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ATTD 2019 Invited Speaker Abstracts

001

NEW AVENUES IN PROTEIN DRUGS FOR DIABETES

ATTD19-0509

TARGETING MORE THAN ONE RECEPTOR

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New avenues in protein drugs for diabetes: targeting more than one receptor

The management of diabetes involves attention to multiple pathogenic factors that affect the control of glycaemia, weight, cardio-renal risk and associated morbidities. Advances in protein therapeutics to simultaneously target more than one cell surface receptor using mixtures of peptides, hybrid peptides or chimeric peptides in a single administration offer new opportunities to address a diversity of medication needs. Examples of stable mixtures of peptides with different physicochemical properties are the fixed-ratio combinations of insulin with a glucagon-like peptide-1 receptor agonist (GLP-1RA), which improve glucose-lowering efficacy while reducing insulin dose, avoiding weight gain and lowering risk of hypoglycaemia compared with insulin alone. Other mixtures and hybrids of two or more complementary peptides are receiving investigation as potential therapies for the treatment of type 2 diabetes, mostly based on analogues of gastro-intestinal and adipose-derived hormones. Chimeric molecules with agonistic effects at two or more receptors are also advancing in clinical studies. These include dual agonists at GLP-1 and gastric inhibitory polypeptide (GIP) receptors, dual agonists at GLP-1 and glucagon receptors, and triple agonists at GLP-1, GIP and glucagon receptors. Combinations of antibodies with peptide hormones are also offering promising effects. The design of future peptide therapeutics provides opportunities to diversify and individualise treatment programmes with particular attention to the balance of effects at different receptors and the immunological implications of these agents.

002

NEW AVENUES IN PROTEIN DRUGS FOR DIABETES

ATTD19-0492

SMART INSULINS

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Smart or glucose-responsive insulins have become a dream of diabetologists and patients with diabetes ever since the first introduction of a potential concept for such an insulin in 1979. Indeed, a simple insulin delivery system directly governed by prevailing blood glucose levels would be a major breakthrough in diabetes therapy as acute complications of insulin therapy, in particular hypoglycaemia, could be prevented transforming and would therefore make insulin a both safe and efficacious treatment option.

Several challenges have to be overcome for a successful development of a smart insulin, many of which are related to safety issues. For instances, large amounts of insulins have to be stored in the body and have to be quickly released at hyperglycaemia, but have to be cleared equally fast from the blood compartment when blood glucose levels decline. Glucose sensing has to be done with sufficient accuracy and precision. Biocompatibility and potential toxicity issues have to be solved if foreign material and chemical reactions are involved in the binding and release of insulin or in glucose sensing. Finally, application of a smart insulin should be simple and preferably done by patients themselves.

In view of all these challenges, it may not be surprising that even 40 years after the first concept paper on smart insulins no development has come close to market yet. Nevertheless, new and promising designs of smart insulins have been introduced and tested in *in-vitro* and animal studies, and most recently in a clinical study in healthy people and patients with type 1 diabetes. The presentation will give an overview on various smart insulin development and will discuss potentials and challenges.

003

NEW AVENUES IN PROTEIN DRUGS FOR DIABETES

ATTD19-0490

STABLE GLUCAGON

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Automated insulin delivery is the current state of the art for the treatment of type 1 diabetes. These systems are designed to reduce patient burden, A1C, and hypoglycemia. In normal physiology, the human pancreas secretes not only insulin to maintain normal glucose homeostasis, but also glucagon, which raises glucose predominately by breaking down hepatic glycogen. Multiple research groups have developed and tested automated glucagon delivery in conjunction with automated insulin delivery to further reduce the risk of hypoglycemia. This dual-hormone approach more closely mimics normal physiology and may be more successful in maintaining normal glucose homeostasis. The glucagon formulations that are currently commercially available are not stable in liquid form and are only

approved for the treatment of severe hypoglycemia. A stable form of glucagon is necessary to enable the commercialization of automated glucagon delivery. In this talk, I will discuss the stable glucagon formulations currently in development and their potential role as a treatment to prevent and treat hypoglycemia.

004

TIME IN RANGES (TIRS)

ATTD19-0515

TIME IN RANGE AS AN OUTCOME IN CLINICAL TRIALS

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Although HbA1c has been recognized for many years as a gold standard for assessing glycemic control in clinical trials, it has certain limitations; and for some studies (e.g., short duration studies or crossover trials), it may not be a feasible outcome. As continuous glucose monitoring (CGM) has gained wider use and acceptance, CGM metrics should be considered as appropriate outcome measures for clinical trials.

Time in range (TIR) is a common CGM metric for assessing overall control. Generally TIR refers to the percentage of glucose values between 70 and 180 mg/dL (3.9 to 10 mmol/L). TIR is largely a measure of hyperglycemia since time above 180 mg/dL (10 mmol/L) generally is 5–10 fold greater than time below 70 mg/dL (3.9 mmol/L). Surveys of individuals with type 1 diabetes have shown that TIR is easily understood and preferred over other metrics of hyperglycemia or overall glucose control.

One drawback of TIR as an outcome measure for regulatory purposes has been that it had not been associated with clinically relevant outcomes. However, recently two studies, one utilizing the longitudinal dataset from the Diabetes Control and Complications Trial (DCCT) of individuals with type 1 diabetes and the other a cross-sectional study of individuals with type 2 diabetes, have shown strong associations of TIR with diabetic microvascular complications. With these compelling data, the time has arrived for TIR to be accepted as an outcome metric in clinical trials.

005

TIME IN RANGES (TIRS)

ATTD19-0512

TIME IN RANGE(S) VS. HBA1C: ARE OUR PATIENTS READY TO CHANGE?

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HbA1c has been the most fundamental biomarker of both diabetes research and care for the past 35 years, and its discovery dates back to 50 years ago. From the 1980s until now every physician, no matter their specialty, has been taught about the use of A1C, and most patients with diabetes use this as their ''report card'' for how well their diabetes is controlled. While limitations of A1C have been understood since the beginning of it's use, it has been the ''CGM era'' where we have really learned more of the subtleties of the test's pitfalls.

CGM on the other hand is a relatively new tool, and it is only recently that we have had consensus on the best metrics for evaluating glycemia. In 2017 an international consensus paper was published noting the time-in-range (TIR) ''buckets'' as an alternative way to evaluate diabetes control but using CGM.

Since it has been only two years since the international consensus conference, and less than that since it's publication, is it premature for us to consider our patients are ready to change?

In December, 2018 a 3-question survey was sent to about 100 health-care providers with 3 questions regarding moving to TIR from A1C: 1. Are our patients ready to change? 2. Are endocrinologists ready to change? 3. Are non-endocrinologists ready to change? Although these are all ''yes/no'' answers, many respondents provided detailed reasoning for their answers and the results of the survey and selected comments will be presented.

It took decades for A1C to become the core metric that it is, even now used for the diagnosis of diabetes. While the data suggests use of TIR at the least may be a good alternative and possibly a better way to assess overall diabetes control and risks for complications, it appears for those patients who use CGM the use of TIRs are sensical and easily adaptable. For the majority of providers and payers this transition may not be as easy.

006

NUTRITION AND FOOD TECHNOLOGY

ATTD19-0505

COMPLEMENTARY SENSORS TECHNOLOGIES FOR FOOD CONSUMPTION MONITORING

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Diet composition, eating behaviors and accurate prandial insulin dosing are of crucial importance for proper diabetes management. Prandial insulin dosages depend mainly on the amount of carbohydrates consumed. However, some patients require insulin adjustments according to protein, fat and dietary fibers content of the meal. Most often, patients underestimate their food and carbohydrates intake and give lower doses of insulin than required. Various solutions, including smartphone apps for food record, do not provide a better estimation as they usually rely on the user subjective evaluation of the meal content.

Wearable devices in healthcare is a fast-growing field with many aspects related to diabetes. Wearable sensors for automatic food monitoring are currently under development. These include smart bracelets or watches that capture hand to mouth gestures, able to identify the beginning and the duration of a meal; swallowing and chewing sensors based on sound or jaw motion; tooth-mounted sensors that can detect specific nutrients eaten and Image processing devices, using camera-based glasses or smartphones, that can photo the meal and connect to an app that analyzes the portion size and composition.

Currently, these sensor-based dietary assessment technologies are not accurate enough to be used, but in the near future they are likely to be of great benefit for diabetes control. Integration of such devices with closed loop systems may free the patient from manual inputs before the meals, allow better adjustment of insulin doses for meals and improve diabetes control as well as the life quality of the patients.

007

JDRF PARALLEL SESSION - TOWARD NEXT-GENERATION PHYSIOLOGIC AUTOMATED INSULIN DELIVERY (AID) SYSTEMS: A PROMISING FRONTIER

ATTD19-0508

CURRENT STATUS OF PHYSIOLOGIC INSULIN DELIVERY: CLINICAL BENEFITS AND CHALLENGES

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Intra-peritoneal (IP) insulin infusion can be considered as the mode of insulin delivery which is the closest to physiology. Indeed, most of infused insulin goes to the liver through the portal venous system which results into a positive portal-systemic gradient. The liver captures about 70% of delivered insulin while the rest circulates toward the general circulation in which insulin levels are close to physiological levels. As a consequence, hepatic glucose production is better modulated and the occurrence of hypoglycemia is reduced compared to subcutaneous (SC) insulin infusion. Hence higher rates of insulin infusion are possible at meal times with lower risk of induced hypoglycemia. Besides, it is likely that lower basal plasma insulin levels explain the restoration of glucagon secretion at exercise and in case of hypoglycemia whereas it is usually blunt during long-term SC insulin therapy. The clinical benefits of IP insulin from implanted pumps or through IP catheters include a combination of close-to-normal HbA1c levels and less than 10 severe hypoglycemia per 100 patient-years as well as reduced blood glucose variability thanks to highly reproducible insulin pharmaco-kinetics and -dynamics. When used in closed-loop insulin delivery systems, tightly controlled blood glucose can be reached including at meal times with no meal announcement. The challenges are mainly related to the still fewly available systems for IP insulin infusion (MiniMed model 2007 pumps and DiaPort devices) worldwide. It contrasts with the dramatic reduction of adverse events related to IP infusion during the last decade: less IP catheter obstructions and reduced complications at implantation site (implanted pumps). Improved physical stability of highly concentrated insulin in implanted devices is expected to allow less frequent pump refills. Current development of IP glucose sensors and smaller insulin pumps for IP insulin infusion could participate in the availability of fully implanted artificial beta cells in a near future.

008

COGNITION IN DIABETES

ATTD19-0520

IMPACT OF HYPERGLYCEMIA ON COGNITIVE FUNCTION

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Background: Mild cognitive alterations have been reported in T1D children as compared to healthy, age –matched controls. The cause of these cognitive differences is unclear.

Objective: The effect of acute hyperglycemia on VSWM was investigated by fMRI in comparison to age- matched control group by MRI.

Methods: Twenty T1D participants (age 14.64 ± 1.785 y) and 20 age-matched healthy controls (age 14.4 ± 2.817 y) participated in the study. All participants performed one structural MRI and two fMRI sessions. Fasting blood samples (IL-6, fibrinogen) were obtained in T1D participants prior to and after completion of fMRI. T1D participants performed the first fMRI in euglycemic and the second in hyperglycemic clamp, whereas the BG of healthy control group was not manipulated.

Results: During hyperglycemic clamp increase of IL-6 (mean fasting 3.1 ng/L, SD 2.49; mean after clamp 13.5 ng/L; SD 13.49) but not of fibrinogen (mean fasting 3.1g/L; SD 0.50; mean after clamp 3.12 g/L; SD 0.43) was noted in T1D participants.

Behavioral data showed a significant decrease (p 0.0048) in VSWM capacity of T1D participants during hyperglycemia. The fMRI analysis showed decreased activation in parietal cortex during encoding phase of the task and increased activation of the same regions during retrieval phase when 2 target positions were presented in both hyperglycemia and euglycemia with more pronounced decrease during hyperglycemia.

Conclusion: The level of IL-6 increased after acute hyperglycemia. The acute hyperglycemia lowers VSWM capacity in T1D children. The proposed mechanism is poorer activation of brain during encoding phase of the task.

009

COGNITION IN DIABETES

ATTD19-0503

BRAIN AND COGNITIVE CONSEQUENCES OF TYPE 1 DIABETES (T1D) – THE DIRECNET PROJECT

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The Diabetes Research in Children Network has been conducting a multiple time point longitudinal study focused on brain and cognitive consequences of type 1 diabetes (T1D) in a large group of children diagnosed with diabetes at a young age (n = 144) and age-matched controls (N = 70). We have previously detected significant differences in total and regional brain gray matter (GM) and white matter (WM) volumes, and altered WM microstructure at baseline in our cohort of children with T1D. Further, children with T1D showed a significantly slower rate of GM and WM growth 18 months after baseline. Both cross-sectional and longitudinal differences in key brain imaging metrics were associated with measures of hyperglycemia. Using standardized batteries of neurocognitive testing, we found that specific measures of executive function were inversely correlated with HbA1c area under the curve. In a subset of this cohort (57 T1D, 14 control) who underwent resting-state functional MRI, we demonstrated increased functional connectivity in children with diabetes, which was positively associated with measures of cognitive functioning, suggesting a compensatory mechanism for hyper-intrinsic connectivity in the brain. We are now completing a two-year extension of this study, following these children as they grow and develop through puberty. That the adverse effects of chronic hyperglycemia can be demonstrated in

the developing brain so early in the course of diabetes highlights the need for optimizing glycemic control specifically in our younger patients.

010

NOVEL BIOMARKERS FOR DIABETES

ATTD19-0519

GLYCATED ALBUMIN: FROM BIOCHEMISTRY TO CLINICAL APPLICATIONS

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Background: Glycated Albumin (GA) has been suggested as an additional or alternative biomarker to circumvent some of the limitations of HbA1c. The much shorter half-life of albumin compared to haemoglobin makes it more responsive to changes in glycemic status. Moreover, GA shows a stronger correlation with continuous glucose measurement over 1 to 2 days than HbA1c, so it may reflect glycemic variability and glucose excursions more accurately. Although GA represents a promising biomarker for the evaluation of glycemic status in both experimental and clinical settings, its introduction in clinical practice requires further validation in relation to basic interpretative criteria and diagnostic accuracy.

Objectives: i) to define upper reference limit (URL) of GA with a direct approach; and ii) to evaluate diagnostic accuracy of GA in predicting diabetes in asymptomatic subjects at risk of suffering from diabetes. Risk factors were impaired glucose tolerance; BMI >25 kg/m^2; previous HbA1c 39–47 mmol/mol or impaired glucose tolerance; family history of diabetes; previous gestational diabetes; history of CVD; hypertension; atherogenic dyslipidemia.

Methods: One thousand thirty-four consecutive blood donors were recruited for reference range definition. Three hundred thirty-four asymptomatic subjects at risk for diabetes were recruited for GA diagnostic accuracy evaluation. GA was measured on plasma-EDTA by quantILab® Glycated Albumin (Instrumentation Laboratory, A Werfen Company).

Results: The calculated GA URL in blood donors was 14.5% (95% CI: 14.3–14.7). GA showed a modest correlation with age ($r = 0.2$; $P < 0.001$) and higher values in women than in men (12.2% *vs* 12%, $P = 0.01$). Among subjects at risk for diabetes, GA median levels were 13.2% (IQR:12.2–14.4). Eighteen subjects (5.4%) were classified as diabetics based on their HbA1c. GA was significantly correlated with HbA1c ($r = 0.31$; $P < 0.0001$). According to ROC curve analysis, GA identified subjects with diabetes with a sensitivity of 72.2% (95% CI: 46.5–90.3) and a specificity of 71.8% (95% CI: 66.5–76.7) (AUC: 0.80; 95% CI:0.75–0.84; $P < 0.0001$) at the cut-off of 14%.

Conclusion: The knowledge of GA distribution in healthy subjects is essential to promote its introduction in both research and clinical practice. GA can predict diabetes in asymptomatic subjects with high accuracy.

References

Bellia C, Zaninotto M, Cosma C, et al. Definition of the upper reference limit of glycated albumin in blood donors from Italy. Clin Chem Lab Med. 2017 Nov 27;56(1):120–125.

Bellia C, Zaninotto M, Cosma C, et al. Clinical usefulness of Glycated Albumin in the diagnosis of diabetes: Results from an Italian study. Clin Biochem. 2018 Apr;54:68–72.

011

NOVEL BIOMARKERS FOR DIABETES

ATTD19-0514

NOVEL BIOMARKERS IDENTIFIED BY INTERNATIONAL PREVENTION-STUDIES

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With the successful conduct of well-designed studies of birth cohorts and at-risk individuals, our understanding of the natural history of pre- and early type 1 diabetes (T1D) has advanced considerably over the past decade. Genetic risk scores can predict with increasing precision and accuracy who is at risk for T1D, and early staging (stages 1–3) based upon islet autoantibody status allows for improved mechanistic and natural history studies as well as improved clinical trial design for prevention studies. However, better biomarkers are needed to improve mechanistic understanding of the disease, for enhanced understanding of progressors and non-progressors among those at-risk for T1D, and, for the design of smaller and more focused preventive efforts using earlier endpoints. With their unique populations, studies conducted within the TrialNet, TEDDY (The Environmental Determinants of Type 1 Diabetes in the Young) and nPOD (Network for Pancreatic Organ Donors with Diabetes) umbrellas have identified potential novel gene, immunologic, pancreatic exocrine and metabolic biomarkers. High throughput technologies for genetic, transcriptomic, and proteomic studies and big data analyses has already and will better enable genome-wide examinations of genetic polymorphisms, global gene changes, and protein expression changes in order to better predict T1D risk, understand mechanism and evaluate therapeutic outcomes. Recent and exciting findings from these networks will be presented.

012

CLOSED-LOOP SYSTEMS – WHERE ARE WE NOW?

ATTD19-0499

VALUES VS. AFFORDABILITY OF DIABETES TECHNOLOGY

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Affordability is one the main factors that determines the wide variations in access to diabetes technologies and other diabetes treatments between and within countries. As technology becomes more sophisticated in the future (e.g. with the introduction of closed-loop insulin delivery systems), affordability will be increasingly a major consideration and constraint in technology usage. Health economics in recent years has largely focussed on value for money i.e. the cost effectiveness of technologies such as insulin pump therapy or sensor-augmented pump therapy vs. a comparator treatment like as multiple daily insulin injections. But technologies can be cost-effective but not affordable in a

locality because of, for example, a large number of patients in an area with poorly-controlled diabetes or because of competing costs from patients with other conditions. A new budget impact model measures affordability as the monetary impact of adopting a specific diabetes therapy or improving diabetes control by a specific amount over the short-to-medium term, with flexible input of such local variables as population size, glycemic control and expected change in glycemic control, and with allowance for savings achieved from reduced diabetes complications.

013

NEW MODELS OF IMPLEMENTING CGM

ATTD19-0516

CGM USE FOR TYPE 1 DIABETES – DIRECT TO CONSUMER

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Despite the compelling evidence of the benefits of CGM, only a minority of individuals with type one diabetes in the U.S. use CGM and very few with type 2 diabetes do. In the most recent T1D Exchange registry data, only about 30% of individuals with T1D were using CGM at endocrinology centers with a strong T1D focus. The percentage is almost certainly lower in community endocrinology practices and substantially lower in primary care practices in the U.S.

New approaches are needed to expand the use of CGM, particularly for individuals with T1D who are not being followed by an endocrinologist, since its use will benefit most users and improve glycemic control and reduce severe hypoglycemia.

A study is starting in the U.S. in which adults with T1D not using CGM whose diabetes is being managed in a primary care setting will be recruited for a study to evaluate the initiation of CGM at home, with remote training being performed by certified diabetes educators.

014

ADJUNCTIVE THERAPIES FOR T1D

ATTD19-0524

EMERGING ROLE OF ADJUNCTIVE THERAPIES FOR T1D

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There are approximately 150-200 million people, worldwide, needing insulin therapy for managing their diabetes. About 90% of them are patients with type 2 diabetes (T2D). Only about 0.5–1% are using some sort of insulin pump therapy despite the approval of the first artificial pancreas by the FDA in September of 2016. The first hybrid closed-loop system has been available in the US for the past year, which has significantly reduced nocturnal hypoglycemia with improvement in glucose values as reflected in both A1c and time-in-range (TIR). The continuous glucose monitors have come a long way and now the majority of them have an accuracy (MARD <10%) closer to blood glucose meters (BGM). The newer iCGM systems do not require calibrations and are approved by the FDA as standalone systems and if future systems qualify for iCGM, the approval process may avoid PMA submission. We still need a consensus for uniform reporting of CGM downloads so that a common provider can interpret CGM information appropriately just like we do for EKG.

Since the majority of people with Type 1 diabetes do not achieve target A1cs (<7 or 6.5%) and more than 2/3 of the patients with Type 1 diabetes are getting overweight or obese, it is important to find adjunctive therapies for patients with Type 1 diabetes, which might help achieving target A1cs without any increase in weight. There were several studies that were reported in the last year with SGLT 1 and 2 inhibitors used adjunctively with insulin in patients with Type 1 diabetes. DEPICT (dapagliflozin reported in Lancet 2017) in Type 1 diabetes clearly showed improvement in A1c, TIR, and weight loss with a small increase in ketoacidosis. The second trial using a dual SGLT 1 and 2 inhibitor (inTandem 3-Sotagliflozin in Type 1 diabetes reported in NEJM 2017) showed significant reduction in A1c, hypgoclyemia, especially severe (less than 55mg/d) and weight loss. There was a small increase in diabetic ketoacidosis (DKA), which is known with all SGLT 2 inhibitors. Lastly, EASE 2 and 3 trials were reported in Diabetes Care, 2018 of using Empagliflozin in T1D and showed similar benefits and risks like Dapa and Sota except authors recommended a smaller dose of 2.5 mg a day to be considered for T1D (due to no increase in DKA risk, but efficacy on A1c was about 50%) based on a small sample size in EASE 3. If these drugs are approved for patients with Type 1 diabetes, this may be the new class of adjunctive therapies for patients with Type 1 diabetes that may allow subjects to achieve target A1cs without increasing hypoglycemia and/or weight. The risk for DKA will need to be mitigated and proper education for patients and providers may need to be provided. I'm excited about the future for people with diabetes.

015

ADJUNCTIVE THERAPIES FOR T1D

ATTD19-0513

THE CONCEPT OF SGLT IN DIABETES

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Central in the therapy of people with type 1 diabetes is the replacement of all functions of the destroyed beta-cell in order to achieve a physiological metabolic profile. Simply put, the functions of the beta-cell cover continuous sensing of glycaemia followed by the release into the portal system of appropriate amounts of insulin, aimed at suppressing endogenous glucose production, lipolysis and protein catabolism. In recent years, better tools have become available to allow people with type 1 diabetes to take over these complicated tasks of the beta-cell. Tools include capillary blood glucose monitoring, now even continuous glucose monitoring systems and supportive educational tools and techniques accompanied by decision making tools.

Insulin analogues have been developed to mimic more closely the insulin excursions induced by a functioning beta-cell at mealtimes or during steady-state. These analogues have greatly improved quality of life in people with type 1 diabetes, mainly

reducing hypoglycemic risk and allowing a more flexible lifestyle.

Several issues still exist with present day insulin therapy, with insufficient matching of insulin profiles to insulin needs resulting in many people with type 1 diabetes not reaching HbA1c targets and suffering from recurrent hypoglycemia. This risk of hypoglycemia, in particular nocturnal hypoglycemia, impacts on quality of life and contributes to weight gain via defensive snacking. Another, perhaps even more important problem is the fact that exogenous insulin is administered in the periphery, whereas the beta-cell secretes it in the portal system. As the liver is the primary target for insulin effect, higher peripheral insulin levels are induced by exogenous insulin for similar hepatic effects as when the beta-cell secretes insulin, leading to peripheral over-exposure of tissues like adipose tissue and muscle to anabolic insulin, leading to undesired weight gain in many patients.

Intuitively, clinicians have been experimenting with non-insulin adjunctive therapies in type 1 diabetes, typically by introducing agents used in people with type 2 diabetes. As such, metformin has been used, with however, few and rather discouraging data on long term effects. Recently, novel agents, like GLP-1 receptor agonists and SGLT2/SGLT1-2 inhibitors have been or are being tested as adjunct therapies, with interesting results.

016

PSYCHOLOGICAL INTERVENTION TO INCREASE THE USE OF TECHNOLOGY BY T1D PATIENTS

ATTD19-0504

ADHERENCE TO INSULIN PUMP BEHAVIORS IN YOUNG CHILDREN WITH TYPE 1 DIABETES MELLITUS: OPPORTUNITIES FOR INTERVENTION

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Background: Research shows that use of insulin pumps and accompanying bolus calculator software can improve glycemic outcomes in persons with type 1 diabetes mellitus (T1D). However, for optimal insulin pump management, it is essential to input into the pump a current blood glucose level (SMBG) and a carbohydrate estimate if also consuming a meal/snack. Previous research shows inconsistencies in the percent of days where adolescents inputted these values into their pump and administered insulin. Here, we describe similar pump adherence behaviors in a large sample of families of young children with T1D.

Methods: We collected pump data covering between 14–30 consecutive days from 116 children and examined adherence to each essential pump adherence behavior (e.g., SMBG, carbohydrate entry, and insulin use) as well as adherence to the combination of these three behaviors.

Results: Young children had a mean age of 5.2 ± 1.4 years. Families completed SMBG ≥4 times on 99% of days, bolused insulin ≥3 times on 95% of days, and entered carbohydrates ≥3 times on 93% of days. In contrast, families corrected for hyperglycemia (≥13.9 mmol/l) only 63% of the time and completed these three pump adherence behaviors in combination for only 43% of boluses. The percent of days with ≥4 SMBG, ≥3 carbohydrate entries, and percent of boluses where families completed the three pump adherence behaviors in combination correlated negatively with children's mean daily glucose.

Conclusions: Families of young children with T1D had variable rates of pump adherence behaviors and lower adherence to recommendations to correct for hyperglycemia. Therefore, families of young children with T1D may benefit from interventions that target pump adherence behaviors or include these treatment targets within a multicomponent intervention to help them to achieve optimal child glycemic control.

017

PSYCHOLOGICAL INTERVENTION TO INCREASE THE USE OF TECHNOLOGY BY T1D PATIENTS

ATTD19-0497

PSYCHOSOCIAL ASPECTS AND DIABETES TECHNOLOGY- HEAD TO HEAD OR HAND IN HAND?

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The ultimate goal of assessing the psychosocial aspects of diabetes technology is to optimise outcomes – both biomedical and quality of life – for people living with diabetes and for those who love them. In order to achieve this, it is necessary to explore the relationship between technology and the psychosocial aspects of that technology in the context of user experience, clinical guidelines and the inclusion of patient-reported outcome measures (PROMs) alongside medical outcomes in research trials. Without assessing the psychosocial aspects of a person's everyday experience with diabetes technologies, there will remain a gulf between the intended use of the device and the actual uptake and continued use of such devices. New technologies must be developed with the end user experience in mind, not simply in terms of human factors (how an individual engages with the device itself) but also in terms of how each user and their families are able to incorporate the technology into their everyday lives to minimise diabetes-related burden, improve outcomes and optimise quality of life. At the same time, it is necessary to consider the balance between outcomes versus cost and both sides of that equation very much depend upon the stakeholder. My talk will address a crucial question i.e. how do we best support individuals with T1D to use technologies to their best advantage, whilst minimising the burden on everyday living and maintaining cost-effectiveness?

018

PSYCHOLOGICAL INTERVENTION TO INCREASE THE USE OF TECHNOLOGY BY T1D PATIENTS

ATTD19-0506

PREVENTING POOR PSYCHOSOCIAL AND GLYCEMIC OUTCOMES IN TEENS WITH TYPE 1 DIABETES

K. Hood[1]

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Diabetes devices and closed loop systems demonstrate increased time in range, reduced hypoglycemia, and psychosocial benefits. However, the uptake of certain devices (CGM for example) are low and there have been issues with sustained use in first generation closed loop systems. The purpose of this presentation is to review evidence to date on barriers to uptake and

sustained use, as well as critical factors that may promote optimal use of devices and closed loop.

019

PATIENT DECISION SUPPORT: CONCEPT AND TOOLS

ATTD19-0494

DECISION SUPPORT SYSTEM FOR PATIENTS WITH DIABETES: CONCEPT, GOALS AND FEASIBILITY

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Our thesis is that the temporal density of the available data determines the treatment that can be implemented. For example, episodic blood glucose (BG) readings can yield information about the risk associated with hypo- and hyperglycemic excursions based on the dispersion of the data. Continuous glucose monitoring (CGM) yields dense data sets with data points that are regularly spaced in time (e.g. every 5 minutes) known as time series. This adds complexity to the analysis, but also presents opportunities to control the dynamics of BG fluctuations in real time. Both *Advisory* and *Closed-Loop Control* technologies are based on the common idea that BG variability is a process in time that has two principal components: risk, associated with the amplitude of BG fluctuations, and time indicating the rate of event progression. An Advisory or a Control *algorithm* then adapts the amount and timing of insulin delivery to mitigate the magnitude of postprandial glucose excursions and prevent hypoglycemia.

In this presentation we review the basics of automated diabetes decision support, the methods and components used by decision support algorithms, as well as results from studies testing the feasibility and utility of decision support for patients with diabetes. We conclude that the feasibility of Advisory Systems for diabetes has been demonstrated by recent clinical trials, including pilot studies and larger-scale multi-center investigations using CGM and insulin delivery via insulin pumps or multiple daily injections.

020

PATIENT DECISION SUPPORT: CONCEPT AND TOOLS

ATTD19-0501

A BETTER CARE FOR DIABETES

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Current decision support systems for insulin dosing in type 1 diabetes fall short to meet the recommended therapeutic targets. In my presentation, I will give a brief overview of the state of the art in decision support for insulin therapy aiming to tackle with the problem of intra-day and inter-day variability. In particular, I will focus on the science, engineering and clinical work currently being done at Imperial College London on bolus-basal insulin decision support using Run-to-Run control and Case-based Reasoning.

021

PATIENT-REPORTED OUTCOME MEASURES (PROMS) AND OUTCOME DRIVEN MEDICINE

ATTD19-0496

EVALUATION OF PATIENT-REPORTED OUTCOME MEASURES (PROMS)

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Patient-reported outcome measures (PROM) are a crucial part of outcomes driven medicine; representing the patient perspective in terms of quality of life, psychosocial functioning and successful uptake and continued use of diabetes devices and therapies. Process evaluation of PROMs and their interpretation in outcomes-driven medicine however is less well-understood. Increasingly Payers are demanding PROMs as part of their considerations for reimbursement and regulatory approvals bodies are increasingly examining PROMs as part of their approvals processes. It is important, therefore, that we are able to respond robustly and effectively to ensure people with diabetes continue to receive access to the care they require for optimal biomedical and psychological outcomes. The ability to understand and interpret what represents a meaningful difference in PROM across the different measures used is crucial. Outcomes of well-being, psychosocial functioning, quality of life, technology acceptance and functional health status for example and how they link to psychological constructs and behaviour change theory must be transparent. My talk will focus on the How, What, Why, When and For Whom in PRO assessment and associated contribution to decision-making processes.

022

PATIENT-REPORTED OUTCOME MEASURES (PROMS) AND OUTCOME DRIVEN MEDICINE

ATTD19-0511

PROMS, APPS AND EXERCISE IN DIABETES

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High quality wearable technologies, applications (apps) and connected smart phone technologies that focus on exercise tracking and management in diabetes are in critical need. To date, several high-quality apps have been developed by the fitness industry that work seamlessly with wearables (i.e. foot pods, smart watches, power meters, chest band heart rate monitors, etc.) and app-based data trackers for monitoring daily step count, heart rate, exercise performance, exercise recovery, sleep quality and energy expenditures. A few emerging apps and technologies are focusing on physically active customers with diabetes that attempt to integrate diabetes-specific metrics such as continuous glucose monitoring, self-monitoring of blood glucose, food intake and insulin dosing. Some even provide evidence-informed recommendations on insulin dose titration and carbohydrate snacking to help improve glucose control during planned exercise. This presentation highlights emerging technologies that help patients living with diabetes engage more safely and more effectively with physical activity.

023

PATIENT-REPORTED OUTCOME MEASURES (PROMS) AND OUTCOME DRIVEN MEDICINE

ATTD19-0493

A MOBILE APP FOR THE SELF-MANAGEMENT OF TYPE 1 DIABETES AMONG ADOLESCENTS: LESSONS LEARNED FROM A RANDOMIZED CONTROLLED TRIAL

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Many young people with type 1 diabetes mellitus (T1DM) struggle to achieve blood glucose (BG) targets. Because adolescents also demonstrate a strong propensity for new technology, one wonders if mHealth apps are well-suited adjuncts to the management of T1DM in this population.

We hypothesized that a tailored approach and inclusion of an adherence mechanism would be needed for an app to be successful. Thus, we interviewed adolescents with type 1 diabetes and their family caregivers and utilized thematic analysis to identify priority design principles. This user-centred approach identified themes such as youths having roles related to data collecting rather than decision making; the need for fast, discrete transactions; and the importance of overcoming decision inertia. Design of the mobile app included simple, automated transfer of glucometer readings and gamification, whereby routine behaviors and actions are rewarded and encouraged.

The app, *bant*, was first evaluated in a 12 week pilot study. Satisfaction was high and frequency of self monitoring of blood glucose (SMBG) increased during the short trial. User feedback led to a refined app, which included out-of-range BG trend alerts, coaching around potential causes and fixes of these trends, and a point-based incentive system to support T1DM self-management.

We then conducted a 12 month randomized controlled trial among 92 adolescents. Forty-six youths were enrolled into the treatment arm, and app satisfaction was assessed at 6 and 12 months using a 7-point Likert scale. At trial end, users ordered *bant*'s 12 features based on perceived usefulness. 79% (30/38) and 76% (34/45) of respondents reported being ''satisfied'' or ''very satisfied'' with *bant* at 6 and 12 months, respectively. The trending feature was ranked the most useful component by 45% (20/44) and second most useful by 38% (15/39) of subjects. At 3 months, 76% (35/46) were moderately or highly engaged (uploaded ≥3 of 7 days) and 24% (11/46) had low or very low engagement (uploaded <3 of 7 days). On average 35% (16/46 subjects) remained moderately or highly engaged over the 12 month trial.

Linear mixed models showed no changes in primary (HbA1c) and secondary (frequency of hypoglycemia, measures of self-care, quality of life) clinical outcomes. However, exploratory analysis demonstrated a significant association between increased SMBG and improved HbA1c in the intervention group. For the subgroup of *bant* users performing SMBG ≥5 daily, there was a significant improvement in HbA1c of 0.58% ($P = .02$), while the parallel subgroup in the control arm experienced no significant change in HbA1c (decrease of 0.06%, $P = .84$).

In summary, *bant* shows promising ability to engage a subset of adolescents and compliment their current clinical care. Throughout the design and testing of *bant*, many lessons were learned about the deployment of smartphone apps. Those lessons, along with the results of our clinical trials, will be presented during this session.

024

DIABETES EDUCATION

ATTD19-0500

THE IMPORTANCE OF EDUCATION IN CLOSED-LOOP

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Education and support initiatives are being developed for closed loop technologies, as hybrid closed loop (HCL) therapy is now approved in multiple countries. Research and programmatic development are needed to optimize delivery of education for both clinician and individuals with type 1 diabetes.

Clinician education must include both general principles of closed-loop therapy and device specifics. The CARES (Calculate, Adjustment, Revert, Education, Sensor) paradigm can be useful for distinguishing closed-loop from traditional pump therapy and highlighting clinically meaningful distinctions between devices (Table). Clinicians must also consider their critical role in expectation-setting in order to poise individuals for optimal use of closed loop systems.

Programs should include both initial closed-loop training and ongoing support. For example, a pediatric center ''HCL system initiation'' program uses group training and videoconference paradigms to train individuals on HCL use. Phone follow-ups emphasize carbohydrate ratio adjustments, responding to alerts, and reducing hyperglycemia. Another strategy is to provide targeted education and intervention for specific closed-loop adherence or glycemic challenges. A novel multicenter study of a videoconference-based intervention for families of young children using HCL included focused strategies to address mealtime behaviors, device troubleshooting, exercise and activity, and hypoglycemia mitigation.

Ongoing work is needed to understand beneficial components of closed-loop training programs. Both clinicians and patients require fundamental understanding of the benefits and limitations for closed-loop systems, and systematic ways to optimize their use.

Updated CARES Paradigm for Closed-Loop Education	
C: Calculate	How does closed-loop algorithm calculate insulin delivery? Which components of insulin delivery are automated (e.g. basal, high glucose corrections, food boluses, etc.)?
A: Adjustment	How can user adjust insulin delivery? What parameters can be adjusted in closed-loop mode (e.g. carbohydrate ratios, insulin action time, basal rates, sensitivities)? What is fixed in the system?
R: Revert	When should user choose to revert to open loop? When will the system default to open loop? How does user optimize time in closed-loop?
E: Education	Where can users and clinicians find additional education? What are key education points for the closed loop device (e.g. essential training, tips and tricks, best practices, etc.)?
S: Sensor	What are pertinent sensor characteristics (e.g. calibration and therapeutic blood glucose requirements, duration of sensor wear, etc.)?

025

DIABETES EDUCATION

ATTD19-0491

EDUCATION THROUGH FACEBOOK AND OTHER SOCIAL MEDIA

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Type 1 diabetes (T1D) management is challenge for both patients and health providers (HP). Technology and social media can provide an additional opportunity to support care and improve communication with HP. Social media enables support and interaction in the online community. The social media platforms and discussion forums are very popular in young people, which provide unique opportunities for online diabetes education, intervention, and support. The social media use in healthcare identifies positive effects and outcomes: fosters patient's education, provides psychosocial support; enhances patient's empowerment and reduces illness stigma.

Social media has additional unique support, which cannot be offered in regular clinic visits, such as: perspective from the patient's point of view and an almost unlimited amount of time to listen and share experience.

Facebook is the largest social media platform and important source of information, support and engagement for patients with chronic diseases. The communication between T1D patients and HP using Facebook allowed active patient participation in the decision-making process with improved glucose control in patients using insulin pump. Combined use of Facebook and Viber can significantly decrease HbA1c level compared to patients using Facebook only, where patients on insulin pump were more likely to use both social media for T1D management.

We believe that in today's challenging healthcare environment of limited budgets and resources with a desire to provide better diabetes care, new methods of patient interaction using social media can be beneficial. Social media can be additional communication tool between T1D patients and HP and can improve glucose control.

026

THERAPIES IN TYPE 2 DIABETES

ATTD19-0523

PUMPS IN T2D

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The treatment with continuous subcutaneous insulin infusion (CSII) using insulin pump has been proven to achieve near normoglycemia in type 1 diabetes patients. In contrast, this therapeutic approach was not implemented to a larger scale in insulin-treated type 2 diabetes (T2D), and there is the lack of the data on the requirements for optimal insulin pump therapy in the different metabolic settings of T2D (insulin resistance, obesity, dyslipidemia etc). However, the growing number of patients with T2D showing the failure on previous insulin treatment has inspired the studies of the metabolic effects of insulin pump treatment in these individuals. After small-scale inconclusive studies, the OpT2mize trial has convincingly demonstrated an ability of insulin pump treatment to significantly improve HbA1c, but also blood glucose daily variability compared to multiple daily injection insulin therapy. In addition, the study of the use of insulin pump therapy in newly diagnosed T2D with intensive removal of hyperglycemia resulted in more frequent and longer clinical remission of the disease. The metabolic changes underlying the improvement of blood glucose control remain yet unclarified. In this context, our studies have demonstrated slower reduction of blood glucose in response to the acute insulin administration with the pump, but significantly better reduction of HbA1c and insulin resistance in the subgroup of highly insulin resistant patients. Our results signify that CSII might be more efficient in patients with higher insulin resistance and that a flexible approach in decreasing blood glucose is a prerequisite for achieving treatment targets.

027

THERAPIES IN TYPE 2 DIABETES

ATTD19-0518

ADD ON TO BASAL INSULIN: PATIENT CENTERED CONSIDERATIONS

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Therapeutic intensification add-on to basal insulin: shared decision making for success

Managing blood glucose levels in people with longstanding type 2 diabetes often requires treatment intensification. For people on basal insulin there are now many options, the most crucial step is to recognize the need for additional therapy and engage the patient in shared decision making. The consequences of therapeutic inertia include life shortening and disabling cardiovascular and microvascular complications. Once the decision is made to intensify therapy delays should be minimized. At each step of treatment intensification, it is important to do a formal reassessment of diet, physical activity, sedentarism and sleep and support the patient in additional strategies for behavior change. The next step is to assess patient characteristics, most importantly the existence of atherosclerotic cardiovascular disease or heart failure. For the 20% of people with concurrent heart disease in diabetes, the use of either a GLP-1 receptor agonist or a SGLT2 inhibitor should be considered. A brief overview of the new and emerging CVOTs will be discussed and optimal choices in light of predominant CVD or CHD. Other critical patient characteristics that will inform shared decision making are the A1c lowering needed, the need for weight loss or minimizing weight gain, the risk of hypoglycemia, the ability to carry out a complex regimen, renal function, concurrently conditions and cost. Once the strategy has been set the clinic should support the patient for cost-effective access to the medication, instruction to minimize side effects and maximize safety and follow up in 3–6 months to determine efficacy. If the strategy is either not tolerated or not adhered to a new strategy should be envisioned by the patient and provider.

028

THERAPIES IN TYPE 2 DIABETES

ATTD19-0510

THE ROLE OF ABA1C POINT OF CARE TESTING IN THE MANAGEMENT OF DIABETES AND CARDIOVASCULAR DISEASE

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Diabetes is a highly prevalent disease also implicated in the development of several other serious complications like cardiovascular or renal disease. It also places a tremendous financial burden on both patients and health care systems. Glycated hemoglobin A1c (HbA1c) testing has for decades been considered to be one of the most important laboratory medical advances in diabetes care and plays a key role in the management of diabetes. HbA1c values represent average glycemic control over the past 2–3 months. They reflect a composition of both pre- and postprandial blood glucose levels. Regular HbA1c measurement is recommended by international guidelines for all patients with diabetes for the assessment of glycemic control by providing information on long-term glycemic status and reliably predicting a potential risk for diabetes-related complications. One potential disadvantage of traditional HbA1c laboratory testing is that results are not available at the time of the patient visit due to the turn-around time required for testing and reporting. This delay in communicating results can delay intensification or modification of treatment and reduce patient adherence to the treatment plan. In response to this, HbA1c testing at the point-of-care is currently increasing. The American Diabetes Association (ADA) recommends point-of-care (POC) testing for HbA1c to offer more timely treatment changes. The rapid availability of HbA1c results permits the discussion of the results face-to-face, and has the potential to improve patient-doctor dialogue and patient satisfaction, thereby facilitating improved glycemic control. HbA1c testing at POC was shown to potentially improve diabetes management if undertaken within an adequate comprehensive quality management system. Continued evidence of the accuracy improvements of various POC systems and cost-effectiveness evaluations, together with the implementation of effective quality control measures will support the expansion of these POC testing systems as a key method for HbA1c testing in daily practice.

029

WHAT PATIENTS DO WITH CGM DATA AND WHAT THEY SHOULD DO

ATTD19-0507

MEDICAL NEED FOR TRAINING COURSES FOR PATIENTS TO MAKE OPTIMAL USAGE OF CGM (RTCGM AND ISCCGM)

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Continuous glucose data provides a more comprehensive overview about glycemic control (e.g. trend arrows, previous course of glucose, exposure to hypo-, eu-, or hyperglycemic glucose values, glycemic variability) than traditional measures like A1c or results of SMBG. These new parameters that become accessible to people with diabetes via flash sensor-based glucose monitoring (FSGM) or continuous glucose monitoring (CGM) can facilitate treatment and adjustments. However, the abundance of glucose data that are provided by FSGM or CGM systems can also be perceived as challenging, burdensome or overwhelming by people with diabetes. Given the amount and new quality of glucose data, it seems crucial that people with diabetes know how to interpret and apply these data. This presentation will provide an overview about psychological and practical challenges in using continuous glucose data. In addition, first results of a multi-centre, randomised, parallel trial evaluating a new education and treatment programme for people with diabetes using FSGM will be presented. In this trial, all participants used FSGM; the intervention group received the new education programme, named FLASH, whereas the control group received no education. At the six-month follow-up, the between-group difference in HbA1c reduction was significant, favouring FLASH education compared to the control group receiving no education (−0.28%, 95% CI 0.16 to 0.40 vs. −0.11%, 95% CI 0.00 to 0.22%; between-group difference: −0.17% 95% CI: −0.01 to −0.33; p = 0.033). Participation in FLASH education also resulted in significant improvements in time spent in the target glucose range, in diabetes-related distress scores and in satisfaction with the glucose monitoring method. FLASH education also resulted in significant improvements in the use of glycaemic information provided by FSGM and in reduced SMBG fingerstick testing. Diabetes education programmes like the newly developed FLASH programme are an effective tool to make optimal use of continuous glucose data.

030

WHAT PATIENTS DO WITH CGM DATA AND WHAT THEY SHOULD DO

ATTD19-0517

DECISIONS IN THE PSYCHOLOGY OF GLUCOSE MONITORING

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Using a continuous glucose monitoring system requires 5 decisions:

1. Decide to use this technology in general; 2. Decide to insert this particular sensor; 3. Decide to download the data during the lifespan of the sensor; 4. Decide to cogitate about the data; 5. Decide to do something based on this reflection. Each of these decisions relates to the achievement of an action. For philosophers, deciding to act requires the formation of an ''intention-in-action'', which itself follows that of a more general ''prior-intention'' (1). For example, the formation of the ''prior-intention'' is caused by the desire to avoid diabetes complications, and this ''prior-intention'' leads to the formation of the ''intention-in-action'' to perform actions 1–5 described above. These decisions depend on many elements (for example, decision 2 requires the sensor to be available).

This conceptual framework explains the force of habit in the realization of repetitive actions such as glucose monitoring (2). It applies not only to Continuous Glucose Monitoring (CGM) but also to the discontinuous measurement of blood glucose (DGM). However, decision 4 is different for CGM and DGM: the patient can write in his treatment logbook a false, normal, blood glucose to escape the anxiety secondary to seeing a high value and the need to cogitate about the data, but this is not possible in continuous monitoring. Decisions 4 and 5 are particularly interesting: they may represent the main burden of glucose monitoring, explaining that decision 3 is actually not taken. These decisions 3–5 will be rendered useless in a closed-loop system, explaining the interest of this technology: closed-loop bypasses the step of the formation of intentions, and thus avoids the cognitive and emotional efforts linked to decision.

References

1. Searle, J. (1983). Intentionality: An Essay in the Philosophy of Mind. New York, Cambridge University Press.
2. Reach, G. (2005) The role of habit in therapeutic adherence. Diab Med 2005;22:415–420.

031

DATA DIABETES SCIENCE

ATTD19-0495

BUILDING A VIRTUAL IMAGE OF PATIENT – THE VIP APPROACH TO PRECISION MEDICINE FOR DIABETES

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Arguably, diabetes mellitus is the best quantified human condition: the genetic underpinning of type 1 diabetes is well described and genetic markers for type 2 diabetes are emerging; elaborate *in silico* models describe the action of the human metabolic system, real-time signals such as continuous glucose monitoring are available, and artificial pancreas systems control blood glucose fluctuations in patients' natural environment. The data relevant to diabetes are generally structured in three time scales: (1) Static characteristics derived from the genotype of a person; (2) Episodic updates, typically every few months, through electronic health records that are used for periodic treatment adjustment, and (3) Real-time data, such as self-monitoring or, particularly, continuous monitoring records, which enable precise description of the dynamics of the metabolic system and ultimate personalized medicine applications, such as real-time decision support or closed-loop control.

We therefore propose to link these currently distinct developments into one coherent new concept – *Diabetes Data Science* – and to introduce tools for building a *Virtual Image of a Patient (VIP)*. The VIP approach allows disparate data sets to congregate and create an *in silico* ''individual,'' – a virtual match of a real person that allows treatment optimization to occur in computer simulation prior to be offered to physicians and patients. The major objective of the VIP model is to broaden the understanding of Precision Medicine for Diabetes beyond its traditional definition as a therapy initialized by a person's genotype, to approaches that are continually updated with electronic health records and real-time monitoring driving personalized treatment algorithms.

032

ULTRA RAPID ACTING INSULINS AND TECHNOLOGY

ATTD19-0522

RAPID ACTING INSULIN, EXERCISE AND CLOSED-LOOP

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Regular physical activity is important for people of all ages and especially for those with chronic diseases. For individuals with type 1 diabetes is physical activity challenged by numerous factors causing glucose fluctuations during and after exercise, including activity type (aerobic, anaerobic or mixed), duration of the activity, level of hydration, the secretion of counter regulatory hormones as well as the amount of insulin and nutriments in the body when the physical activity is performed (1,2). The burden of regularly adjusting insulin therapy before, during and after physical activity based on current treatment recommendations (3) is a significant challenge, especially in the pediatric and adolescent populations, due to varying spontaneous activity levels, developmental and hormonal changes, varying lifestyle modalities and other factors.

Artificial pancreas is, based on results from numerous clinical studies in the past decade, becoming a part of unsupervised clinical care for people with type 1 diabetes (4,5) and has proven to be safe and effective also when challenged with different types of physical activity (6,7). The majority of present artificial pancreas systems require manual insulin bolus for meals to deliver insulin in so-called hybrid closed-loop manner (5). While improvements seen in glycemic control with these state-of-the-art devices are reassuring, users of hybrid closed-loop systems still experience the everyday burden of feed-forward actions, such as carbohydrate counting or exercise announcement and still require pre-meal and pre-exercise insulin adjustments to avoid glycemic excursion (8–11). To fully ''close the loop'', these systems might benefit from shortening the time to peak action for prandial insulin coverage and also faster insulin clearance rate, which were recently reported with novel ultra-rapid insulin analogs (12–14). Nevertheless, data on ultra-rapid insulin analogs with closed-loop insulin therapy during physical activity are scarce.

In this presentation we will present data on the possible benefits and limitations of ultra-rapid insulin analogs for closed-loop insulin therapy, challenged by unannounced/uncovered meals and unannounced physical activity.

References

1. Bally L, Zueger T, Buehler T, Dokumaci AS, Speck C, Pasi N, et al. Metabolic and hormonal response to intermittent high-intensity and continuous moderate intensity exercise in individuals with type 1 diabetes: a randomised crossover study. Diabetologia [Internet]. 2016 Apr 6 [cited 2017 Jan 3]; 59(4):776–84.
2. Riddell MC, Gallen IW, Smart CE, Taplin CE, Adolfsson P, Lumb AN, et al. Exercise management in type 1 diabetes: a consensus statement. Lancet Diabetes Endocrinol [Internet]. 2017 Jan 23 [cited 2017 Feb 5];5(5):377–90.

3. Zaharieva DP, Riddell MC. Insulin Management Strategies for Exercise in Diabetes. Can J Diabetes [Internet]. 2017 Oct 1 [cited 2017 Oct 4];41(5):507–16.
4. Bergenstal RM, Garg S, Weinzimer SA, Buckingham BA, Bode BW, Tamborlane W V., et al. Safety of a Hybrid Closed-Loop Insulin Delivery System in Patients With Type 1 Diabetes. Jama [Internet]. 2016 Oct 4 [cited 2016 Dec 7]; 316(13):1407.
5. Bekiari E, Kitsios K, Thabit H, Tauschmann M, Athanasiadou E, Karagiannis T, et al. Artificial pancreas treatment for outpatients with type 1 diabetes: systematic review and meta-analysis. BMJ [Internet]. 2018 Apr 18 [cited 2018 Apr 20];361:k1310.
6. Dovc K, Macedoni M, Bratina N, Lepej D, Nimri R, Atlas E, et al. Closed-loop glucose control in young people with type 1 diabetes during and after unannounced physical activity: a randomised controlled crossover trial. Diabetologia [Internet]. 2017 Aug 24 [cited 2017 Aug 25];60(11): 2157–67.
7. Breton MD, Cherñavvsky DR, Forlenza GP, DeBoer MD, Robic J, Wadwa RP, et al. Closed Loop Control During Intense Prolonged Outdoor Exercise in Adolescents With Type 1 Diabetes: The Artificial Pancreas Ski Study. Diabetes Care [Internet]. 2017 Aug 30 [cited 2017 Sep 3];dc170883. A
8. Olinder AL, Kernell A, Smide B. Missed bolus doses: devastating for metabolic control in CSII-treated adolescents with type 1 diabetes. Pediatr Diabetes [Internet]. 2009 Mar [cited 2018 Jun 26];10(2):142–8.
9. Forlenza GP, Cameron FM, Ly TT, Lam D, Howsmon DP, Baysal N, et al. Fully Closed-Loop Multiple Model Probabilistic Predictive Controller Artificial Pancreas Performance. Diabetes Technol Ther [Internet]. 2018 Apr 16 [cited 2018 May 2];20(5):1–9.
10. Weinzimer SA, Steil GM, Swan KL, Dziura J, Kurtz N, Tamborlane W V. Fully automated closed-loop insulin delivery versus semiautomated hybrid control in pediatric patients with type 1 diabetes using an artificial pancreas. Diabetes Care [Internet]. 2008 May 1 [cited 2018 Feb 14]; 31(5):934–9.
11. Cameron FM, Ly TT, Buckingham BA, Maahs DM, Forlenza GP, Levy CJ, et al. Closed-Loop Control Without Meal Announcement in Type 1 Diabetes. Diabetes Technol Ther [Internet]. 2017 Aug 2 [cited 2017 Oct 3];19(9): dia.2017.0078.
12. Bode BW, Johnson JA, Hyveled L, Tamer SC, Demissie M. Improved Postprandial Glycemic Control with Faster-Acting Insulin Aspart in Patients with Type 1 Diabetes Using Continuous Subcutaneous Insulin Infusion. Diabetes Technol Ther [Internet]. 2017 Jan [cited 2017 Apr 10]; 19(1):25–33.
13. Heise T, Zijlstra E, Nosek L, Rikte T, Haahr H. Pharmacological properties of faster-acting insulin aspart vs insulin aspart in patients with type 1 diabetes receiving continuous subcutaneous insulin infusion: A randomized, double-blind, crossover trial. Diabetes, Obes Metab [Internet]. 2017 Feb [cited 2017 Feb 5];19(2):208–15.
14. Mathieu C, Bode BW, Franek E, Philis-Tsimikas A, Rose L, Graungaard T, et al. Efficacy and safety of fast-acting insulin aspart in comparison with insulin aspart in type 1 diabetes (onset 1): A 52-week, randomized, treat-to-target, phase III trial. Diabetes, Obes Metab [Internet]. 2018 Feb 4 [cited 2018 Feb 13];

033

(ISPAD) DIABETES TECHNOLOGY IN PEDIATRICS: ISPAD GUIDELINES UPDATE AND THE FUTURE

ATTD19-0502

INSULIN PUMPS

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The first application of technology to improve the care of those living with type 1 diabetes (T1D) can arguably be traced to the dawn of insulin pump therapy in the late 1970s. Yet, integration of this technology into the clinical care of youth remained minimal until the turn of the century. Data on the use of pump therapy have shown improvement in glycemia in observational studies; however, randomized control trials have demonstrated conflicting results. More recently, registry data has reinforced that lower A1c levels are demonstrated in pump users. Additional benefits of pump therapy, extending beyond A1c, should be considered in youth. Indeed, pumps serve as the foundational building blocks in the midst of a technological revolution based on integration of sensor data allowing for automation of insulin delivery.

034

DO IT YOURSELF IN DIABETES

ATTD19-0521

THE EUROPEAN PERSPECTIVE OF DIY FOR CLOSED-LOOP

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The availability of official hybrid closed loop systems is limited in routine care of patients with T1D. This situation has led to massive expansion of non-certified Open Source Hybrid Closed Loop Systems amongst these patients.

In contrast to the USA, where Loop is the most popular, In Europe AndroidAPS is the most common. This open source hybrid closed loop, which was created by Milos Kozak, is based on the OpenAPS algorithm which works with a model predictive control (MPC). The AndroidAPS app can be downloaded to any smartphone with Android 5 and the pump is fully controlled by the smartphone with AndroidAPS application. The CGM and CSII data can be visualized on smartphone as well. This algorithm, along with its additional features, does not have either a Certification Europe (CE) marking or FDA approval. However, the number of patients with T1D using this uncertified product is still increasing and physicians are being more and more frequently confronted with T1D patients using this system. Pivotal data has shown the effectiveness of this system. Nevertheless, long term safety data is still missing.

This presentation will show the preliminary results of In Silico modeling by a UVA/Padova simulator of the AndroidAPS hybrid closed loop, as well as an update of ongoing studies with AndroidAPS. The Good News project, an international multicenter safety study of AndroidAPS, will also be introduced.

035

DO IT YOURSELF IN DIABETES

ATTD19-0498

"#WEARENOTWAITING:" DIY DIABETES DATA AND RESEARCH

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Over the last several years, dozens of patients have developed numerous novel tools and technologies to make living with type 1 diabetes easier. By sharing their work through open source methods, thousands of people with diabetes have been able to benefit from accessing and visualizing their data in new and novel ways, in addition to making new combinations of diabetes devices interoperable. These tools range from remote monitoring tools to DIY closed loops such as OpenAPS. While most of these tools are often designed for real-time use, the data created and collected by these tools enable for significant new research into areas of diabetes previously not addressed by traditional researchers. This presentation will address the background of the #WeAreNotWaiting movement and the evolution of these diabetes tools and technologies, as well as some of the current research and potential future areas of research that this data can empower.

036

Advanced Medical Technologies to Be Used in Hospitals

ATTD19-0098

ROLE OF COMPOSITE GLYCAEMIC INDICES: A COMPARISON OF THE COMPREHENSIVE GLUCOSE PENTAGON ACROSS DIABETES SUBTYPES AND HBA1C

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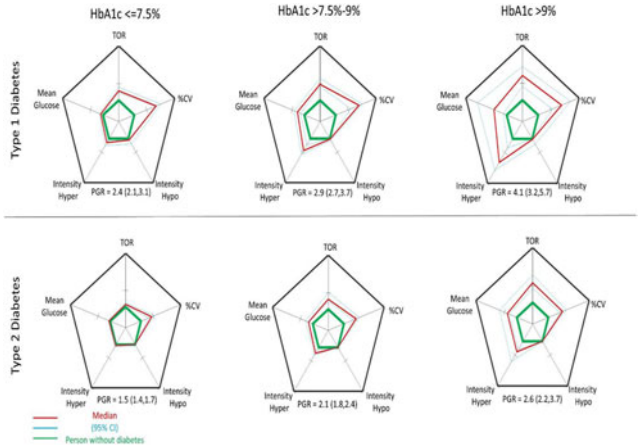
Background: Complex changes of glycaemia occur in diabetes which no single measure can fully capture. The Comprehensive Glucose Pentagon (CGP) measures multiple aspects of glycaemia to generate the Prognostic Glycaemic Risk (PGR), which constitutes the combined relative risk of hypoglycaemia and long-term complications. We compare components of CGP and PGR across Type 1 and Type 2 Diabetes (T1, T2D) and HbA1c.

Methods: Subjects: n = 60 T1D and n = 100 T2D who underwent CGM. Mean glucose, %CV, Intensity of Hypoglycaemia and Hyperglycaemia (INT_{hypo} & INT_{hyper}, $\sqrt{(AUC)^2+(Time)^2}$), Time out-of-Range (TOR, <3.9mmol/L & >10mmol/L) and PGR were calculated. PGR scores (median, 95% CI) for diabetes subtypes and HbA1c tiers were compared.



Results: While HbA1c was lower in T1D (T1D-vs-T2D: 8.0 ± 1.6% vs 8.6 ± 1.7%, p = 0.02), mean glucose and median INT_{hyper} were similar across T1D and T2D (both p > 0.05). INT_{hypo}, %CV and TOR were all higher in T1D [T1D-vs-T2D: 905(571, 1566) vs 18(0, 81) mg/dlxmin^2; 40.5 ± 9.4 vs 29.6 ± 7.6%; 699 ± 272 vs 591 ± 364 min/day respectively, all p < 0.05]. Across each HbA1c tier, the PGR remained consistently and significantly higher in T1D (Figure 1). Whilst mean glucose remained the same across HbA1c tiers, %CV, TOR, INT_{hyper} and INT_{hypo} were significantly higher for T1D. Even within the same HbA1c tier, the spread (95%CI) of each parameter in T1D was wide (Figure 1).

Conclusion: T1D clearly demonstrates wider variation across multiple glycaemic parameters in comparison to T2D. HbA1c alone cannot capture this variation. Composite indices like CGP may enable ready comparison of multiple important glucose outcomes.

037

Advanced Medical Technologies to Be Used in Hospitals

ATTD19-0366

FAMILY MIRNA 132 AND 134 EXPRESSIONS AND THEIR RELATION TO DIABETES MELLITUS AND MILD COGNITIVE IMPAIRMENT

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Background: Understanding miRNAs-related pathways could serve as novel targets for drug development for devastating health conditions.

Objective: is to assess miRNA family 132 & 134 expression among diabetics and its association with mild cognitive impairment (MCI).

Methodology: This study recruited 150 diabetics and 150 healthy age and sex matched individuals. Micro RNA family 132 & 134 expressions were assessed and MCI was detected using, ACE III cognitive test.

Results: Among diabetics, family 134 miRNA (134, 323, 382) expressions are positively highly significant correlated with each other P < 0.001. Among controls, the family miRNA132 (128, 132 and 874) expressions were significantly correlated with each other.

Expression level of miRNA 874 was found to be significantly higher among diabetics compared to controls, P < 0.0001. Logistic regression analysis revealed that higher miRNA 874 and miRNA 323 expressions were the significant predicting factors for DM with AOR 1.1 (1.05–1.12) and 1.1 (0.99–1.22) respectively. The prevalence of MCI was significantly higher among diabetics (27.6%) compared to controls (6.7%) with OR 5.3, P < 0.001. Among controls, total ACE III score was significantly positively correlated with miRNA128 and significantly negatively correlated with miRNA 134 expressions. While, among diabetics, total ACE III score was not correlated with the miRNA expressions. Higher miRNA 874 expression, female gender and lower education level were the significant predicting factors for MCI among diabetics with AOR 1.01 (0.99–1.2), 2.3 (0.97–5.7) and 0.62 (0.39–1.003) respectively.

Conclusion: MiRNA expression can be used as a minimally invasive test for early detection of DM and MCI.

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038

Artificial Pancreas

ATTD19-0215

OPEN – OUTCOMES OF PATIENTS' EVIDENCE WITH NOVEL, DO-IT-YOURSELF ARTIFICIAL PANCREAS TECHNOLOGY

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Digital innovations in healthcare up until recently have typically followed a 'top-down' pathway, with manufacturers leading the design and production of technology-enabled solutions and patients involved only as 'users' of the end-product. However, this is now being disrupted by the increasing influence and popularity of more 'bottom-up' and patient-led open source initiatives. A leading example is the growing movement of people with diabetes (PwD) who create their own ''do-it-yourself'' artificial pancreas systems (DIY APS) through remote control of medical devices with an open source algorithm.

The EU-H2020 funded project ''OPEN'' brings together an international and intersectoral consortium of patient innovators, clinicians, social scientists, computer scientists and patient advocacy organizations to establish an evidence-base surrounding the impact of DIY APS on PwD and wider healthcare systems. Its aims include the following: 1) to examine the clinical and quality of life outcomes, as well as lived experiences, of DIY APS users through a variety of quantitative and qualitative approaches; 2) to make technological improvements in DIY APS through improving the user experience as well as the predictive capacity of such systems; 3) to explore barriers to scale-up, such as socioeconomic, gender, ethnic and age-related inequalities in access to technologies needed for DIY looping, and how they might be resolved.

The DIY APS movement is an exemplary case study of historical significance, and this research will have important lessons and implications in a context where informed and connected patients are driving and challenging current care models and paradigms of medical innovation and regulation.

039

Blood Glucose Monitoring and Glycemic Control in the Hospitals

ATTD19-0429

DAILY GLUCOSE VARIABILITY IS ASSOCIATED WITH NOCTURNAL HYPOGLYCAEMIA

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Background and aims: Even with the advent of insulin pumps and long-acting insulin analogues, nocturnal hypoglycaemia is still common in patients with type 1 diabetes (T1D). Our aim was to assess the relationship between nocturnal hypoglycaemia and glucose variability (GV) in T1D.

Method: We analysed 10778 hours of continuous glucose monitoring of patients with type 1 diabetes (T1D) and extracted 3601 hours between 0 and 8 a.m.. All data points were collected on iPro$_2$TM.

Results: Most patients were female (n = 40; 57.1%), and mean age, duration of disease and A1C was 30.3 ± 9.6years, 17.1 ± 9.2years and 7.9 ± 1.1%. Mean glucose levels decreased during the night in patients treated with insulin pumps (0–2a.m.: 168.8 mg/dL; 2–4a.m.: 172.8 mg/dL; 4–6a.m.: 165.4mg/dL; 6–8a.m.: 158.3 mg/dL) and multiple daily injections [MDI] (0–2a.m.: 159.2 mg/dL; 2–4a.m.: 160.6mg/dL; 4–6a.m.: 153.2 mg/dL; 6–8a.m.: 147.4mg/dL). However, the time spent in hypoglycaemia was substantially lower for patients treated with insulin pumps than MDI (5.5% vs 11.1%), and it was lowest between 2–4a.m. (3.7%). and highest between 6–8a.m (7.8%) for the former and two blocks of time were noticeable between 0–4a.m. (9,4%) and 4–8a.m. (12.8%) for the latter. Time spent in hypoglycaemia at night was correlated with 24 h glucose variability indexes (ie, CONGA [r = –0.10, p = 0.015], LI [r = –0.10, p = 0.015], JINDEX [r = –0.09, p = 0.022], LBGI [r = 0.07, p = 0.090], HBGI [r = –0.09, p = 0.030], GRADE [r = –0.12, p = 0.022], MODD [r = –0.06, p = 0.162], MAGE [r = –0.11, p = 0.009], ADDR [r = –0.17, p < 0.001], MValue [r = –0.08, p = 0.051], MAG [r = –0.14, p = 0.001]).

Conclusion: Daily glucose variability was associated with the time spent in hypoglycaemia at night, therefore patients at increased risk of nocturnal hypoglycaemia would benefit from strategies aiming to decrease glucose variability.

040

Clinical Decision Support Systems - Advisors

ATTD19-0163

TOWARDS AUTOMATED MACRONUTRIENT ASSESSMENT

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Introduction: The role of nutrition is crucial for the management of metabolic diseases such as diabetes and obesity. However, accurate assessment of dietary intake remains challenging. Conventional approaches are often burdensome, indicating a pressing need to develop a more effective tool.

Methods: We tested the accuracy of a novel automated image-based macronutrient assessment tool in a pre-clinical setting at the Bern University Hospital Kitchen. Fifty breakfast variants, each consisting of 4 out of 40 food items from 7 categories (bread, cereals, spreads, fruits, cheese, mash and yogurt) were assessed in terms of macronutrient and energy content. Each meal was scanned 4 times. Reference data was derived from the true weight and information from a nutritional database. Primary outcome was mean difference in estimated carbohydrate (CHO) content with 95% limits of agreement [LoA]. Secondary outcomes were deviations in protein, fat and energy estimation and method reproducibility.

Results: The mean(SD) error in estimated CHO content per menu was 2.6 (6.5)g with LoA [−15.8, 21.1]. Protein, fat and energy estimations varied by 1.4 (2.4)g [−3.7, 5.7], 1.0 (1.9)g [−4.8, 7.6] and 25.2 (45.5)kcal [−100.1, 150.5] from reference method. The coefficients of variation between repeated scans were 15.5 (10.9)%, 14.2 (9.0)%, 15.2 (9.8)% and 13.9 (8.1)% for CHO, fat, protein and energy content, respectively. Accuracy was lowest for yogurt food items. When excluding yogurt items, LoA were [−10.3g, 10.0g], [−3.7g, 4.9g], [−3.1g, 4.1g] and [−68.5kcal, 82.6kcal] for CHO, fat, protein and energy content.

Conclusion: Image-based automated macronutrient assessment showed promising accuracy over a wide range of different food items. Its potential clinical impact remains to be determined under real-life settings.

041

Clinical Decision Support Systems - Advisors

ATTD19-0214

FEASIBILITY OF SAFETY SYSTEM WITHIN A NOVEL PERSONALISED DECISION SUPPORT TOOL FOR INSULIN DOSING

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Background: The Patient Empowerment through Predictive Personalised Decision Support (PEPPER) integrated system is designed to provide personalised bolus advice for people with Type 1 diabetes (T1DM). The system delivers insulin dosing decision support based on case-based reasoning (CBR), coupled with a safety system which includes predictive glucose alarms, low glucose suspend for insulin pump users, and personalised carbohydrate recommendations. We aimed to assess proof of concept and feasibility of the PEPPER safety system.

Methods: This is a Phase 1 non-randomised open-labelled 8-week study to assess the safety system outcomes (without CBR-based insulin dosing decision support). Eight adults with T1DM on multiple daily injections of insulin participated. Following two weeks of unblinded continuous glucose monitoring (CGM, Dexcom G5), participants completed six further weeks with the PEPPER safety system active. Baseline outcomes derived from the run-in period were compared with end-point.

Results: Participants were (median (interquartile range)) aged 38 (31.8–53.5) years, with a diabetes duration of 22.5 (18.0–26.5) years and HbA1c 63 (57–66)mmol/mol. Percentage time in hypoglycaemia (<3.0mmol/l) significantly decreased from 0.82% at run-in to 0.33% at endpoint ($p = 0.02$), with a significant increase in percentage time in target (3.9–10.0mmol/l; $p = 0.027$). The total number of alarms to carers significantly decreased ($p = 0.005$). There was also a reduction in number of carbohydrate recommendations.

Conclusions: The PEPPER safety system is safe and feasible to use as a component of the overall system and to integrate with the PEPPER adaptive bolus calculator. The data suggest the PEPPER safety system has the potential to enable improvements in hypoglycaemia and percentage time in range.

042

Clinical Decision Support Systems - Advisors

ATTD19-0243

SMART BOLUS CALCULATOR FOR PERSONALIZED INSULIN DOSING USING CONTINUOUS GLUCOSE MONITORING DATA AND PATIENT CHARACTERISTICS

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Background and Aims: In type 1 diabetes (T1D) therapy, insulin meal boluses (IMB) are usually computed by a ''standard formula'' (SF) using current blood glucose (BG) concentration provided by fingerprick devices. In this work, we investigate the potential of integrating continuous glucose monitoring (CGM) data and patient specific parameters to adjust and personalize the IMB dose computed using SF.

Method: Using the UVa/Padova T1D Simulator, we generated in silico data of 100 virtual subjects undergoing single meal, noise-free trials with different conditions in terms of preprandial BG and glucose rate of change (ROC) and meal amount. For each condition, we computed the optimal correction ΔIMB to be applied to IMB obtained with SF, to minimize the BG risk index

(BGRI). We split data into training and test sets. In the training set, we fitted a linear regression (LR) to predict ΔIMB using 10 features (carbohydrate-to-insulin ratio, correction factor, insulin-on-board, carbohydrate-on-board, body weight, meal carbohydrate intake, target BG, basal insulin, preprandial BG and ROC). In the test set, we compared performance of SF and LR in terms of time in hypo/hyperglycemia and BGRI.

Results: Median results show a general improvement of the glycemic performance with LR compared to SF: time in hypoglycemia 5.22% vs. 12.57%; time in hyperglycemia 21.93% vs. 21.92%; BGRI 6.94 vs. 8.75.

Conclusion: We showed how LR can exploit both CGM-derived information and patient characteristics to effectively personalize IMB computation and improve the glycemic outcomes. Future development will involve the assessment of this methodology in more challenging scenarios.

Table 1: Change in % time spent in glycemic ranges and glycemic variability assessed by blinded CGM from baseline to week 24.

	ABC group	MC group	ABC vs MC (P value)
Change in % time spent in ranges assessed by CGM *			
Δ Time in hypoglycemia (%)	-0.5 (-1.7 - 0.7) (P=0.45)	-0.9 (-1.8- -0.5) (P=0.04)	P=0.52
Δ Time in euglycemia (%)	10.4 (1.4 - 19.4) (P=0.03)	5.5 (-4.3 - 15.2) (P=0.26)	P=0.45
Δ Time in hyperglycemia (%)	-9.9 (-19.2 - -0.7) (P=0.04)	-4.5 (-14.6 - 5.5) (P=0.36)	P=0.42
Change in glycemic variability assessed by CGM			
Δ SD (mmol/L)	-0.4 (-0.8 - -0.1) (P=0.01)	-0.32 (-0.6 - -0.03) (P=0.03)	P=0.61
Δ CV (%)	-2.7 (-5.6 – 0.2) (P=0.07)	-3.1 (-5.0 - -1.2) (P=0.02)	P= 0.82

Data are mean (95% CI). CGM: Continuous glucose monitor; SD: Standard deviation; CV: Coefficient of variation; ABC: Advanced bolus calculator; MC: Manual calculation.
*Hypoglycemia: SG≤3.9 mmol/L, Euglycemia: SG 4.0 – 10.0 mmol/L, Hyperglycemia: SG≥10.1 mmol/L

043

Clinical Decision Support Systems - Advisors

ATTD19-0273

EFFICACY OF ADVANCED CARBOHYDRATE COUNTING AND AUTOMATED INSULIN BOLUS CALCULATORS IN TYPE 2 DIABETES: THE BOLUSCAL2 STUDY, AN OPEN-LABEL, RANDOMIZED CONTROLLED TRIAL

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Background and aim: Carbohydrate counting and use of automated bolus calculators (ABC) can help reduce HbA1c in type 1 diabetes but this approach has never been tested in type 2 diabetes. We evaluated the efficacy of advanced carbohydrate counting and use of an ABC compared with manual insulin bolus calculation in persons with type 2 diabetes.

Methods: A 24-week open-label, randomized controlled study was conducted in 79 participants (mean age 62.5 ± 9.6 yrs, HbA1c 72 ± 11 mmol/mol, diabetes duration 18.7 ± 7.6 yrs) with type 2 diabetes treated with basal-bolus insulin. Participants were randomized 1:1 into two groups. ABC group received training in advanced carbohydrate counting and use of an ABC. MC group received training in advanced carbohydrate counting and manual calculation of insulin bolus. Participants wore blinded CGM for 6 days at baseline and at study end. Primary endpoint was change in HbA1c.

Results: After 24 weeks HbA1c significantly decreased 8.8 mmol/mol in ABC group and 9.0 mmol/mol in MC group with no difference between groups (P = 0.96). Change in time spent in glycemic ranges (%) and glycemic variability are given in table 1. Glycemic variability decreased significantly in both groups. There was no significant change in insulin dose or BMI during the study.

Conclusion: Advanced carbohydrate counting and insulin bolus calculation is an efficient, low-cost tool to reduce HbA1c and glycemic variability in persons with basal-bolus insulin treated type 2 diabetes. Similar effects were seen with use of an ABC and with use of manual bolus calculation.

044

Clinical Decision Support Systems - Advisors

ATTD19-0425

THE USE OF AN INSULIN SENSITIVITY-INFORMED BOLUS CALCULATOR REDUCES AFTER-DINNER HYPOGLYCEMIA FOLLOWING AN EARLY-AFTERNOON EXERCISE SESSION: A PROOF-OF-CONCEPT IN SILICO STUDY

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Background: Insulin sensitivity (SI) regulates the impact of insulin treatment decisions on glucose variability in individuals with Type 1 Diabetes (T1D). SI fluctuations – frequent and large in T1D – complicate insulin dosing and can lead to worsened glycemic control. Here, we propose a new bolus strategy based on monitoring SI changes, and present its *in silico* validation in the control of one meal following an exercise session (increased SI).

Methods: A 24-hour simulation was built using the UVa/Padova T1D Simulator. One-hundred *in silico* adults received

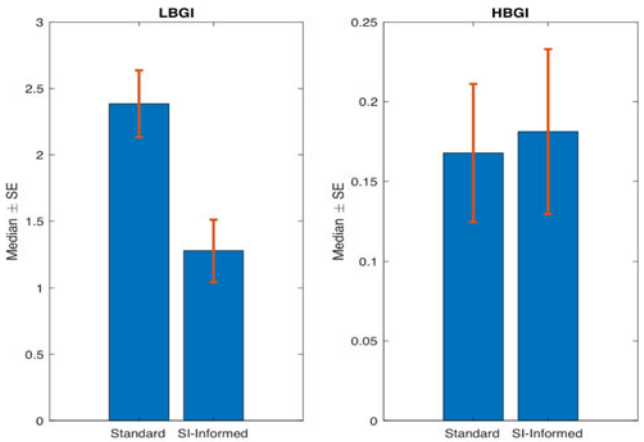

Figure. Postprandial LBGI/HBGI (median ± standard error of the median [SE]) obtained with the use of standard or SI-informed bolus calculator.

breakfast at 7AM, lunch at 12:30PM, and dinner at 7PM; a 45-minute exercise session was simulated at 2:30PM. The dinner bolus was computed using functional insulin therapy or the SI-informed bolus calculator; the latter modulates the standard insulin dose based on the ratio between a real-time estimate of SI and the subject's usual SI at the same time of day. Low and high blood glucose indices (LBGI/HBGI) were computed from sensor data in the 6 hours following dinner to assess hypo- and hyperglycemia exposure.

Results: Postprandial LBGI considerably decreased when the SI-informed bolus calculator was used rather than standard insulin therapy ($\Delta_{LBGI} = 1.1$); HBGI did not show relevant difference ($\Delta_{HBGI} = 0.01$) [see Figure]. The number of hypoglycemia treatments administered in the same postprandial period was reduced from 34 to 6 with the use of the SI-informed calculator.

Conclusions: This *in silico* study shows the potential benefit of modulating insulin boluses in real-time based on the subject's SI, and suggests the possibility of deploying this technique to improve glucose control after physical activity.

045

Closed-loop System and Algorithm

ATTD19-0167

HYBRID CLOSED LOOP THERAPY IN THE REAL WORLD: 6 MONTH CLINICAL OBSERVATION OF YOUTH WITH TYPE 1 DIABETES

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Objective: To describe the impact of the 670G Hybrid Closed Loop (HCL) system on glucose control in a clinical sample of youth with type 1 diabetes (T1D).

Methods: Youth starting the 670G HCL system for T1D care enrolled in an observational study. Data on HCL use and glycemic outcomes were obtained from pump downloads and chart review during 2 routine follow-up clinic visits over 6 months following initiation of HCL.

Use of HCL and glycemic outcomes over time for participants continuing HCL therapy (N=32)
Statistics reported are mean ± SD or median (25th percentile, 75th percentile)

Variable	1st clinic visit after start of HCL	2nd clinic visit after start of HCL	*p*-value
Median # days since HCL initiation	89 (67, 110)	189 (170-218)	na
% time in HCL	71 (57,82)	61 (39,76)	0.004
% sensor wear	81 (71,89)	72 (52,87)	0.03
% sensor glucose <70 mg/dl	1 (0,2)	1 (1, 2)	0.43
% sensor glucose 70-180 mg/dl	61 ± 14	56 ± 15	0.02
% sensor glucose 181-250 mg/dl	23 ± 6	25 ± 6	0.09
% sensor glucose >250 mg/dl	11 (6,17)	14 (5, 23)	0.08
Standard deviation of glucose (mg/dl)	62 ± 12	66 ± 15	0.07
Mean sensor glucose (mg/dl)	169 ± 26	178 ± 30	0.07
# system exits from HCL mode/day	1.0 ± 0.42	0.92 ± 0.42	0.16

Results: Fifty-one youth (mean age 15.7 + 3.5 yrs.; 56% M; baseline A1c 8.6% (7.8, 9.8) with T1D for 7.2 + 4.1 yrs, were included. Nineteen individuals (37%) discontinued use of HCL within 6 months of starting HCL therapy. After adjusting for baseline A1c, the 32 youth who continued HCL exhibited an increase in A1c from 7.8% at the 1st follow-up clinic visit to 8.1% at the 2nd follow-up clinic visit ($p = 0.02$ in a mixed model). Time spent in HCL decreased from 71% to 61% between the 1st and 2nd clinic visits ($p = 0.004$). Sensor wear decreased from 81% to 72% ($p = 0.03$). Time in range (70–180 mg/dl) decreased from 61% to 56% ($p = 0.02$). System exits from HCL mode to standard pump mode occurred once per day.

Conclusions: Youth experienced a decline in HCL use over time, possibly contributing to the reduced sensor time in range and increased A1c over time. Youth may need additional support to maintain sensor wear and manage HCL exits to sustain HCL use over time. Future research is necessary to understand reasons for discontinuation of HCL therapy in youth.

046

Closed-loop System and Algorithm

ATTD19-0175

HIGH-INTENSITY INTERVAL EXERCISE VS. MODERATE-INTENSITY EXERCISE IN ADULTS WITH TYPE 1 DIABETES AND IMPAIRED AWARENESS OF HYPOGLYCAEMIA USING CLOSED-LOOP INSULIN DELIVERY

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Background: People with type 1 diabetes (T1D) and impaired awareness of hypoglycaemia (IAH) have defective hormonal counter-regulation to hypoglycaemia. However, their biochemical responses to exercise have not been well-defined.

Aims: To evaluate counter-regulatory hormone responses and glucose control using hybrid-closed-loop (HCL) among people with T1D and IAH undertaking exercise.

Methods: Nine adults with T1D and IAH (5 men; median [IQR] age 54 [44, 57] years; HbA1c 7.2% [6.5, 7.5]; Gold score 6 [5, 7]) undertook high-intensity interval exercise (HIIE) and moderate-intensity exercise (MIE) stages, 45-minutes duration, in random-order with HCL (Medtronic 670G) activated. Frequent venous samples measured glucose, ketones, lactate and counter-regulatory hormones. Biochemical parameters during and 120-minutes post-exercise were assessed as time-averaged mean AUC; HIIE and MIE results were compared using Wilcoxon signed-rank test.

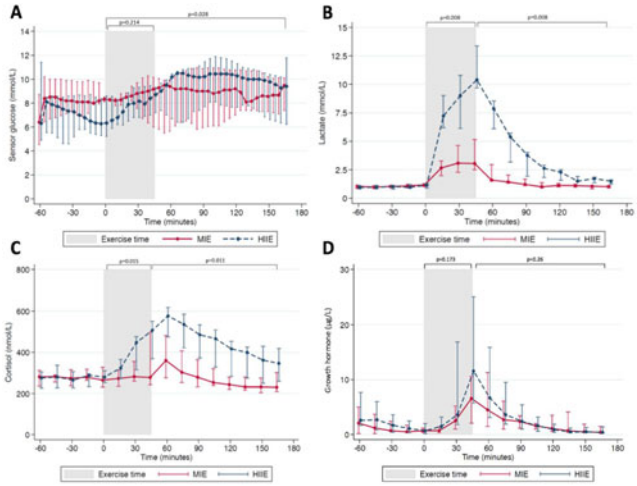

Figure 1: Profiles of sensor glucose, lactate and counter-regulatory hormones prior to, during, and following exercise. Comparisons are for HIIE vs. MIE.

Results: Compared with MIE, HIIE was associated with greater increases in cortisol (385nmol/L*min [296, 428] vs. 295nmol/L*min [234, 313] respectively, p = 0.015) *(Figure 1)*. No significant differences in growth hormone or glucagon were observed. Post-exercise, ketones increased similarly with HIIE and MIE. Increase in sensor glucose from exercise commencement to 120-minutes post-exercise was greater with HIIE than MIE (HIIE +225mmol/L [+173, +504] vs. MIE -144mmol/L [−274, −20], p = 0.028). Sensor glucose was <3.9mmol/L in only one participant during each stage.

Conclusions: Among adults with T1D and IAH, our data suggest preservation of counter-regulatory patterns of response to exercise. This contrasts to documented impaired counter-regulatory responses to hypoglycaemia in this group, suggesting different pathways for the two stimuli. HCL appeared safe and effective with exercise in this study.

047

Closed-loop System and Algorithm

ATTD19-0268

AN INSULIN PUMP WITH PREDICTIVE LOW GLUCOSE SUSPEND TARGETS THE TIME IN RANGE MORE EFFECTIVELY THAN MDI WITH CGM UNDER REPEATED PHYSICAL ACTIVITY.

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Background: Recent studies have shown that MDI with CGM is as effective as CSII with CGM for glycemic control improvement in patients with T1D. A comparison between MDI with CGM and an insulin pump equipped with automatic functions in real life conditions is missing.

Objective: The aim of our study was to compare MDI with CGM vs. CSII with Predictive Low Glucose Suspend (PLGM) in children with T1D at a sports camp.

Methods: Thirty-three T1D patients (13 males aged 7–14 years) were included in the six-day study at a summer sport camp. Patients were divided in two groups: PLGM-group (n = 18) using insulin pump MiniMed®640G with Enlite sensor and CGM-MDI-group (n = 15) monitored with DexCom G4 or G5 sensors. All patients had similar physical activities several times a day. Hypoglycemia was treated with dextrose using an identical protocol for both groups. All CGM data were uploaded afterwards and statistically processed.

Results: The groups did not significantly differ in mean glycemia (7.5 ± 1.1 vs 8 ± 1 mmol/L for PLGM vs. MDI, respectively; p = 0.2) or time spent in target range 3.9 to 7.8 mmol/L (59 vs 49%; p = 0.06). However, the PLGM group spent a significantly longer time in the range 3.9 to 10 mmol/L (80 vs 65%, p < 0.004) and significantly less time in hypoglycemia <3.9 mmol/l (3.5 vs 11%, p = 0.008) despite a lesser use of dextrose for prevention and treatment of hypoglycemia (10g vs 40g/patient/day; p < 0.02).

Conclusion: Our study showed that the main modality leading to better glycemic control during and after physical activity is an insulin pump with PLGM.

048

Closed-loop System and Algorithm

ATTD19-0370

GLYCEMIC OUTCOMES AND SYSTEM ADHERENCE BETWEEN AGE GROUPS IN PEDIATRIC SUBJECTS USING A HYBRID CLOSED-LOOP PUMP

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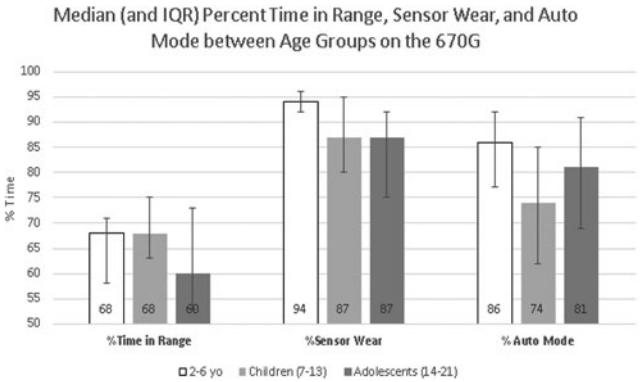
Objectives: Automated insulin delivery systems help individuals with Type 1 Diabetes increase euglycemia throughout day and night. We compared use of the Medtronic MiniMed 670G Hybrid Closed-Loop (HCL) system between children ages 2–6, 7–13, and 14–21 during home use.

Methods: Subjects were grouped into 3 categories, ages 2–6 (N = 18), 7–13 (N = 19), and 14–21 (N = 10). Subjects used the



670G pump and Guardian 3 Sensor in HCL mode (''Auto Mode''). Data was obtained during a 2-week block in the month after completion of the pivotal trial.

Results: There was significantly higher sensor wear in the youngest subjects, 94% in 2–6 year olds (yo) vs 87% in 7–13yo and 14–21yo ($p = 0.005$), and 2-6yo spent more time in HCL than 7–13yo, 87% vs 74% ($p = 0.028$). Pump wear was 100% for both 2–6 and 7–13yo, and 93% for 14–21. Percent time <70 mg/dl was low for all three groups (3.7% for 4–6yo, 2.1% for 7–13yo, 2.9% for 14–21yo). There was no statistical difference in either time in range (70–180mg/dl, 68% in 2–6yo, 68% in 7–13yo, 60% in 14–21yo) or mean glucose (158 mg/dl in 2–6yo, 158 mg/dl in 7–13yo, 164 in 14–21yo).

Conclusions: This study found that sensor wear and time spent in HCL was highest in 2–6yo. All groups maintained low rates of hypoglycemia, ≥60% time in range, and similar mean glucose levels. This aligns with our clinical experience that management of HCL systems in younger children is primarily done by parents, which helps with adherence. Overall the system works well in all age groups when it is worn.

049

Closed-loop System and Algorithm

ATTD19-0488

GLYCEMIC OUTCOMES DURING MINIMED 670G SYSTEM USE IN CHILDREN AGED 2–6 YEARS WITH T1D

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Background and Aims: Three-month use of the hybrid-closed loop MiniMed™ 670G system improved glycated hemoglobin (HbA1c) levels, day and night time glucose variability, and time in target glucose range (TIR) compared to baseline, in patients with type 1 diabetes (T1D) aged ≥14 years.[1] Recently, the system was approved for use in patients with T1D aged ≥7 years. Safety of the system when used at home by children with T1D aged 2-6 years of age was evaluated.

Method: Data from patients (N = 42, 2–6 years of age) who completed a 2-week baseline run-in phase in open-loop Manual Mode followed by a three-month study phase with closed-loop Auto Mode enabled were analyzed. Overall glycemic control and HbA1c between the baseline run-in and study phase were compared.

Results: The mean ± SD HbA1c reduced from 8.0 ± 0.9% (64.0 ± 13.9 mmol/mol) to 7.5 ± 0.6% (58.5 ± 16.9 mmol/mol) and overall mean TIR (70–180mg/dL [3.9-10mmol/L]) increased from 55.4 ± 13.3% to 63.6 ± 9.3%, compared to baseline. Percentage of time spent >180 mg/dL (<10.0 mmol/L) decreased from 41.0 ± 14.7% to 33.0 ± 9.9% and that ≤70 mg/dL (<3.9 mmol/L) decreased from 3.6 ± 2.6% to 3.4 ± 1.6%.

Conclusion: In-home MiniMed™ 670G system use in patients with T1D 2-6 years of age, similar to that observed in adults and youth with T1D, has been safe and associated with improved glycemic metrics.

Reference

1. Garg et al., *Diabetes Technol Ther*. 2017;19:155–163.

050

Devices Focused on Diabetic Preventions

ATTD19-0248

A CONSENSUS MODEL TO IMPROVE THE PREDICTION OF TYPE 2 DIABETES ONSET: VALIDATION ON THE MULTI-ETHNIC STUDY OF ATHEROSCLEROSIS DATA

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Objective: Several predictive models of type 2 diabetes (T2D) onset exist to identify subjects at risk of developing T2D. However, they often cannot be applied (missing model prediction) because some of their input variables are missing or not defined for certain groups of subjects (e.g. different racial/age groups). To overcome this limitation, we developed a consensus model that combined multiple existing models for T2D onset prediction. We assessed the consensus model validity on the Multi-Ethnic Study of Atherosclerosis (MESA) dataset.

Method: Subjects without diabetes at MESA entry visit were divided into a training set (4124 subjects) and a test set (1031 subjects). Eight models of T2D onset from the literature were recalibrated using the T2D incidence in the training set and then applied on the test set. For each subject, the consensus model prediction was obtained as the weighted average of the predictions of the recalibrated models applicable to that specific subject, assigning larger weights to the models using variables collected in medical examinations. Performance metrics were the concordance index (C-index) and the expected to observed event ratio (E/O). The number of subjects with missing model prediction (NM) was also assessed.

Results: The consensus model (C-index = 0.825, E/O = 0.828; NM = 0) presented no missing predictions and performed similar to the existing model with best discriminatory ability (C-index = 0.828, E/O = 0.807; NM = 462) and remarkably better than the existing model with minimum NM (C-index = 0.704, E/O = 0.697; NM = 1).

Conclusion: We proposed a consensus model for T2D onset prediction, which overcomes the problem of missing values and produces more robust risk predictions.

051

Glucose Sensors

ATTD19-0059

REAL-WORLD REDUCTION OF PROLONGED HYPOGLYCEMIA WITH FLASH GLUCOSE MONITORING: THE IMPORTANCE OF SCANNING AGAIN WITHIN THE NEXT HOUR

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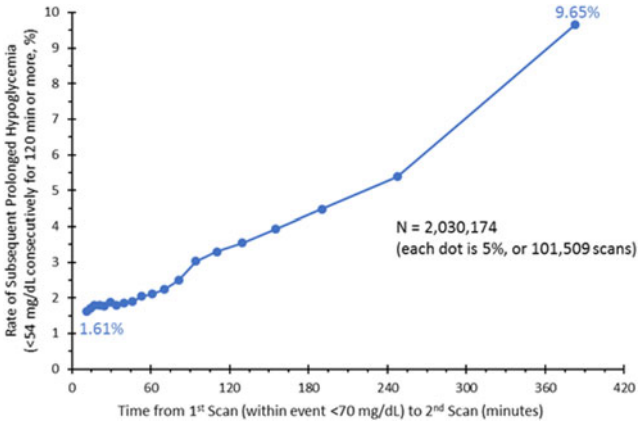
Aims: This analysis evaluates flash glucose monitoring (Freestyle LibreTM) scan timing following discovery of low glucose, with the specific aim to determine the reduction of prolonged hypoglycemia episodes by those who scan within the hour following a hypoglycemic scan reading.

Materials and methods: De-identified data provided glucose readings from 40,341 readers and 275,777 sensors. 2.03 million alert hypoglycemia events (at least two consecutive 15-minute readings below 70 mg/dL) had a scan during the event. Any subsequent ''prolonged'' serious clinically-relevant hypoglycemia (120 or more consecutive minutes below 54 mg/dL) event was determined, along with the time to the next scan (more than 10 minutes later). Odds ratios of prolonged hypoglycemia were determined. In addition 20 equal-sized bins rank-ordered by time to 2nd scan were found, and the fraction of prolonged hypoglycemia events was determined for each.

Results: The median time to the next scan was 57 minutes [mean (SD) 91 (96) minutes, IQR: 27–119 minutes] and 59,109 (2.9%) had subsequent prolonged hypoglycemia. A 2nd scan within the next 60 minutes reduced the likelihood of prolonged hypoglycemia by 56% (OR: 0.44, 95%CI 0.43–0.44, $p < 0.0001$). The soonest scans had a rate of 1.61% of prolonged hypoglycemia, while the latest scans had rate of 9.65% of prolonged hypoglycemia, a relative rate increase of 599%.

Conclusion: This analysis shows that scanning a 2nd time within the next hour is effective at reducing the rate of prolonged hypoglycemia, and that waiting longer increases the rate.



052

Glucose Sensors

ATTD19-0060

SHARING OF REAL-TIME CONTINUOUS GLUCOSE MONITORING DATA IMPROVES DEVICE UTILIZATION AND GLYCEMIC PARAMETERS IN YOUTH

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Background and Aims: Those caring for children and adolescents with diabetes often use glucose concentration and trending information in management decisions. Continuous glucose monitoring (CGM) systems from Dexcom® offer real-time sharing and monitoring capability through the mobile app feature, Share, and the companion Follow app. We explored associations between data sharing/monitoring, CGM utilization, and estimated glucose values (EGVs).

Methods: Anonymized device utilization and EGVs from a convenience sample of 15,777 mobile app users ages 2–18 years that were voluntarily uploaded in the first half of 2018 were analyzed. Data from patients using the G6 sensor were excluded. The presence or absence of a real-time monitor (a ''Follower'') was established on 6/15/2018. Each day with ≥1 valid EGV was counted as a day of device usage. Between-group comparisons were made with two-sided Welch's t-tests assuming unequal variances.

Results: Overall, 94.8% of the population used the Share feature and had at least 1 Follower. The mean numbers of Followers for patients ages 2–5, 6–12, and 13–18 were 2.8, 2.8, and 2.4, respectively. The presence of at least one Follower was consistently associated with lower mean EGVs, more EGVs in euglycemia (70–180 mg/dL), fewer EGVs in hypoglycemia and hyperglycemia, and significantly more device utilization (Table).

Table. Effects of Follower(s)

	Age (years)	Number of Followers	
		0	1 or more
n, %	2-5	79 (7.5%)	975 (92.5%)
	6-12	354 (5.0%)	6660 (95.0%)
	13-18	395 (5.1%)	7314 (94.9%)
Device Utilization (days/week)	2-5	4.8	6.2**
	6-12	4.7	6.2**
	13-18	4.9	5.9**
Mean EGV (mg/dL)	2-5	190.0	186.8
	6-12	192.2	184.1**
	13-18	193.4	186.5*
Percent <70 mg/dL	2-5	4.0	3.2
	6-12	3.4	3.1
	13-18	3.9	3.2*
Percent 70-180 mg/dL	2-5	47.7	49.8
	6-12	46.7	51.0**
	13-18	46.3	49.7*
Percent >180 mg/dL	2-5	48.3	46.9
	6-12	49.9	45.9**
	13-18	49.8	47.0*

*, p<0.05 and **, p<0.001 compared to 0 followers

Conclusion: Real-time sharing and following of CGM data may improve device utilization and glycemic parameters by facilitating timely interventions by parents and/or caregivers or by improving self-care behaviors among youth with diabetes.

053

Glucose Sensors

ATTD19-0100

PREDICTIVE FACTORS OF THE ADHERENCE TO THE REAL-TIME CGM SENSORS: A PROSPECTIVE OBSERVATIONAL STUDY (PARCS STUDY)

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We investigated factors that may influence CGM sensor adherence in a prospective observational study.

Method: Forty-six patients with type 1 diabetes mellitus using insulin pumps without CGM were recruited. After switching to the sensor-augmented pump MiniMed 620G (Medtronic, Inc), they were followed for one year. PAID (20 items) was used to evaluate the emotional burden of diabetes, and HFS (HFS-B, HFS-W) was used to evaluate the fear of hypoglycemia. CGM data was downloaded to PCs for analysis. Patients wearing the sensor for 60% or more of the time were considered adherent, whereas those who wore it for less than 60% of the time were considered non-adherent. *P*-values less than 0.05 were considered significant.

Results: Patients were aged 44.0 ± 15.0 years old, and 73.9% were female with a mean HbA1c of 7.7 ± 1.0%. The adherent group comprised 60.9% of the patients. There was no significant difference in age, gender, BMI, HbA1c, total daily insulin dose, annual mileage, income, reimbursement, or HFS (HFS-B, HFS-W) score at baseline between the adherent group and non-adherent group. The PAID score at baseline was significantly higher in the adherent group (40.0 ± 18.5 vs. 28.3 ± 14.1, $P = 0.044$). No severe adverse event (hospitalization due to diabetic ketoacidosis or severe hypoglycemia) was observed. There was no significant difference in the change in HbA1c after 1 year between the groups (–0.40 ± 0.48 vs. –0.25 ± 0.50, $P = 0.328$).

Conclusion: Higher CGM sensor adherence may be associated with heavier emotional burden of diabetes before starting to use CGM. (UMIN-CTR: UMIN000016588)

054

Glucose Sensors

ATTD19-0154

REAL-WORLD HYPOGLYCEMIA AVOIDANCE WITH A PREDICTIVE LOW GLUCOSE ALERT DOES NOT DEPEND ON FREQUENT SCREEN VIEWS

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[2]Dexcom- Inc., Clinical Affairs, San Diego, USA

Background: Requiring users to have frequent interaction with their glucose monitoring devices to improve control is burdensome. We evaluated hypoglycemia reduction associated with a predictive low glucose alert to determine its dependence on screen view frequency in a new integrated continuous glucose monitoring (iCGM) system.

Methods: We examined estimated glucose values (EGVs) from a convenience sample of 15,000 patients who used Dexcom G6 (Dexcom, Inc.) and its mobile app for at least 30 days between 5/1/18–8/31/18 with or without the ''Urgent Low Soon'' alert (ULS) enabled. The ULS is activated when an EGV ≤55mg/dL is forecasted within 20 minutes. Screen view frequency was determined as the frequency with which the trend screen was accessed on the app. Multiple screen views within any 5-minute interval were counted as one. Hypoglycemia exposure for patients in the top and bottom quartiles of screen view frequency (>8.25 and <3.30 per day, respectively) was calculated as the percentage of EGVs below various thresholds.

Results: The ULS feature was left in the enabled (default) state by >93% of users and its use was associated with significantly lower frequencies of EGVs <55 and <70 mg/dL, regardless of whether patients viewed their screens frequently or infrequently (Table). There were small (on average less than 2 minutes/day) differences in time in hypoglycemia between infrequent and frequent screen viewers.

	Infrequent Screen Viewers (<3.30 per day)			Frequent Screen Viewers (>8.25 per day)		
	ULS Disabled	ULS Enabled	p-value*	ULS Disabled	ULS Enabled	p-value*
N	252	3566	-	166	3652	-
Mean screen views/day	2.5 (0.5)	2.5 (0.5)	0.56	14.1 (6.8) †	13.3 (5.8) †	0.16
Time <55 mg/dL (%)	1.1 (1.5)	0.7 (1.2)	<0.001	1.2 (1.6)	0.6 (1.0) †	<0.001
Time <70 mg/dL (%)	4.3 (4.0)	2.6 (3.1)	<0.001	4.8 (4.4)	2.5 (2.8)	<0.001

Values are mean (SD). * computed using two-sided Welch's t-test, ULS Disabled vs. ULS Enabled. †, p<0.005, vs. Infrequent Screen Viewers

Conclusion: Features such as the predictive ULS alert of the G6 CGM system are associated with significant reductions in hypoglycemic exposure. These benefits do not require frequent device interactions, unencumbering iCGM users.

055

Glucose Sensors

ATTD19-0188

RELATIONSHIP BETWEEN HBA1C AND ESTIMATED HBA1C IN PATIENTS WITH TYPE 1 DIABETES USING FLASH GLUCOSE MONITORING

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Aims: To analyse the relationship between measured HbA1c and estimated HbA1c (eA1c).

Methods: Nine hundred thirty-seven adults with type 1 diabetes on multiple daily insulin injection (75.6%) or insulin pump (24.4%) from the FUTURE trial (NCT02898714) were included.

HbA1c was measured using Tosoh G8 HPLC Analyzer (Biosciences, Inc., CA) and eA1c was derived from four weeks FreeStyle® Libre™ (Abbott Diabetes Care, CA) data at two time points, 6 months apart. Haemoglobin glycation index (HGI) was calculated as HbA1c-eA1c (both expressed as %) and values of ±0.42% (±3SD) were defined significant.

Results: Although HbA1c and eA1c correlated at both time points ($r = 0.814$, $p < 0.0001$; $r = 0.800$, $p < 0.0001$), up to 49.2% and 56.9% of paired samples differed >|0.42%|, respectively. Bland-Altman plots suggest a proportional bias to more negative HGI values for higher HbA1c. HGI grid-analysis (figure 1) shows 20.3% of patients with HGI >0.42% (zone B) and 8.4% of patients with HGI <–0.42% (zone C) at both time points, suggesting a fast and slow glycosylation phenotype, respectively. Thirty-five patients first presented with a positive difference and second a negative difference (zone D) or vice versa (zone A). In most patients (68%) an aberrant eA1c calculation due to missing sensor data (data capture 68.2 ± 15.8% vs 88.7 ± 15.8% for whole group, $p < 0.0001$) or possible false low glucose measurements during nights accounted for this conversion.

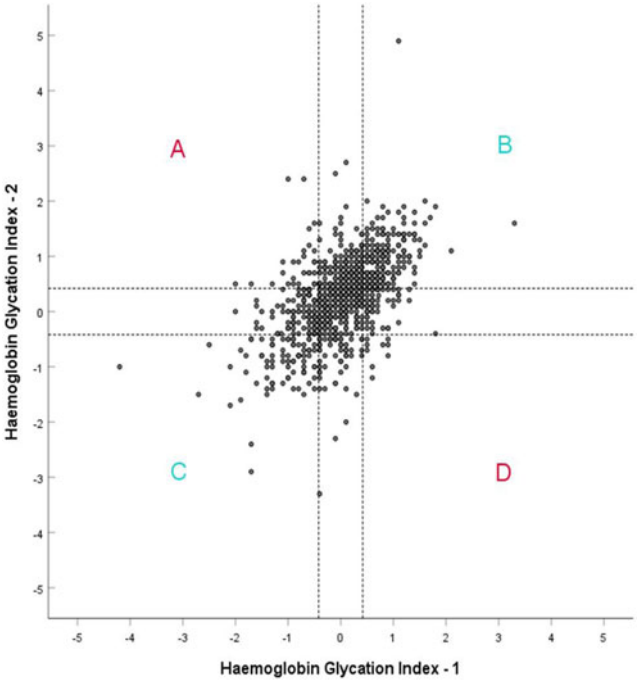

Figure 1: Grid-analysis of Haemoglobin Glycation Index for time point 1 (x-axis) and 2 (y-axis)

Conclusion: HbA1c and eA1c are correlated but often major differences exist between both parameters resulting from variations in glycosylation phenotype or aberrant eA1c calculation. Both parameters are therefore not interchangeable and should be used complementary.

056

Glucose Sensors

ATTD19-0232

ASSESSMENT OF THE PERFORMANCE OF AN IMPLANTABLE CGM SYSTEM WITH A NEW GLUCOSE CALCULATION ALGORITHM

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Background: PRECISE II was a prospective, multi-center blinded study that evaluated safety and accuracy of the novel implantable Eversense CGM system through 90 days of continuous sensor wear in participants with type 1 or type 2 diabetes (T1D, T2D). A mean absolute relative difference (MARD) of 8.8% with positive safety was achieved.

Methods: The glucose calculation algorithm (referred to as SW602) was updated after the conduct of the study. The algorithm converts raw data collected by the Sensor into glucose readings. Changes within SW602 algorithm targeted accuracy improvement in 1) early Sensor life and 2) hypoglycemic range throughout the Sensor life. The efficacy measures of percent of system agreement within 15 mg/dL or 15% of Yellow Springs Instrument (YSI) reference glucose measurements (15/15% metric) and MARD between paired Eversense and YSI reference measurements through 90 days were evaluated with SW602.

Results: Ninety participants received the CGM system. SW602 applied to the PRECISE II raw sensor data (15,753 matched pairs) resulted in 87% of CGM values within 15/15% of reference values over the total glucose range of 40–400 mg/dL. Performance in the very low hypoglycemic range (<54 mg/dL) showed 89% of CGM values within 15mg/dL. The overall MARD value against reference glucose values improved to 8.5% (95% CI: 8.0, 9.1).

Conclusions: The new glucose calculation algorithm, SW602, applied to the PRECISE II study sensor values of Eversense CGM system demonstrated an improved MARD of 8.5% compared to 8.8% with the original software through the sensor's 90 days wear time.

057

Glucose Sensors

ATTD19-0280

INCREASING USE OF CONTINUOUS GLUCOSE MONITORING (CGM) AMONG ADULTS WITH TYPE 1 DIABETES: DIFFERENCES BETWEEN THE US T1D EXCHANGE REGISTRY AND THE GERMAN/AUSTRIAN DPV INITIATIVE

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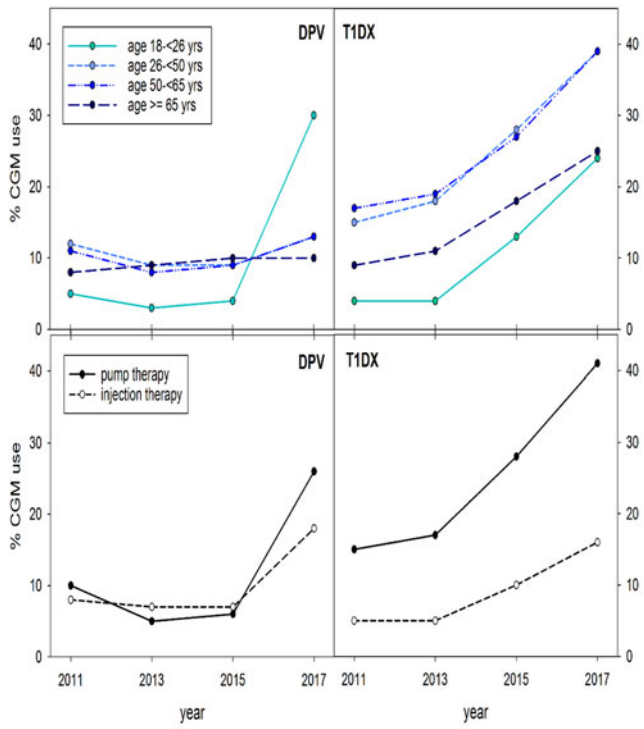
Objectives: To assess change in CGM use over the past seven years in adults with type 1 diabetes (T1D) in the US T1D Exchange (T1DX) and the German/Austrian DPV registries.



Methods: Data from N = 39,627 adults (≥18 years, T1D duration ≥1 year) were analyzed (DPV: N = 23,034; T1DX: N = 16,593). Percentage of CGM use in the years 2011, 2013, 2015, and 2017 was analyzed by registry, age group (18≤26, 26≤50, 50≤65, ≥65 years), and insulin delivery method (pump, injections). Multiple linear regression was used to compare mean HbA1c by CGM use.

Results: Overall frequency of CGM use increased from 11% in 2011 to 32% in 2017 in the T1DX, and from 9% to 21% in the DPV. Increase in CGM use was observed across all age groups for T1DX, but only in young adults (18≤26 years) in the DPV (5% in 2011 vs. 30% in 2017, $p < 0.001$; Figure, upper panel). CGM use was more frequent in pump vs. injection users across all years in the T1DX (Figure, lower panel, all $p < 0.001$), but only in 2011 and 2017 in the DPV (both $p < 0.001$). In 2017, mean HbA1c, adjusted for age and gender, was lower in CGM users vs. non-users in both registries (T1DX: 7.7 vs. 8.4%; DPV: 7.7 vs. 8.1%, both $p < 0.001$).

Conclusions: CGM use has increased considerably among adults with T1D in the T1DX, but less so in DPV with the exception of the young adult age group. The differences in CGM use are likely reflective of differences in insurance coverage, provider beliefs and patient preferences.

058

Glucose Sensors

ATTD19-0316

CGM AT DIAGNOSIS OF TYPE 1 DIABETES: IMPACT ON GLYCEMIC AND PSYCHOSOCIAL OUTCOMES

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Initiation of CGM is shifting closer to onset of type 1 diabetes (T1D). This pilot RCT assessed the impact of non-adjunctive CGM use on youth recently diagnosed with T1D and their caregivers.

Data from 55 study participants, ages 2-17 (11.1 ± 3.6 years, 50% female, 69% non-Hispanic white) and a caregiver were collected at baseline, 3 and 6 months. Participants were randomized 2:1 to intervention (n = 42, started Dexcom G5 within 40 days of diagnosis) or control (n = 13, no real-time CGM and use blinded Dexcom G4 for 1 week/month for 6 months). Parents completed online validated surveys about their diabetes-related distress (PAID-PR) and confidence to manage hypoglycemia (Hypoglycemia Confidence) in their children, and what they perceived as their child's health-related quality of life (QOL; PedsQL Proxy). HbA1c was collected at each time point.

There were no significant differences at 6 months in time-in-range (70–180mg/dL) or HbA1c, but the CGM group spent significantly less time <70mg/dL at 3 months (2% vs 7%, $p < 0.001$) and at 6 months (2% vs 5%, $p = 0.002$). Further, parents with children using CGM had significantly greater confidence in managing hypoglycemia ($p = 0.02$) than controls. However, a trend toward greater perceived diabetes-related distress in CGM parents versus controls was also observed ($p = 0.05$). Both groups reported steadily increasing QOL over six months; no differences between the groups.

Results highlight benefits of CGM early in the T1D course on hypoglycemia and caregiver confidence in managing hypoglycemia across multiple situations, yet caregivers likely need additional support to cope with additional burden of using real-time CGM.

059

Glucose Sensors

ATTD19-0379

EFFECTIVENESS AND SAFETY OF A NOVEL PERCUTANEOUS OPTICAL FIBER CONTINUOUS GLUCOSE SENSOR (FIBERSENSE) IN CLINIC AND HOME USE IN INDIVIDUALS WITH DIABETES AND PREDIABETES

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Objective: To evaluate the effectiveness and safety of the FiberSense, system, a percutaneous fiber-optic real-time continuous glucose sensor for home use in diabetic and prediabetic individuals for 29 days.

Methods: 8 type 1, 10 type 2 insulin-treated diabetic and 4 prediabetic individuals were enrolled. 4 additional insulin-treated diabetes patients on peritoneal dialysis with icodextrin were enrolled to evaluate maltose interference. Each wore a FiberSense sensor on the upper arm or abdomen for up to 29 days. Subjects attended four in-clinic measurement sessions on days 1, 7, 14 and 28 where FiberSense readings were compared against a standard laboratory method (YSI glucose) every 10 minutes during a glucose challenge. Self-monitored capillary blood glucose was performed at least four times a day. Non-dialysis subjects wore a commercial comparator CGM (Dexcom G4) during one of the study weeks.

Results: In an analysis of 19 (16 diabetes, 3 prediabetes) subjects who completed up to 29 days of sensor wear (mean 28.4 days; 10 on abdomen and 9 on upper arm), the pooled mean absolute relative difference (MARD) against YSI glucose was 14.9% (15.5%; 95%CI upper bound) across the full glycemic range (n = 1716) as compared to MARD 15.1% (16.4%, 95%CI upper bound) (n = 511) with Dexcom CGM. Consensus Error Grid analysis yielded 99.6% of paired FiberSense measurements in zones A plus B. There were no serious device-related adverse events or sensor site reactions.

Conclusions: These early results provide encouraging evidence that FiberSense CGM is acceptable and comparable in clinical accuracy to existing commercial CGM over 29-day home use.

060

Glucose Sensors

ATTD19-0414

DIFFERENCES BETWEEN INTERSTITIAL AND CAPILLARY GLUCOSE DURING DIFFERENT TYPES OF SUPERVISED EXERCISE

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Continuous and flash glucose monitoring (CGM and FGM) accuracy may be altered by posture and by metabolic changes in interstitial fluid glucose concentrations during exercise. The aim of the study is to evaluate difference in the interstitial and blood glucose during different type and intensity of exercise. 20 subjects (12F/8M, 46.4 ± 13.5years, 5CGM, 15FGM) with type 1 diabetes have been recruited for a 3-day educational camp focused on physical activity (PA) and management of insulin intensive therapy (CSII/MDI). Subjects wore heart-rate monitor during exercise sessions and recorded glycaemic values both with sensor and capillary measurement. All subjects performed activities: low intensity walking, moderate to vigorous intensity jogging and high intensity (uphill running) and a mixed-intensity activity (mountain hike) for 6 hours. The operator collected data before, during and after every training session. Variables are summarized as median and IQR. Concordance were tested using a nonparametric method (Kendall's test). During every task recorded capillary and sensor values were concordant (blood glucose vs sensor pre exercise p = 0,017, post p = 0,013). Analyzing the data according to the type of sensor, we found a constant concordance for the values measured with FGM ($p < 0.05$). We found a greater discrepancy, in all types of exercise, both with FGM and with CGM, when blood glucose values above 180mg/dl. During exercise sessions on field there is a good concordance between interstitial and blood glucose values even if significative differences were found for higher glycemic values. This phenomenon could lead to bias in insulin management and it requires in-depth studies.

061

Glucose Sensors

ATTD19-0417

ADOLESCENTS AND YOUNG ADULTS WITH TYPE 1 DIABETES (T1D) EXPERIENCE SUBSTANTIAL GLYCEMIC VARIABILITY

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Objectives: Teens and young adults (YAs) with T1D have previously demonstrated inconsistent use of continuous glucose monitors (CGM). Given improved CGM performance of modern devices, we initiated an RCT to compare CGM use with BG monitoring on A1c outcomes in 14-24 year olds with T1D. We analyzed blinded CGM data collected at baseline in the trial to assess glycemic indices.

Methods: Data from 138 young persons across 14 sites in the USA were summarized. Major eligibility criteria for the RCT included ages 14≤25 yrs, T1D duration ≥1 year, no use of CGM in previous 3 months, and A1c 7.5% to <11.0% (58≤97 mmol/mol). All participants wore a blinded Dexcom G4 CGM (505 algorithm) for up to 14 days to collect at least 200 hours of CGM data.

	Percent of Time Median (IQR)	Hours or Minutes per day Median (IQR)
Time in Range 70-180 mg/dL/ 3.9-10.0 mmol/L	35% (28%, 47%)	8.5 (6.8, 11.2) hours/day
Time >180 mg/dL/ >10 mmol/L	60% (46%, 69%)	14.4 (10.9, 16.6) hours/day
Time >250 mg/dL/ >13.9 mmol/L	33% (21%, 45%)	7.9 (5.1, 10.7) hours/day
Time <70 mg/dL/ < 3.9 mmol/L	3.6% (1.7%, 7.2%)	52 (24, 103) minutes/ day
Time <54 mg/dL/ <3 mmol/L	1.0% (0.3%, 3.2%)	14 (5, 46) minutes/ day

Results: Participants (49% male) had a median age 18 yrs and median T1D duration 9 yrs; 61% were non-Hispanic white, 60% had private health insurance, 55% used insulin pumps, and 34% used CGM in the past. Median BG monitoring was 4 X/day and mean A1c was 8.9 ± 1.0% (74 ± 10.9 mmol/mol). Mean CGM glucose was 213 mg/dL(11.8 mmol/L) with median coefficient of variation (CV) 42% (IQR 37–46%). Teens/YAs spent majority of time in hyperglycemic range and <1 hour/D in hypoglycemic range (Table).

Conclusions: Given that the overwhelming majority of teens/YAs fail to achieve target A1c levels, use of CGM offers an opportunity to guide T1D management in order to increase glucose time in range and reduce glycemic variability; strategies to maximize CGM use are needed.

062

Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0324

EARLY DETECTION OF HYPOGLYCEMIA IN TYPE 1 DIABETES USING HEART RATE VARIABILITY MEASURED BY A WEARABLE DEVICE

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Objectives: People with type 1 diabetes (T1D) are at risk of severe hypoglycemia. Changes in heart rate variability(HRV) occur at the initiation of hypoglycemia due to sympathetic nervous system activity. We investigated the use of HRV detection by a wearable device as an early alert for hypoglycemia.

Research Design And Methods: Proof of principle study including 23 patients with T1D (14 women, mean age 42 ± 11 years, mean diabetes duration 26 ± 10 years). Patients were asked to wear the VitalConnect HealthPatch during five consecutive days. Hypoglycemic eventswere defined as glucose ≤70 mg/dL (≤3.9 mmol/l) by finger stick measurement and verified by continuous glucose monitoring. HRV was analyzed in standardized periods before a hypoglycemia was recorded.

Results: Sixty-six hypoglycemic events were recorded. Hypoglycemia caused a detectable increase in LF:HF and/or decrease in RMSSD in 36 (55%) of the hypoglycemic events. Eighteen hypoglycemic events (27%) showed a decrease in LF:HF or an increase in RMSSD. Ten events (15%) were unclassified. There were 2 events (3%) that clearly did not display a change in HRV. Physical activity, glucose peak level before hypoglycemia, sex, diabetes duration and rate of declining glucose level all affected the difference LF:HF in linear modeling.

Conclusion: Hypoglycemic events cause early changes in HRV that can be detected by a wearable device in patients with type 1 diabetes. Measuring real time HRV seems promising for early detection of hypoglycemic events in people with diabetes.

063

Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0334

LEVERAGING A BIG DATA SET TO DEVELOP A MACHINE LEARNING ALGORITHM TO PREDICT HYPOGLYCEMIA IN TYPE 1 DIABETES

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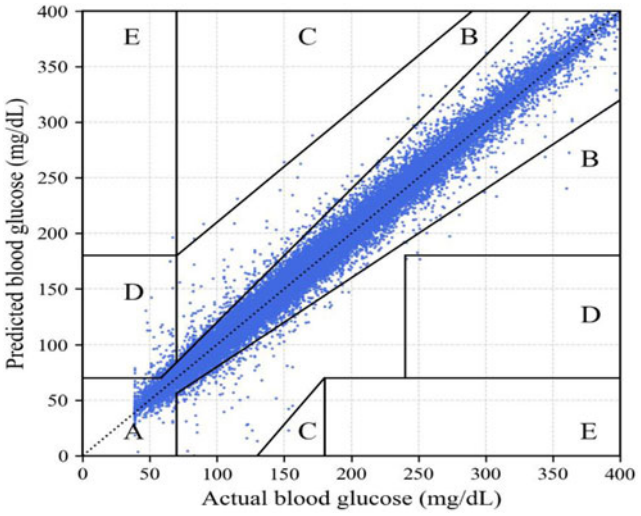
Background: We developed a machine-learning-based predictive algorithm for people with Type 1 Diabetes (T1D) that incorporates past glucose measurements and insulin doses to alert patients to hypoglycemia 30 minutes in advance.

Methods: We trained a long-short-term-memory recurrent neural network using historic continuous glucose monitoring (CGM) values and optionally insulin data to predict glucose concentrations along a 30-minute prediction horizon. We used a subset of the 4,000+ *Tidepool Big Data Donation Dataset (TBDDD)* to optimize the network. The subset of the *TBDDD* is a repository that contains information from 124 T1D data donors (age 31 ± 19 years, 15 ± 14 years since diagnosis), corresponding to 27,466 days of time-date-matched CGM and insulin dosed to people using multi-vendor CGM and pump devices.

Results: We evaluated the accuracy of the algorithm on a separate dataset collected from 10 people with T1D during a 4-week trial under free-living sensor-augmented insulin-



pump therapy (age 34 ± 6 years, 6F, 31 ± 20 hypoglycemia events). The algorithm predicted 99% of glucose values within the A region of the Clarke Error grid (RMSE = 7.55 mg/dL, MAE = 4.89 mg/dL). The algorithm predicted hypoglycemia with an accuracy of 90.87 ± 0.06% with less than 1 false positive per week, surpassing the performance reported by commercial CGM algorithms. Incorporating insulin as an extra feature into the algorithm improved accuracy by 1%, indicating that CGM alone can yield excellent prediction results (t = -2.49, p = 0.03).

Conclusions: Hypoglycemia can be accurately predicted 30 minutes in advance using machine-learning models trained on big-data sets, yielding prediction accuracy that surpasses state-of-the-art technologies when evaluated on an independent dataset.

064

Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0360

SIMPLE, MOBILE BASED ARTIFICIAL INTELLIGENCE ALGORITHM IN THE DIAGNOSIS OF DIABETIC RETINOPATHY

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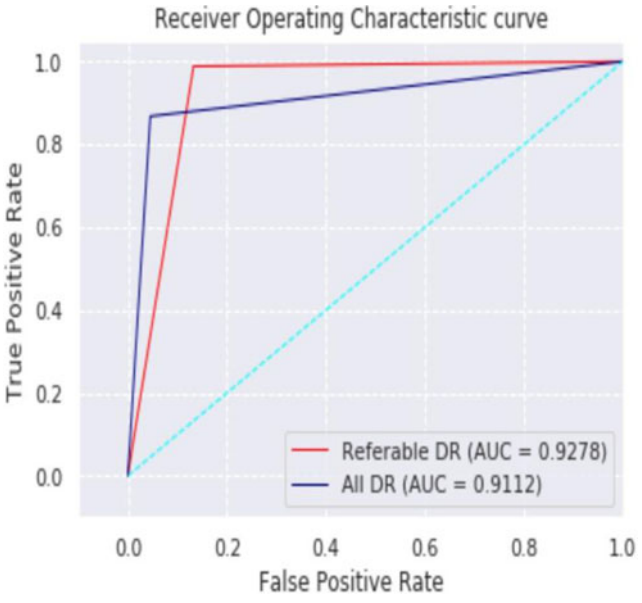
[2]Primer Academy of Medical Sciences, Medical Education, Bangalore, India
[3]Retina Institute of Medical Sciences, Ophthalmology, Bangalore, India

Background: Screening is key for early detection of diabetic retinopathy (DR). The aim of this study is to evaluate the performance of an offline artificial intelligence (AI) algorithm for the diagnosis of DR.

Methods: Dilated retinal images of 304 patients with diabetes were captured using the Remidio smart-phone based fundus camera at Diacon Hospital, Bangalore, India. The images were graded by an ophthalmologist as per the International Diabetic Retinopathy Classification System. Images [posterior pole (macula centered), nasal field and superotemporal field of each eye of each patient] were run offline on the AI software developed by Medios Technologies. The diagnosis of the AI was compared with the ophthalmologist's diagnosis.

Results: Analysis included images from 297 patients (7 clinically ungradable), of which 121 had DR. Performance (fig ROC) of the AI for referable cases of DR [moderate non-proliferative DR (NPDR) or more severe disease or the presence of diabetic macular edema (DME)] was as follows - Sensitivity 98.84% (95% CI 97.62%–100%), Specificity: 86.73% (95% CI 82.87%–90.59%). Performance of the AI for all cases of DR (mild NPDR or more severe disease or the presence of DME) was as follows - Sensitivity: 86.78% (95% CI 82.92%–90.63%), Specificity: 95.45% (95% CI 93.09%–97.82%). Sensitivity for the diagnosis of severe NPDR, proliferative diabetic retinopathy and DME was 100%.

Conclusion: The Medios AI can open up new doors to make DR screening more accessible. Larger studies are required for further validation.



065

Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0388

USING A SUPPORT VECTOR REGRESSION MODEL TO PREDICT NOCTURNAL HYPOGLYCEMIA IN PATIENTS WITH TYPE 1 DIABETES

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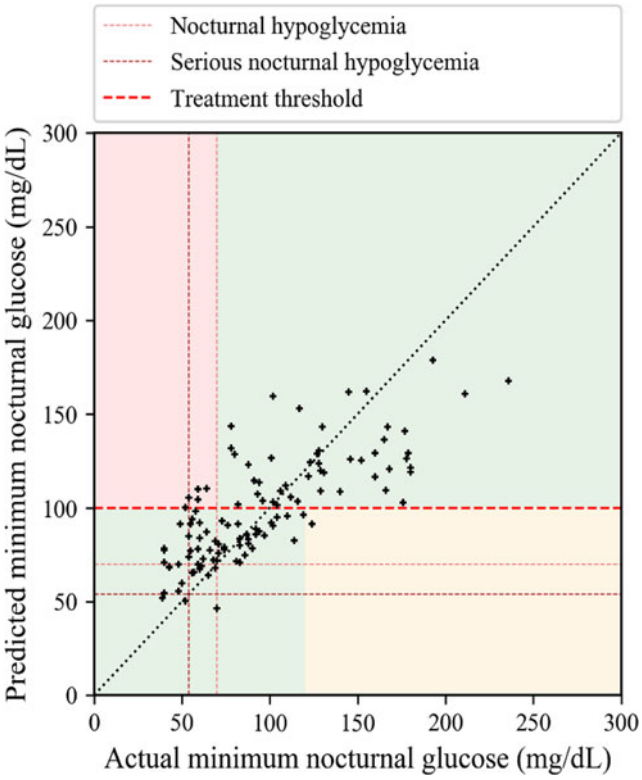
Background: We present a support vector regression (SVR) model to predict nocturnal hypoglycemia (<70 mg/dL) prior to bedtime in patients with type 1 diabetes (T1D) using continuous glucose monitoring (CGM).

Methods: We trained an SVR model to predict the minimum nocturnal glucose concentration (MNGC) using CGM-derived features. Key features included the glucose at bedtime, mean glucose computed for time frames of 1 to 15 hours before bedtime, and time in hyperglycemia (>180 mg/dL) during 6 hours prior to bedtime. Model parameters were tuned using a subset of the *Tidepool Big Data Donation Dataset* that contains over 27,000 days of CGM data from 124 T1D donors (age 31 ± 19 years, 15 ± 14 years since diagnosis).

Results: Performance was evaluated on data from 10 T1D patients collected during a 4-week trial under free-living sensor-augmented insulin-pump therapy (age 34 ± 6 years, 6F, 18 ± 10 years since diagnosis). Carbohydrates were not consumed after bedtime for 115 nights and these were considered for evaluation. The SVR model was able to predict 86.84% of nocturnal hypoglycemia events by setting a minimum predicted MNGC of 100 mg/dL. There was high correlation between the actual and predicted MNGC (R = 0.76, p < 0.01); the RMSE was 28.24 mg/dL.



Conclusions: CGM data is useful when developing a SVR model to predict nocturnal hypoglycemia using the MNGC in patients with T1D. The proposed model can be used as a decision support tool to help patients decide whether hypoglycemia treatment recommendations are given to patients before bedtime to prevent nocturnal hypoglycemia.

066

Insulin Pumps

ATTD19-0014

PREDICTORS OF AN INCREASED TIME IN RANGE IN TYPE 1 DIABETES PATIENTS ON SENSOR-AUGMENTED INSULIN PUMP WITH PREDICTIVE LOW-GLUCOSE SUSPEND FUNCTION: A REAL-WORLD DATA ANALYSIS

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Background and aims: The aim was to analyse the effect of the sensor-augmented pump with predictive low-glucose suspend function (SAP-PLGS) on the percentage of time in range 70–180 mg/dl (TIR) in sensor data in real-life clinical practice.

Table 1. Differences between patients with time in range (70-180 mg/dl) in the lowest quartile (< 59%) and with time in range (70-180 mg/dl) in the highest quartile (> 77%).

	Time in range (70-180 mg/dl)		
	Lowest quartile (< 59%) n = 40	Highest quartile (> 77%) n = 39	p
Age (years)	38 ± 15	30 ± 18	0.031
Diabetes duration (years)	23 ± 12	17 ± 12	0.029
Time on CSII before SAP-PLGS	5.5 ± 5.0	2.8 ± 4.5	0.013
HbA1c (%) before SAP-PLGS	7.7 ± 0.7	6.7 ± 0.6	0.001
Daily insulin dose (U/kg) before SAP-PLGS	0.6 ± 0.2	0.7 ± 0.2	0.035
Bolus insulin (%) before SAP-PLGS	45 ± 13	56 ± 12	0.001
Boluses before SAP-PLGS (number/day)	4.8 ± 1.9	6.3 ± 1.9	0.009
Boluses with bolus advisor before SAP-PLGS (number/day)	3.9 ± 1.8	5.5 ± 2.0	0.002
Bolus insulin during SAP-PLGS (%)	48 ± 13	58 ± 11	0.001
Sensor use during SAP-PLGS (days/week)	5.8 ± 1.0	6.3 ± 0.5	0.004
Suspension "before low" during SAP-PLGS (hours/day)	1.9 ± 1.3	3.4 ± 1.8	0.001

Material and Methods: All the type 1 diabetes patients treated with SAP-PLGS at 3 referral hospitals were evaluated. Fourteen days of data from SAP-PLGS downloads were analysed and percentage of TIR (70–180 mg/dl), time <54 mg/dl, <70 mg/dl, >180 mg/dl and >250 mg/dl were calculated.

Results: 162 patients were included, 46 children, median time on SAP-PLGS: 12 months, age: 32 ± 17 years, 62% females, diabetes duration: 19 ± 13 years, HbA1c: 7.1 ± 0.7%.

TIR was 67 ± 13%, <54 mg/dl: 0.9 ± 1.0%, <70 mg/dl: 3.4 ± 2.7%, >180 mg/dl: 30 ± 14% and >250 mg/dl: 7.4 ± 6.9%. TIR was significantly higher in children compared to adults (71 ± 11% vs. 66 ± 14%, p = 0.013) and time >180 mg/dl was significantly lower in children (26 ± 12% vs. 31 ± 15%, p = 0.011). The sensor use was 6.0 ± 0.8 days/week.

Differences between patients with TIR in the lowest quartile (<59%) and patients in the highest quartile (>77%) were estimated (Table 1). In a multivariate logistic regression analysis, the predictors of a higher TIR were a lower HbA1c before SAP-PLGS (p = 0.001), a higher percentage of bolus insulin before SAP-PLGS (p = 0.003) and a higher time in suspension ''before low'' during SAP-PLGS therapy (p = 0.001).

Conclusion: SAP-PLGS achieves an high percentage of time in range in children and adults in a real-world clinical setting. Predictors of an increased percentage of time in range could help to select the optimal candidates for the system.

067

Insulin Pumps

ATTD19-0097

GLUCOSE TIME-IN-RANGE AFTER TYPE 1 DIABETES EDUCATION IS NOT DIFFERENT BETWEEN ADULTS USING INSULIN PUMPS AND MULTIPLE DAILY INJECTIONS

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K. Kumareswaran[3,8], R. MacIsaac[1,2], R. McCallum[19], C. Sims[1], J. Speight[13,14], S. Stranks[5,6], S. Trawley[14,20], G. Ward[2,21], V. Sundararajan[1], T. Jones[10,11,12], D. O'Neal[1,2]

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[2]St Vincent's Hospital Melbourne, Department of Endocrinology & Diabetes, Melbourne, Australia
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[5]Flinders Medical Centre, Southern Adelaide Diabetes and Endocrine Services, Adelaide, Australia
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[10]Princess Margaret Hospital for Children, Department of Endocrinology and Diabetes, Perth, Australia
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Background: Insulin pumps provide greater dosing flexibility than multiple daily injections (MDI), albeit at greater expense. We compared sensor glucose levels after type 1 diabetes (T1D) education among adults with T1D using insulin pumps versus MDI.

Methods: Adults aged 25–70 years with T1D using pre-existing pump therapy or MDI (and willing to consider pump), not currently using real-time continuous glucose monitoring (CGM), were eligible. Those using MDI were given glucose meters incorporating a bolus dose calculator (Accu-Chek® Aviva Expert, Roche). All participants received diabetes and carbohydrate-counting education with insulin dosing advice, then wore masked CGM (Enlite® Sensor 3, Medtronic) for 3 weeks. The primary outcome was CGM time-in-range of 3.9–10.0 mmol/L.

Results: Ninety-two adults participated (49 women; mean ± SD age 45 ± 12 years; BMI 26.2 ± 4.5 kg/m^2; HbA_{1c} 7.8 ± 1.0% [62 ± 11 mmol/mol]). There were no significant differences in sex, age, BMI or HbA_{1c} between pump ($n = 48$) and MDI ($n = 44$) users. After T1D education, there were no significant CGM differences between pump and MDI users: time-in-range 54 ± 12% vs 53 ± 13% ($p = 0.56$); mean sensor glucose 9.6 ± 1.4 mmol/L vs 9.6 ± 1.4 mmol/L ($p = 0.99$); CGM coefficient of variation 39 ± 5% vs 40 ± 7% ($p = 0.47$); median [IQR] glucose time <3.9 mmol/L 4.2% [1.3–7.6%] vs 4.2% [2.4–7.7%] ($p = 0.45$); nor for time in any hypoglycaemic or hyperglycaemic range, or any CGM metrics during day or night only. However, a trend towards less nocturnal hypoglycaemia associated with pump therapy was observed.

Conclusions: Among adults with T1D, after T1D education and insulin dosing advice, individuals using MDI can achieve equivalent time-in-range to pump users in the absence of real-time CGM.

068

Insulin Pumps

ATTD19-0130

ULTRA RAPID LISPRO (URLI) SHOWS FASTER INSULIN ABSORPTION AND IMPROVED POSTPRANDIAL GLUCOSE LOWERING VS LISPRO DURING INSULIN PUMP USE IN PATIENTS WITH T1D

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URLi (LY900014), a novel ultra-rapid mealtime insulin in Phase 3 development, is shown to reduce postprandial glucose after subcutaneous injection. This study evaluated the pharmacokinetics and pharmacodynamics (PD) of URLi via continuous subcutaneous insulin infusion (CSII) (Medtronic 640G). In a double-blind, randomized cross-over study, 24 adult patients with T1D received URLi or lispro (Humalog®) for 3 days. Mixed meal tolerance tests (MMTT) were conducted on Days 1 & 3 after catheter insertion using a standard (1.5 U/min) single-wave bolus with the same individualized doses.

URLi showed faster insulin lispro absorption on both days compared to lispro. URLi reduced time to early half-maximal

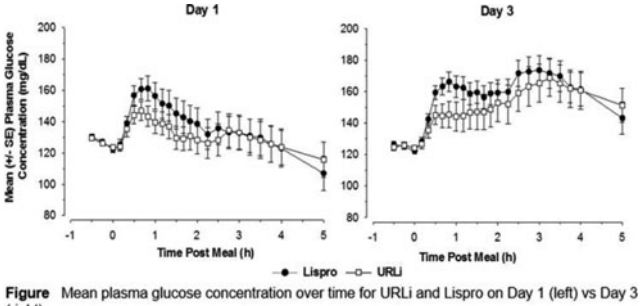

Figure Mean plasma glucose concentration over time for URLi and Lispro on Day 1 (left) vs Day 3 (right).

drug concentration by 37% (−8.5 min) and 32% (−5.3 min) compared to lispro on Days 1 and 3 (both $p < 0.0001$). Area under the insulin lispro concentration time curve (AUC) for the first 15 min was >50% higher than lispro after dosing with URLi on Days 1 and 3 ($p < 0.005$).

URLi reduced 1-hour postprandial glucose excursion during the MMTT by 45% on Day 1 (p = NS) and 47% on Day 3 ($p = 0.059$) compared with lispro (Fig). Accelerated URLi absorption was associated with trends toward lower postprandial glucose excursion for the entire MMTT (57% and 20% reductions in ΔAUC [0–5h] on Days 1 & 3; both NS). The study was not powered for PD assessment which may contribute to the lack of statistical significance.

No differences were seen in the number or severity of hypoglycemic events or local tolerability between URLi and lispro.

069

Insulin Pumps

ATTD19-0164

PRELIMINARY ANALYSIS OF THE USE OF PREDICTIVE LOW GLUCOSE MANAGEMENT ALGORITHM IN PREGNANCIES OF WOMEN WITH TYPE 1 DIABETES

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Background: Meticulous glycemic control in pregnant women with type 1 diabetes (T1D) is crucial. However, tight control exposes pregnant women to an increased risk of hypoglycemia. We studied the effects on glucose patterns in women using sensor integrated pumps with predictive low-glucose management (PLGM) algorithm.

Methods: We retrospectively analyzed anonymized data from 7 pregnant T1D women using MiniMed 640G system and followed at our Diabetes and Pregnancy Clinic between March 2017 and March 2018, who voluntarily uploaded data on the Carelink platform during each trimesters of pregnancy (tr1, tr2 and tr3).

Results: Patient compliance with CGM use increased in each trimester, from a mean of 69% of the time in tr1 to 90% in tr3. The median PLGM suspensions per patient daily was 3.3 (2.5 – 4.4). The percentage of PLGM suspensions that prevented glucose values <70 mg/dL at any time of the day was 71%, 72%, and 77% in tr1, tr2 and tr3, respectively. Effectiveness in preventing hypoglycemia was higher when the suspension was not preceded by a bolus in the previous two hours. The use of PLGM resulted in a median time spent <70 mg/dL or <55 mg/dL of 3.9% (1.2 – 4.6) and of 0.7% (0.1–1.1), respectively.

Conclusions: PLGM appears to be effective in preventing hypoglycemia and could be a useful tool to improve glucose management in pregnant women with T1D. As documented outside pregnancy, the effectiveness of PLGM is higher when hypoglycemia results from an inadequate basal rate, rather than an inadequate bolus.

070

Insulin Pumps

ATTD19-0220

EFFECT OF NATIONWIDE REIMBURSEMENT OF SENSOR-AUGMENTED PUMP THERAPY IN A PAEDIATRIC TYPE 1 DIABETES POPULATION ON HBA1C, HYPOGLYCAEMIA AND QUALITY OF LIFE: THE RESCUE-PAEDIATRICS STUDY

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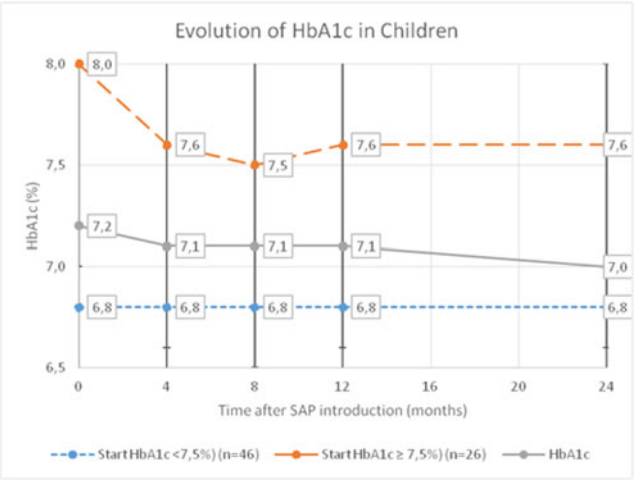
Background: Long-term real-life data of sensor-augmented pump therapy (SAP) in paediatric type 1 diabetes (T1D) patients are lacking.

Objectives: To assess the impact of SAP in a nationwide study of paediatric T1D patients on HbA1c, hypoglycaemia and quality of life until 24 months[1].

Methods: Between December 2014 and February 2017, 75 children entered Belgian reimbursement system for SAP and were followed for 12 (n = 73) and 24 months[2] (n = 25). Study endpoints included evolution of HbA1c, hypoglycaemia and quality of life[3].

Results: Seventy-three (97%) patients used SAP 12 months. Baseline HbA1c (7.2 ± 0.7%) decreased to 7.1 ± 0.8% at 4 months ($p = 0.024$), remained stable at 8 months ($p = 0.03$) and 12 months ($p = 0.15$), and decreased to 7.0 ± 0.8% at 24 months ($p = 0.55$). Patients with a baseline HbA1c<7.5% (n = 46), had a mean HbA1c of 6.8 ± 0.5% and it stayed the same after 4, 8, 12 and 24 months. Subjects with a baseline HbA1c≥7,5% (n = 26, mean HbA1c 8.0 ± 0.4%) showed improvement at 4 months (7.6 ± 0.7%; $p = 0.005$), at 8 months (7.5 ± 0.6%; $p = 0.005$) and then stabilised at 7.6 ± 0.7% at 12 ($p = 0.062$) and 24 months



(p = 0.5). Time in hypoglycaemia (<70 mg/dl) decreased from 6.6 ± 6.1% at baseline to 5.8 ± 4.1% at 12 months (p = 0.037) and to 4.5 ± 5.4% at 24 months (p = 0.009). Time in severe hypoglycaemia (<50 mg/dl) did not change over time (1 ± 2%). Overall quality of life did not change, but only total scores were evaluated.

Conclusions: Reimbursement of SAP in paediatric T1D patients improved HbA1c and decreased time in hypoglycaemia without affecting overall quality of life.

[1] RESCUE study, ClinicalTrials.gov: NCT02601729
[2] Antwerp group
[3] Impact, satisfaction, worry, parents questionnaires

071

Insulin Pumps

ATTD19-0404

640G MINIMED SYSTEM EFFECTIVENESS IN CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES: EDUCATION PLUS TECHNOLOGY ENSURE HIGHER %TIME IN TARGET RANGE (70-160 MG/DL)

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Introduction: After a long lead-in period, artificial pancreas (AP) technology is well on its way to revolutionizing the treatment of diabetes, but no AP is currently approved. Recently data about the use of a hybrid closed-loop (CL) insulin delivery has been presented. We evaluated Minimed 640Gsystem (Medtronic, CA, USA) for the comparable management of children with diabetes.

	All patients (n=62)	Compliant patients (n=39)	Non compliant patients (n=23)	P
Age (years)	11.42±3.35	11.22±3.29	11.86±3.37	0.93
Diabetes duration (years)	6.01±3.36	6.67±3.34	5.89±4.14	0.64
HbA1c baseline (%)	8.2±1.7	7.4±0.7	8.8±1.9	**0.04**
HbA1c last followup (%)	7.3±0.8	6.9±0.8	7.6±0.6	**0.03**
HbA1c <7,5% (%)	79,0	97,4	47,8	**0.001**
HbA1c <7% (%)	40,3	56,4	13,1	**0.001**
%time in target (71-160 mg/dl)	59.7	74.8	51.4	**0.02**
%time in hypo (<70 mg/dl)	3.2	2.9	3.3	0.76
%time in hyper (>161 mg/dl)	37.1	22.3	45.3	**0.01**

Methods: We prospectively analyzed data of all patients who started 640G system at Cremona Hospital after its introduction in Italian market after May 2015. Patients were evaluated according compliance (>70%) of sensor usage.

Results: After 3 yrs (range 6–36 months, mean 22.5 ± 4.8 months), 62 children and adolescents (mean age 11.42 ± 3.35 yrs, range 3–18 yrs, diabetes duration 6.01 ± 3.36 yrs, baseline HbA1c 8.2 ± 0.7%, final HbA1c 7.3 ± 1.8%, p = 0.001) used PLGM system. All patients have been instructed about the use of the system according our recommendations (Pediatr Diabetes 2017). The patients who used the system over 70% showed about 75% of time spent in target range (Table). No severe hypoglycemia or diabetic ketoacidosis events were recorded during the observation period.

Table - Clinical characteristics and time in range, in hypo and hyper in 62 pediatric patients using PLGM system

Conclusions: PLGM system, if used most of the time after a systematic educational pathway, attains results that are similar to those obtained using hybrid CL or fully AP, showing that waiting for an AP or a more performant hybrid CL system, we already have tools for the best possible care of patients with type 1 diabetes.

072

Insulin Pumps

ATTD19-0456

EFFECTIVENESS AND SAFETY OF 6-MONTH MINIMED 640G SYSTEM USE IN ADULT PATIENTS PRONE TO HYPOGLYCEMIA

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Background: Many adult patients with T1D are prone to hypoglycemia. This is the largest randomized controlled trial (RCT) to investigate the effectiveness and safety of the MiniMed™ 640G system with SmartGuard™ Suspend before low technology compared to insulin pump therapy, in decreasing hypoglycemia in hypoglycemia-prone patients.

Methods: This prospective, multi-center, RCT enrolled 169 patients (aged 24–75 years) with T1D duration ≥10 years, and HbA1c level 5.8-10.0% (40-86 mmol/mol), with impaired hypoglycemia awareness or who experienced a severe hypoglycemic event in the last 12 months. After a two-week baseline run-in, 153 eligible patients (mean±SD of 48.2 ± 12.4 years) were randomized to MiniMed™ 640G pump without continuous

	MiniMed™ 640G Pump (Control) N=77	MiniMed™ 640G System Suspend before low (Intervention) N=76	P
Hypoglycemic events per week*, N			
Run-in phase	3.81 ± 3.0	3.79 ± 3.8	0.9689
Study phase	4.13 ± 3.36	1.12 ± 1.23	<0.0001
Rate of severe hypoglycemia, per 100 pt-years	52.1	8.5	0.0036
Percentage of time spent across ranges per day			
<54 mg/dL (<3.0 mmol/L)	3.6 ± 3.5	0.7 ± 0.8	<0.0001
≤55 mg/dL (≤3.1 mmol/L)	4.2 ± 3.7	0.9 ± 0.9	<0.0001
≤70 mg/dL (≤3.9 mmol/L)	9.1 ± 6.0	2.8 ± 2.0	<0.0001
70-180 mg/dL (3.9-10.0 mmol/L)	57.8 ± 11.7	59.9 ± 11.3	0.0474
>180 mg/dL (>10 mmol/L)	33.2 ± 13.8	37.2 ± 12.1	0.0702
>240 mg/dL (>13.9 mmol/L)	13.1 ± 8.6	13.1 ± 7.1	0.9464

Sensor data are shown as mean ± standard deviation.
*Defined as sensor glucose values ≤55 mg/dL (≤3.1 mmol/L) for more than 20 consecutive minutes.

glucose monitoring or CGM (Control) or MiniMed™ 640G system with SmartGuard™ Suspend before low (Intervention), for six months. The mean number of sensor hypoglycemic events, severe hypoglycemic episodes, and overall glycemic control were evaluated for both groups.

Results: Results of the Control (N = 77, aged 47.4 ± 12.5 years) and Intervention (N = 76, aged 49.0 ± 12.2 years) therapies during the study phase are shown in the table. Mean number of sensor hypoglycemic events/week was 4.13 and 1.12 ($P < 0.0001$), respectively. The reported mean number of severe hypoglycemic episodes was 18 and 3 ($P = 0.0036$), respectively. Change in HbA1c did not differ significantly between groups ($P = 0.4439$) and no DKA event was reported during the study.

Conclusion: Six-month use of Suspend before low effectively reduced hypoglycemia in hypoglycemia-prone adults in comparison to pump therapy without CGM, with no increase in HbA1c. These results show that MiniMed™ 640G system therapy clinically benefits patients impacted by hypoglycemia exposure.

073

New Insulin Analogues

ATTD19-0192

THE ULTRA-RAPID INSULIN BIOCHAPERONE LISPRO BOLUSED BY INSULIN PUMP SHOWS FAVOURABLE PHARMACODYNAMICS AND PHARMACOKINETICS VS FASTER ASPART AND INSULIN ASPART

G. Meiffren[1], O. Klein[2], C. Seroussi[1], A. Ranson[1], J. Arrubla[2], J. Correia[1], M. Gaudier[1], O. Soula[1], R. Soula[1], B. Alluis[1], B.W. Bode[3], T. Heise[2]

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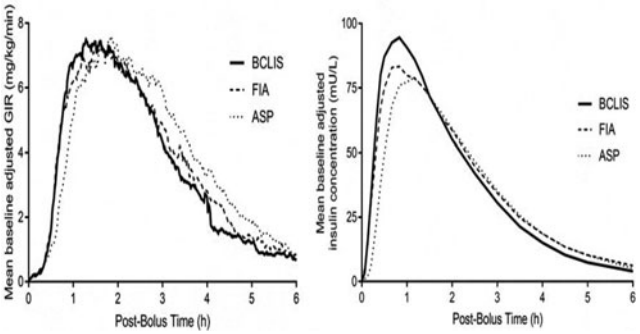
BioChaperone Lispro (BCLIS) is an ultra-rapid insulin lispro formulation designed to better mimic the physiological timing of prandial insulin action than current insulin analogs. This clinical trial is the first to investigate the pharmacodynamic and pharmacokinetic properties of the two ultra-rapid insulins BCLIS and faster aspart (FIA) and of the insulin analog aspart (ASP).

Forty-three participants with type 1 diabetes were enrolled in this phase 1, double blind, randomised, crossover clinical trial. Subjects received a 0.15 U/kg bolus dose on top of a 0.01 U/kg/h basal infusion of each insulin formulation administered with a pump under automated euglycaemic clamp conditions (blood glucose target 5.5 mmol/L). PK was assessed using a validated assay.

Figure: Mean baseline adjusted glucose infusion rate (GIR) (left) & PK (right) profiles after a subcutaneous bolus dose of BCLIS, FIA or ASP administered with an insulin pump on top of a basal infusion.



BCLIS was associated with higher early exposure (LSM AUCINS 0–1h BCLIS 64; ASP 38; FIA 56 h.mU/L, $p < 0.001$ BCLIS vs ASP; $p = 0.028$ BCLIS vs FIA) and lower late exposure (AUCINS 2–6h 67 vs. 86 vs. 82 h·mU/L, $p < 0.001$; $p = 0.002$) than ASP and FIA (figure). BCLIS demonstrated faster-on and faster-off activities than ASP characterized by a higher AUCGIR 0-2h (514 vs. 435 mg/kg, $p = 0.037$), lower AUCGIR 2-6h (615 vs 804 mg/kg, $p < 0.001$) and an earlier time to late half-maximum GIR (tlate0.5GIRmax 209 vs 232 min, $p = 0.013$). Compared to FIA, BCLIS exhibited a significantly faster-off, with a lower $AUC_{GIR\ 2–6h}$ (615 vs 704; $p = 0.049$) and an earlier tlate0.5GIRmax (209 vs 228 min, $p = 0.042$). All three formulations were well tolerated.

Administered by pump, BCLIS exhibits ultra-rapid PK and PD properties compared to ASP and favorable profiles compared to the ultra-rapid FIA formulation.

074

New Insulin Delivery Systems: Inhaled, Transderma, Implanted Devices

ATTD19-0108

ULTRA-RAPID PROFILE OF INSULIN HUMAN INHALATION POWDER MIMICS TIME-ACTION PROFILE OF PHYSIOLOGIC ABSORPTION OF GLUCOSE FROM MIXED-MEAL TOLERANCE TESTS IN TYPE 2 DIABETES

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Background: Study MKC-TI-118 compared metabolic responses to 2 insulins demonstrating distinctly different pharmacokinetic profiles. Technosphere® insulin (TI) inhalation powder undergoes ultra-rapid absorption with a correspondingly fast onset and quick rise to peak action with a short duration of effect.

Subcutaneous insulin lispro (LIS) is absorbed more slowly with a longer time to peak action and longer duration of glucose-lowering effect.

Method: Twelve patients with type 2 diabetes underwent 2 mixed-meal tolerance tests after receiving LIS 10 U (n = 12) or TI 16 or 24 U (n = 6 per dose) in random order in a cross-over design. Endogenous glucose production (EGP) rate and glucose absorption (Ra) and disposal rates (Rd) were derived from tracer data.

Results: With TI, the maximum Rd and maximum EGP suppression occurred 30-45 minutes after the start of the meal and coincided with the maximum Ra from the meal. With LIS, pharmacodynamic effects peaked after the maximum Ra. TI's better match in timing produced a much tighter control of postprandial plasma glucose (PPG) in the early postprandial period, while LIS produced early postprandial hyperglycemia (Figure). The duration of PPG control is dose dependent. At the high dose, the effect of TI ended approximately 120 minutes after dosing, but the short duration of effect suggests a small supplemental dose could be taken at that time to extend control with little risk of late postprandial hypoglycemia.

Conclusion: These studies confirm that TI, with its well-timed, insulin-mediated glucose disposal and suppression of EGP, can handle early absorption of glucose during mixed meals.

075

New Medications for Treatment of Diabetes

ATTD19-0062

NASAL GLUCAGON: A VIABLE ALTERNATIVE TO TREAT INSULIN-INDUCED HYPOGLYCEMIA IN ADULTS WITH TYPE 1 DIABETES

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Commercially available glucagon requires reconstitution and injection, while investigational nasal glucagon (NG) is a ready-to-use dry-powder spray formulation single use device for nasal administration. This randomized, 2-period, crossover study was conducted to demonstrate non-inferiority between intramuscular glucagon (IMG) and NG as treatment for insulin-induced hypoglycemia (IIH).

Hypoglycemia (plasma glucose (PG) <3.3 mmol/L) was induced by an intravenous insulin infusion. Five minutes after stopping insulin, either 3-mg NG or 1-mg IMG was administered, followed by PG measurements up to 90 min. Treatment success (TS) was defined as increases to PG ≥3.9 mmol/L or increases of ≥1.1 mmol/L from PG nadir within 30 min of receiving glucagon.

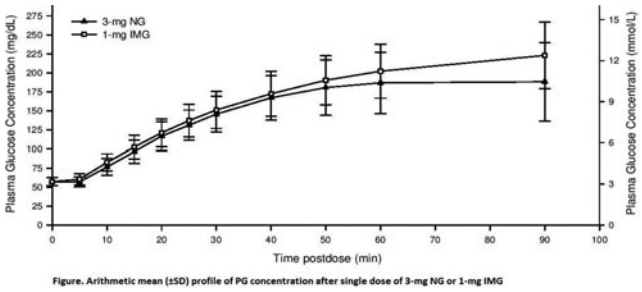

Figure. Arithmetic mean (±SD) profile of PG concentration after single dose of 3-mg NG or 1-mg IMG

The primary efficacy analysis showed all 66 patients achieved TS by 25 min with mean time to TS: 11.4 (NG) and 9.8 (IMG) min. Data demonstrated NG's non-inferiority (upper limit of 2-sided 95% CI of percentage of patients achieving TS [IMG-NG] <10%). Glucose responses were similar within 40-min post-glucagon (Figure).

Forty-eight (NG) and 51 (IMG) adverse events (AEs) were reported, mostly mild and transient, with similar frequency in both groups; AEs (≥5%): nausea (31% NG; 42% IMG), vomiting (14% NG; 17% IMG), and headache (16% NG; 10% IMG). After NG, symptoms (≥10%) from the Nasal and Non-nasal Score Questionnaire included watery eyes; nasal itching, congestion; runny nose; sneezing; redness and itchy eyes; and itchy throat.

NG was as efficacious and safe as IMG for IIH in adults, supporting its use as rescue treatment for severe hypoglycemia.

076

New Medications for Treatment of Diabetes

ATTD19-0201

BIOCHAPERONE TECHNOLOGY ENABLES THE DEVELOPMENT OF PRAMLINTIDE-PRANDIAL INSULIN COMBINATIONS

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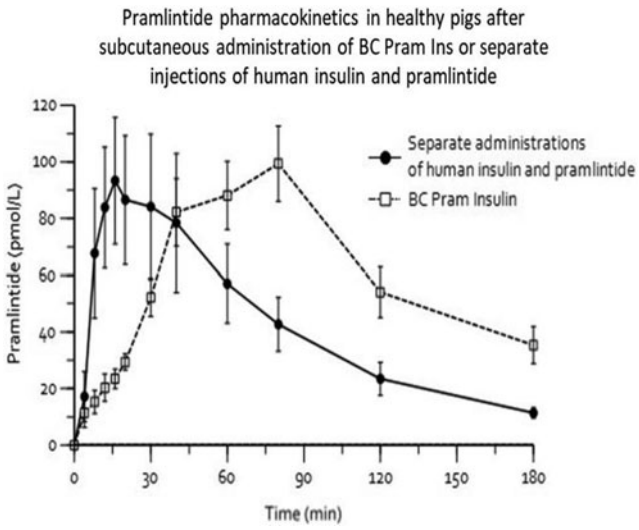
Pramlintide is the only amylin analog approved for the treatment of diabetes. It is used as an adjunct to mealtime insulin by T1D or T2D patients to achieve a better post-prandial glucose control. Pramlintide affects the rate of postprandial glucose appearance by slowing down gastric emptying, inhibiting glucagon secretion, and inducing satiety. The clinical use of pramlintide is limited as it cannot be combined in a single formulation with a prandial insulin due to pH incompatibility, resulting in a burden of additional injections which limits its acceptability by patients. In this work, BioChaperone® technology was used to develop a stable co-formulation of pramlintide and human insulin (BC Pram Ins) at neutral pH. The formulation is physically and chemically stable for at least 6 weeks at 30°C and 9 weeks at 25°C, similar to those of commercial insulin and pramlintide. Under simulated in-use pump conditions at 37°C, BC Pram Ins shows physical and chemical stability for at least 1 week, with insulin and pramlintide recoveries higher than 95%. Following a single subcutaneous administration to fasted healthy pigs, BC Pram Ins results in slower absorption of pramlintide (LSM ratio [95%CI] $\Delta AUC_{Pram0–30min}$: 0.45 [0.20; 1.05]), and a higher late exposure to pramlintide ($\Delta AUC_{Pram60-180min}$: 2.65 [1.44; 4.90]) compared to the separate injections of human insulin and pramlintide.



In conclusion, the in-vitro and preclinical pharmacokinetic properties of BC Pram Ins support its clinical development as an improved treatment compared to prandial insulins for postprandial glycemic control in patients with T1D and T2D.

077

New Medications for Treatment of Diabetes

ATTD19-0267

IMPACT OF BASELINE MEAN AMPLITUDE OF GLUCOSE EXCURSIONS ON OUTCOMES IN PATIENTS WITH TYPE 1 DIABETES TREATED WITH DAPAGLIFLOZIN IN DEPICT-1 AND 2

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Background and Aims: Dapagliflozin as adjunct to adjustable insulin reduced glucose variability and improved glycaemic control compared to placebo, in patients with type 1 diabetes (T1D) in two Phase 3 clinical trials (DEPICT-1 and 2). This post-hoc analysis assessed the correlation between mean amplitude of glucose excursions (MAGE) at baseline and change in HbA1c and MAGE after 24 weeks of treatment.

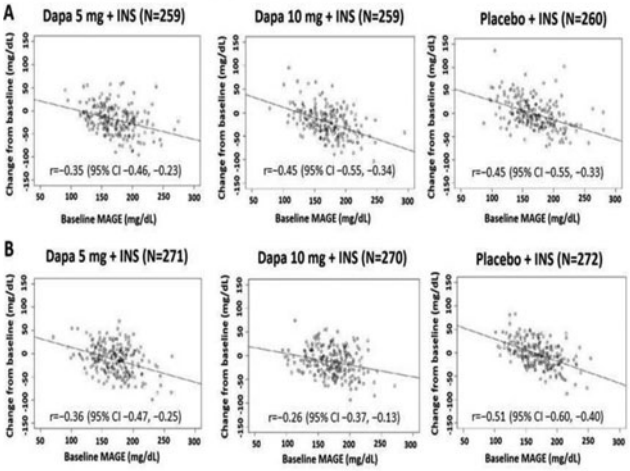
Method: In the two studies patients were randomized to dapagliflozin 5 mg, 10 mg or placebo. Interstitial glucose levels were measured using continuous glucose monitoring (CGM) and MAGE was calculated as the arithmetic mean of the differences between consecutive peaks and nadirs of glucose levels over 24 hours (provided that the differences were greater than one standard deviation of the mean glucose value). Correlation between baseline MAGE and change in HbA1c or MAGE over 24 weeks was assessed using Pearson's product-moment correlation method.

Results: The analysis included 778 patients from DEPICT-1 and 813 patients from DEPICT-2. Patients were ≥18–≤75 years old with inadequately controlled T1D (7.7 ≥ HbA1c ≤11.0%); baseline characteristics were balanced between groups. Baseline MAGE and change in HbA1c over 24 weeks showed no correlation. MAGE at baseline was correlated with change in MAGE over 24 weeks: patients with high baseline MAGE had greater reductions from baseline in MAGE at Week 24 across all treatment groups in both DEPICT-1 and 2 (Figure).

Conclusion: Patients with higher baseline MAGE showed greater improvement in glucose variability, while no correlation was seen between baseline MAGE and change in HbA1c over 24 weeks.

Support: AstraZeneca

Figure. Correlation between baseline MAGE and change in MAGE from baseline at Week 24 (A – DEPICT-1, B – DEPICT-2).



DAPA Dapagliflozin; HbA1c Glycated haemoglobin; INS Insulin; MAGE mean amplitude of glucose excursions

078

Other

ATTD19-0110

SELF-MANAGEMENT SUPPORT DELIVERED DIGITALLY AND IN-PERSON IMPROVES CLINICAL AND ECONOMIC OUTCOMES FOR PATIENTS WITH TYPE 2 DIABETES

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Objective: To demonstrate that digital self-management support for patients with type 2 diabetes can improve clinical and economic outcomes.

Method: The intervention reported on in this study, Better Choices Better Health-Diabetes (BCBH-D) service, originally developed at Stanford University, is an intensive Diabetes Self-management series of 2-hour sessions over 6 consecutive weeks facilitated by 2 specially-trained peers. Participants are exposed to content each week, create and implement action planes, complete exercises, read posted materials, and interact with others in their group. Participants receive Living a Healthy Life with

Chronic Conditions, which contains program content and chapters on a variety of chronic conditions. Subjects were recruited from of a large U.S. national health plan between 2012 and 2014

Results: 242 participants received the program in-person and 1,010 received it digitally. The key results include:

- • Decreased A1C 0.45% at 12 months
- • Decreased A1C 1.27% at 12 months (Initial A1C>9%)
- • Reduced incidence of Depression 27%
- • Improved Medication Adherence by 16%
- • Increased Exercise 43 minutes Per Week
- • Reduced all-cause healthcare utilization and costs in year post intervention
- • Decreased claims across variety of co-morbid conditions and for Emergency Department, out-patient, pharmacy and in-patient
- • Decreased healthcare utilization for comorbid conditions - minimal change for diabetes-related utilization
- • Lower costs in the year post intervention (un-adjusted)
- • Total cost savings attributed to intervention was $815 in the year post intervention*

Conclusion: BCBH-D improves clinical and economic outcomes in adults with type 2 diabetes leading to a lowering of A1C and a 3::1 Return on Investment

079

Other

ATTD19-0276

ASSOCIATIONS BETWEEN DIABETES MELLITUS, COGNITIVE IMPAIRMENT AND ALL-CAUSE MORTALITY AMONG THE POPULATION OF 55 YEARS AND OLDER

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Aim: Evaluate associations between cognitive dysfunction, diabetes mellitus (DM) and all-cause mortality among the population of 55 years and older.

Methods: This study is part of the prospective cohort survey ''Stress, aging and health'' and 1876 participants aged 55 years and older has been included. Cognitive function was assessed on the scale of Mini-Mental State Examination (MMSE), cognitive impairment was recorded for scores less than 24 on the basis of 30 points in total. Diagnosis of DM was based on levels of glycated hemoglobin ≥6,5% and/or taking medication. The mean follow-up was 9 years, 547 deaths occurred. Logistic regression model was used to determine the risk of cognitive impairment in the presence of DM. Association between cognitive impairment, diabetes mellitus and all-cause mortality was evaluated by Cox regression model.

Results: Overall, 19.2% of participants had DM, 19.1% - cognitive impairment and 5% - both of diseases. The odds ratio for cognitive impairment showed the significant linear increase in relation to the presence of DM independent of potential covariates (sex, age) [OR 1.62 (95%CI 1.21–2.16), $p = 0.001$]. The relative risk for all-cause mortality was significantly higher among individuals with both DM and cognitive impairment, after adjustment for sex and age (HR 1.57, 95%CI 1.18–2.07, $p = 0.002$) than in the case of presence only DM or cognitive impairment.

Conclusion: DM was associated with a risk of cognitive impairment among the population aged 55 years and older. The risk for all-cause mortality increased by 57% among individuals suffering from both DM and cognitive impairment.

ATTD 2019 E-Poster Discussion Abstracts

080

Artificial Pancreas

ATTD19-0134

SMALL DOSES OF DASIGLUCAGON CONSISTENTLY INCREASE PLASMA GLUCOSE (PG) LEVELS FROM HYPOGLYCEMIA AND EUGLYCEMIA IN PEOPLE WITH TYPE 1 DIABETES MELLITUS (T1DM)

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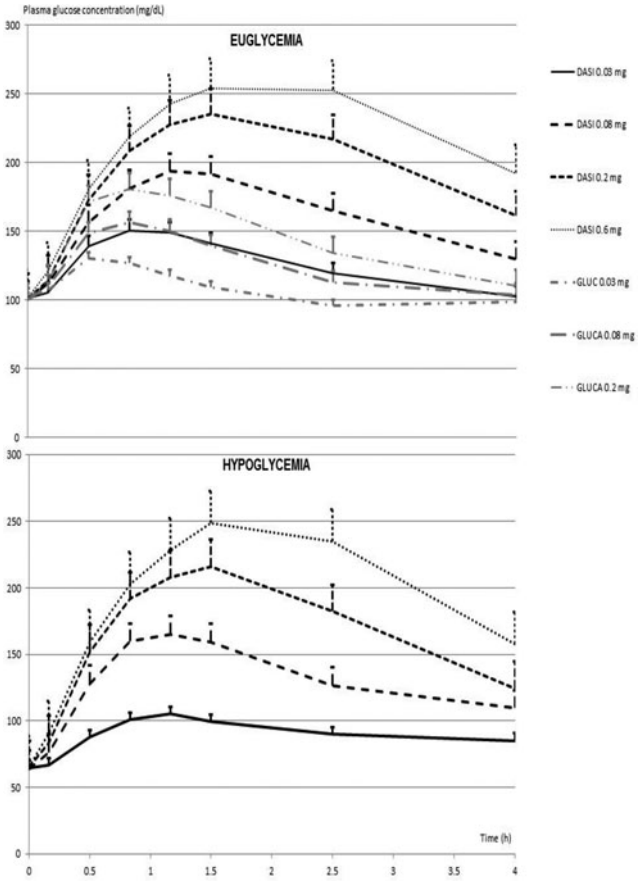
Background and Aims: Currently available glucagon formulations are of limited stability, which hinders their use in dual-hormone artificial pancreas (DHAP) systems to prevent hypoglycemia. We characterized the pharmacokinetic and pharmacodynamic properties of dasiglucagon, a novel, stable and liquid formulated glucagon analog and promising candidate for use in DHAP systems.

Method: In this randomized double-blind trial 17 patients with T1DM received four single subcutaneous doses (0.03, 0.08, 0.2 and 0.6 mg) of dasiglucagon (4 mg/ml formulation) under hypoglycemic (PG 56-66 mg/dL) or euglycemic (PG 100 mg/dL) conditions. For comparison, three doses (0.03, 0.08 and 0.2 mg) of a commercial glucagon (Glucagon, Eli Lilly) were investigated at euglycemia.

Result: Dasiglucagon showed dose-dependent and rapid PG-increases across all doses (mean increase 30 min post-dosing 24–94 mg/dl from hypoglycemia and 39–80 mg/dL from euglycemia, compared to 30–71 mg/dl with Glucagon) (figure). Median time to increase in PG by >20 mg/dL was less than 20 min (18–19.5 min) with 0.03 mg dasiglucagon and 9–15 min with higher doses (Glucagon 13–14 min). In hypoglycemia, 0.03 and 0.08 mg dasiglucagon re-established normoglycemia (PG ≥70 mg/dL) within median times of 14 and 10 min, respectively. All patients achieved a PG ≥70 mg/dL within 30 minutes post-dose at dose levels of 0.08 mg and above.

Conclusion: Dasiglucagon rapidly and effectively increases PG even in low doses and in a titratable and dose-dependent fashion from both hypoglycemia and euglycemia. The PD profile described supports dasiglucagon as a promising candidate for use in dual-hormonal closed-loop AP systems.

Different doses of dasiglucagon and Glucagon (Mean± SEM)



081

Artificial Pancreas

ATTD19-0320

EXPOSURE TO CLOSED LOOP BARRIERS USING VIRTUAL REALITY

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Background: Closed loop insulin delivery (CL) represents a major advancement in type 1 diabetes (T1D) management. Interventions are needed to increase uptake by addressing known barriers.

Methods: A 4-scenario behavioral intervention using virtual reality (VR) was developed to address most prevalent barriers

(Image 1): devices and body image, perceived hassles of using CL, de-skilling fears, and unwanted social attention. Goals of the pilot were to assess feasibility and expose patients to CL. Surveys were conducted pre and post participating in the VR experience.

Results: 20 adults with T1D completed the pilot (Table 1). Reported motion sickness was low (10.33) and not different among younger (<30) versus older (≥30) participants (p = 0.393). The average time to complete VR was 14.1 minutes (8.8-39.9). Willingness to use VR was maintained in 90% (n = 18). VR did not change expectations of CL in 95% (n = 19). VR changed perceived hassles of using CL in 25% (n = 5) with four concerned over alarms and one over connectivity issues. Positive technology attitudes, confidence in managing hypoglycemia, overall perceptions of appearance, and positive affect maintained after the intervention (Table 2). In fact, negative affect significantly decreased after exposure and perceptions of being overweight trended toward significance (Table 2).

Conclusions: The pilot showed this is a feasible and acceptable intervention that exposed persons with diabetes to CL and associated barriers, but maintained enthusiasm for use and expectations of CL.

082

Blood Glucose Monitoring and Glycemic Control in the Hospitals

ATTD19-0072

IMMEDIATE AND SUSTAINED GLYCEMIC IMPROVEMENTS DURING REMOTE PATIENT MONITORING: REAL-WORLD EVIDENCE FROM PILOT PROGRAMS

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Mobile-enabled remote patient monitoring (RPM) has the potential to improve health outcomes and access to care while also reducing hospitalizations and costs. However, whether RPM can improve glycemic outcomes in people with diabetes (PWDs) is not well understood given RPM's relative recency.

We evaluated real-world self-monitored blood glucose (SMBG) data among PWDs enrolled in RPM pilot programs across the United States. Enrolled PWDs were encouraged to sync blood glucose (BG), medication, and lifestyle information using the provided Glooko mobile app. Care teams monitored PWDs remotely and provided coaching as needed. We analyzed cross-sectional SMBG data at multiple times between enrollment (213 PWDs) and 12 months of RPM (41 PWDs).

Among PWDs providing demographic information: median age = 54 years (IQR: 46–60), 42.6% female, 86.0% type 2 diabetes. Average BG decreased over the first two months (from 11.1 mmol/L pre-RPM to 10.1 mmol/L, 9.3 mmol/L, respectively) and remained stable at six (9.4 mmol/L) and twelve months (9.0 mmol/L). Similarly, improvements were observed in the proportion of in-range and hyperglycemic SMBG readings (47.5% between 3.9-10.0 mmol/L; 23.6%> 13.9 mmol/L pre-RPM, respectively) at month 2 (63.9%; 11.4%), and sustained at 6 (65.1%; 9.7%) and 12 months (68.2%; 7.9%).

In the current study, we observe immediate and sustained improvements in glycemic outcomes during RPM. These findings, along with evolving reimbursement models and enthusiasm from healthcare systems, offer optimism for RPM. However, the full scope of RPM's value and the ability of healthcare systems to implement and scale RPM programs remain to be seen.

083

Closed-loop System and Algorithm

ATTD19-0158

GLUCOSE CONTROL IN ADULTS WITH TYPE 1 DIABETES USING A MEDTRONIC ENHANCED-HYBRID CLOSED-LOOP SYSTEM (E-HCL)

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Background: Additional refinements of closed-loop (CL) systems are required to further enhance glucose control and user acceptance among people with type 1 diabetes (T1D).

Aims: To explore Medtronic Enhanced-hybrid CL system (E-HCL) system performance and glucose control in adults with T1D.

Methods: Twelve adults with T1D and sensor-augmented pump experience (7 men; median [IQR] age 48 [39–57] years;

	Open-loop Run-In Period (1 week)	Closed-loop At-Home Period (3 weeks)	p value
Insulin delivery and settings			
Total daily insulin (units)	40.6 (32.8-59.2)	37.6 (32.4-56.1)	0.64
Insulin to carbohydrate ratio	8.8 (7.7-10.0)	8.8 (7.7-9.6)	N/A
Insulin action time (hrs)	3.0 (3.0-3.2)	3.0 (3.0-3.2)	N/A
Automated insulin delivery (%)	N/A	60.7	N/A
Continuous Glucose Monitoring Metrics			
Time 3.9-10.0mmol/L (%)	75.0 (66.6-83.7)	85.3 (79.4-88.4)	0.003
Time <3.9mmol/L (%)	3.0 (1.8-3.8)	4.4 (3.3-6.1)	0.020
Time <3.3mmol/L (%)	0.8 (0.6-1.5)	1.1 (0.7-1.7)	0.388
Time <2.8mmol/L (%)	0.3 (0.1-0.6)	0.4 (0.2-0.5)	0.844
Time >10.0mmol/L (%)	20.5 (14.8-30.6)	9.5 (7.8-15.3)	0.002
Time >13.9mmol/L (%)	2.6 (1.7-5.1)	1.2 (0.3-2.0)	0.006
Time >16.7mmol/L (%)	0.2 (0.0-0.9)	0.1 (0.0-0.3)	0.609
Mean sensor glucose (mmol/L)	8.0 (7.5-8.6)	6.8 (6.6-7.3)	0.002
Coefficient of variation	32.9 (31.0-34.9)	34.3 (31.6-36.7)	0.158
System performance			
Time in CL (%)	N/A	99.98 (98.97-100.00)	N/A
CL exits / 3 weeks (n)	N/A	1.00 (0.00-2.25)	N/A

Table 1: All data are median (IQR)

HbA1c 6.8% [6.2–7.2], 51mmol/mol [44–55]; diabetes duration 31 [13–41] years) participated. E-HCL incorporated refinements to the current generation Medtronic HCL system: enhanced bolus reminders; iterative changes broadening glucose and insulin delivery parameters permitting persistence in CL; automated correction boluses for hyperglycaemia; and non-adjunctive use of sensor glucose. Following 1-week run-in using open-loop, E-HCL was activated at the start of a 1-week supervised hotel phase, followed by 3-weeks at-home. Primary outcome was sensor glucose time-in-target range; run-in and E-HCL at-home were compared by Wilcoxon Signed-Rank Test.

Results (Table 1): E-HCL resulted in greater time-in-target range (85.3% vs. 75.0%, p = 0.003) and lower mean sensor glucose (6.8 vs. 8.0mmol/L, p = 0.002). Time spent <3.9mmol/L was greater with no difference in time <3.3mmol/L or <2.8mmol/L. There were no episodes of severe hypoglycaemia or ketoacidosis. Time spent in CL was 99.98%. Sensor mean absolute relative difference (MARD) was 11.7%. All participants reported 'very' or 'extreme' satisfaction using E-HCL.

Conclusions: In this well-controlled cohort, our findings suggest high time-in-target range, with few CL exits, positive user experience and no major safety concerns using this E-HCL iteration. Further refinements aimed at achieving full CL functionality and longer-term home-based studies are required.

084

Closed-loop System and Algorithm

ATTD19-0170

USING MULTIVARIABLE NONLINEAR MODEL PREDICTIVE CONTROL FOR A BIHORMONAL CLOSED-LOOP ARTIFICIAL PANCREAS

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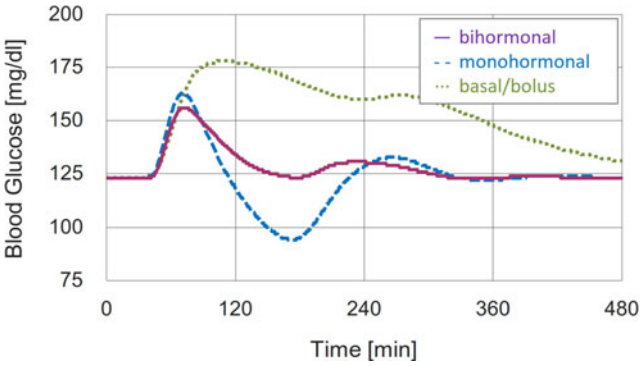
Model predictive control (MPC) is the ''forefront of current research into closed-loop systems'' (Hovorka 2011). However, none of the approaches described in the literature seems to provide a thorough solution to the following challenges: i) account for subcutaneous hormone application, ii) minimize the overall consumption of exogenous hormones (e.g. by avoiding unnecessary counteracting, or by containing BG in a sensible interval rather than forcing it to a specific equilibrium), iii) adopt a sophisticated physiological model to enable consideration of known upcoming disturbances like announced meals.

We employ the UVA/Padova T1DMS simulator (The Epsilon Group, Charlottesville, Virginia USA) to provide proof of concept for a novel multivariable nonlinear MPC algorithm. It bases upon a model similar to the latest Padova model to reconstruct the current state of the virtual patient from past measurements (moving horizon estimation) and to find the optimal control signal in order to avoid both hyper- and hypoglycemia. For both tasks, one has to define expedient cost functions that provide a mathematical formulation of the conflicting goals. The controller receives continuous BG and accepts meal announcements. While most existing bihormonal algorithms use glucagon merely as a rescue system, our controller defines both insulin and glucagon dosage at the same time and thus in a coordinated way, such that the pending effect of any already administered hormone is accounted for in the prediction.



We found the controller to exhibit highly desirable behavior in most situations; the example of a spontaneous meal is shown in the figure.

085

Closed-loop System and Algorithm

ATTD19-0225

THE DESIGN OF AN OPTIMAL MONO- OR BI-HORMONAL MEAL BOLUS DEVELOPED WITH A FULLY INTEGRATED MPC-ALGORITHM AND TESTED IN A GROUP OF VIRTUAL PATIENTS

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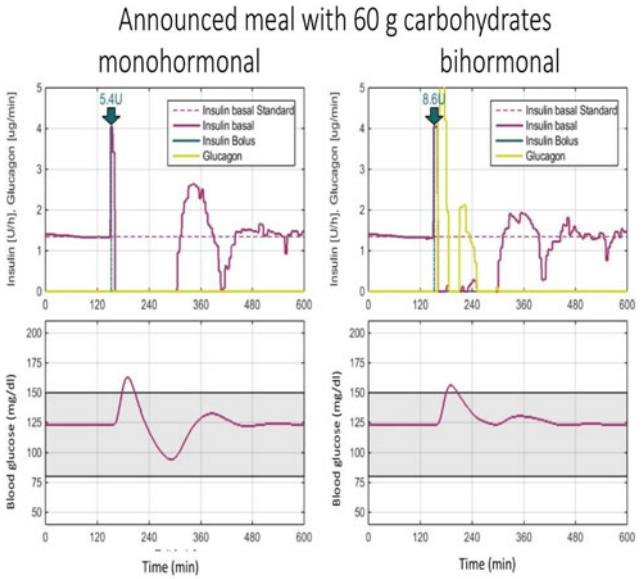
[2]*Ulm University of Applied Sciences, Department of Mechatronics and Medical Engineering, Ulm, Germany*

The optimal configuration of a meal bolus is a matter of discussion. Bi-hormonal algorithms generally prefer glucagon only as a rescue system. With our fully integrated double MPC-algorithm based on the Padova-model we assumed that also postprandial regulations and consumption of both hormones



could be improved. The UVA Padova T1DM Simulator (T1DMS) was used for standard meal situations to test how the bolus design can be optimized with this new algorithm (simultaneously published abstract). Reference was a standard basal/bolus therapy.

Results: 1. The reference demonstrated best regulation with an injection to meal interval of 30 min. 2. The algorithm regulates meals with low carbohydrate (CH) contents by up-regulation of the basal rate. 3. With higher CH contents it constructs a special bolus: the basal rate is immediately set close to zero, the bolus is applied and thereafter the basal rate recovers. 4. Very high (>60 g) CH contents are difficult to cover - here the system prefers a combination of insulin and glucagon (picture) 5. With incorrect carbohydrate estimation the updated system applies immediately after the bolus a (low) additional bolus of glucagon, which regulates the postprandial period safely. 6. The system applies insulin for unannounced meals monohormonal conservatively low whereas the bi-hormonal system is more aggressive - knowing, that the compensation with glucagon is safe.

Conclusion: Our algorithm regulates the postprandial period in this virtual setting adequately. It demonstrates bolus solutions also for standard pump applications. Low dose MPC regulated Glucagon may improve even the course of unannounced and incorrect announced meals.

086

Devices Focused on Diabetic Preventions

ATTD19-0049

SERUM IRAP, A NOVEL DIRECT BIOMARKER OF INSULIN-RESISTANCE AS A SCREENING, DIAGNOSTIC AND DRUG DISCOVERY TOOL

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Insulin resistance (IR) affects more than half of the adult population worldwide. Type 2 diabetes (T2D), which often follows, affects more than 450 million people and represents more than 10 % of the health budget in industrialized countries. A preventive public health policy is therefore urgently needed. Indeed, early management of IR does not only strongly reduce its evolution towards T2D but also strongly reduces the appearance of cardiovascular comorbidity There is however currently no simple and reliable test available for the diagnosis or screening of IR. We therefore developed an ELISA for the quantitative determination of a novel circulating biomarker of IR, IRAP. IRAP is associated with and translocated together with GLUT4 to the plasma membrane in response to insulin. Its extracellular domain is subsequently secreted in the blood stream. In T2D, IRAP translocation in response to insulin is strongly decreased.

Our patented sandwich ELISA is highly sensitive and specific, robust and very cost-effective. Results of pilot studies indicate an excellent correlation between serum IRAP levels and insulin sensitivity. We therefore believe that serum IRAP is a direct marker of insulin sensitivity and that the quantitative determination of its plasma levels should allow large-scale screening of populations at risk for IR and T2D.

Similarly, simple companion tests allowing the assessment of the efficacy of novel drugs aimed at improving insulin sensitivity do not exist yet. As such serum IRAP appears as a useful alternative to the euglycemic hyperinsulinic clamp to monitor insulin sensitivity in human in clinical trials.

087

Glucose Sensors

ATTD19-0153

HYPOGLYCEMIA AVOIDANCE AFTER ADOPTION OF A NEXT-GEN CGM SYSTEM INCLUDING A PREDICTIVE LOW GLUCOSE ALERT

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Background: New features of continuous glucose monitoring (CGM) systems may have measurable effects on usage and outcomes. The G5 and G6 CGM systems (Dexcom, Inc.) are comparably accurate and have adjustable low threshold alerts. A principal difference between the systems is that G6 introduces the ''Urgent Low Soon'' (ULS) alert, which is enabled by default and triggered when an estimated glucose value (EGV) ≤55mg/dL is predicted in the next 20 minutes. We evaluated the impact of the ULS alert by comparing data from patients who transitioned from G5 to G6.

Methods: We examined device settings and EGVs from an anonymized convenience sample of 1424 patients who used G5 and transitioned to G6 between 5/1/18 and 8/31/18. Data from users with the low threshold alert setting of 70mg/dL (n = 658) or 80mg/dL (default; n = 766) were evaluated separately. Receiver users, those who disabled the ULS alert, or those with less than 30 days of data immediately preceding or following the transition to G6 were excluded.

Results: The ULS alert remained enabled among >97% of G6 users and was triggered less than once daily (Table). Hypoglycemia (<55mg/dL and <70mg/dL) and severe hyperglycemia (>250mg/dL) decreased significantly after transitioning to G6, whether users had a low threshold alert set at 70mg/dL or 80mg/dL. Time in range improved significantly for users with a low threshold alert set at 70mg/dL, but not at 80mg/dL.

	Low Threshold Alert Set at 70 mg/dL (n=658)			Low Threshold Alert Set at 80 mg/dL (n=766)		
	G5	G6	p-value*	G5	G6	p-value*
ULS activations/day	-	0.9 (0.8)	-	-	0.6 (0.6)	-
Mean glucose (mg/dL)	165.4 (33.0)	163.0 (31.4)	0.18	174.2 (30.3)	172.2 (29.8)	0.19
Time <55 mg/dL (%)	1.1 (1.6)	0.7 (1.1)	<0.001	0.7 (1.1)	0.4 (0.9)	<0.001
Time <70 mg/dL (%)	3.7 (3.5)	3.0 (3.0)	<0.001	2.3 (2.8)	2.0 (2.5)	0.006
Time in range (70-180 mg/dL) (%)	61.1 (17.9)	63.0 (18.1)	0.05	57.5 (17.5)	58.7 (18.1)	0.18
Time >180 mg/dL (%)	35.2 (19.1)	34.0 (19.1)	0.23	40.2 (18.4)	39.4 (18.9)	0.37
Time >250 mg/dL (%)	12.6 (12.1)	11.1 (11.2)	0.02	14.4 (11.8)	13.0 (11.5)	0.02

Values reported are mean (SD).
*computed using a two-sided Welch's t-test between population means.

Conclusion: The ULS alert of the G6 CGM system may contribute to significant reductions in hypoglycemia and improved glycemic control among CGM-experienced users.

088

Glucose Sensors

ATTD19-0235

ASSESSMENT OF THE HYPOGLYCEMIC PERFORMANCE OF AN IMPLANTABLE CGM SYSTEM

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Background: A previous multi-center, prospective blinded study, PRECISE II, evaluated safety and accuracy of the new implantable Eversense CGM system in participants with type 1 or type 2 diabetes (T1D, T2D) demonstrated excellent accuracy and safety. Data were collected in a new prospective, multi-center unblinded study (PRECISION) to evaluate performance specifically in the hypoglycemic range.

Methods: PRECISION evaluated the accuracy and safety of Eversense among adults with T1D or T2D. Efficacy measures of percent of system agreement within 15 mg/dL or 15% (15/15% metric) of Yellow Springs Instrument (YSI) reference glucose measurements and MARD between paired Eversense and YSI reference measurements through 90 days for reference glucose values from 40 to 400 mg/dL were evaluated. The primary safety endpoint was incidence of device-related or sensor insertion/removal procedure-related serious adverse events (SAEs) through 90 days post-insertion.

Results: Thirty-five participants received the CGM system. Eighty-five percent (85%) of CGM values were within 15/15% of reference values over the total glucose range of 40–400 mg/dL. Hypoglycemic ranges of 40-60 and 61–80 mg/dL demonstrated 92% and 87% within 15 mg/dL and MADs of 8.1% and 8.6%, respectively. Overall MARD value against reference glucose values was 9.6% (95% CI: 8.9, 10.4). All sensors were functional through day 90 with no device- or procedure- related SAEs.

Conclusions: The PRECISION study corroborated the findings from PRECISE II of high accuracy and favorable safety of Eversense CGM system through the 90-day sensor life. In particular, strong accuracy results were achieved in the hypoglycemic ranges and all sensors lasted 90 days.

089

Glucose Sensors

ATTD19-0299

EXPANDED REAL-WORLD USE CONFIRMS STRONG ASSOCIATION BETWEEN FREQUENCY OF FLASH GLUCOSE MONITORING AND GLUCOSE CONTROL

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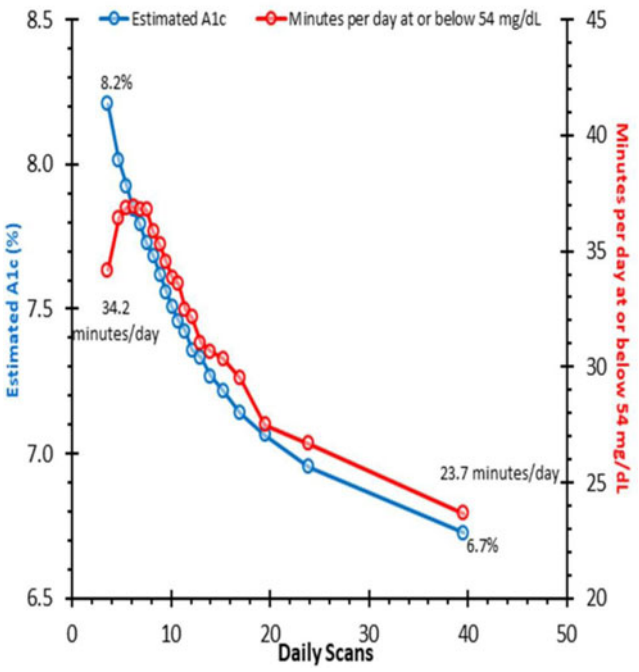
Background and Aims: With the increased availability of data with flash glucose monitoring (FreeStyle Libre™ system), we have investigated glucose testing patterns and metrics in users worldwide, expanding on previous analyses.

Methods: De-identified glucose data comprising of 470,643 readers and 4,112,626 sensors worldwide were analyzed, and 96% of the readers came from 26 countries on 6 continents with at least 2,000 readers. Scan rate per reader was determined and each reader was sorted into twenty equally-sized rank-ordered groups, categorized by scan frequency.

Results: Users performed an average of 12 scans per day (median:10, interquartile range: 7–14). The estimated HbA1c decreased from 8.2% to 6.7% (66.2 to 50.0 mmol/mol) as scan rate increased from lowest to highest scan groups (3.6 and 39.5 scans/day, respectively; $p < 0.001$). The time below 54 mg/dL decreased by 31% ($p < 0.001$), from 34.2 to 23.7 min/day. Time above 240 mg/dL decreased from 6.0 to 2.2 h/day (63%, $p < 0.001$). Time in range increased from 11.7 to 16.8 h/day (44%, $p < 0.001$). Overall, 62.9% of readers had time in range >12 hrs/day, while comparing those below and above 10 scans per day were 51.2% and 72.9%, respectively.

Figure 1. Association between frequency of flash glucose monitoring scans and glucose control measures during real-world usage (totals: 4.8 billion glucose measurements, 1.2 billion monitoring hours, 470,643 readers).



Conclusions: This expanded analysis of real-world use, confirms prior observations that higher rates of scanning to self-monitor glucose strongly associate with improved glucose measures, including decreased mean glucose and time in hyper- and hypoglycaemia as well as increased time in range.

Funded by Abbott Diabetes Care

090

Glucose Sensors

ATTD19-0311

METABOLIC BENEFITS AND DIABETES-RELATED DISTRESS WITH CONTINUOUS GLUCOSE MONITORING USE IN ELDERLY TYPE 1 AND TYPE 2 DIABETES PATIENTS USING MULTIPLE DAILY INJECTIONS OF INSULIN

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Objective: Different challenges in diabetes care arise depending on the patients' age. Understanding older adults' perceptions of technology is important to assist with introducing it to this population and maximizing the potential of devices that can improve glycaemic control and quality of life. The aim was to determine the effectiveness of continuous glucose monitoring (CGM) introduction in elderly multiple daily injections (MDI) users.

Methods: 25 participants (mean age 67 ± 6 years, HbA1c = 7.1 ± 0.7%, diabetes duration 33 ± 15 years) with type 1 (n = 14) and type 2 (n = 11) diabetes; treated by basal bolus MDI were enrolled in the study. Use of a CGM device in *blinded mode* was subsequently followed by *real-time* CGM. CGM data were analysed to determine glycaemic control parameters, diabetes-related emotional distress was measured by validated questionnaires. Differences were assessed with paired samples T-test; results were reported as mean ± SD.

Results: Significant improvements in time spent in target range (TIR = 4.4–7.2 mmol/L) (34.8 ± 14.4% vs. 42.2 ± 12.7%; $p < 0.05$) and in hypoglycaemia (TIH) (13.5 ± 12.2% vs 8.5 ± 6.3%; $p < 0.05$) as well as reduced glycaemic variability expressed by glycaemic variation (CV) (37.3 ± 11.1% vs. 32.9 ± 6.3%; $p < 0.05$) were observed. Patients expressed overall positive experience with new technology introduction, that did not add to diabetes related distress (measured by *Problem Areas in Diabetes Questionnaire*). Majority of included elderly were eager to adopt new diabetes technology.

Conclusion: Introduction of CGM use in well controlled elderly with long standing diabetes results in significant clinical benefit in glucose control (improved TIR, TIH and CV) without imposing an additional *diabetes treatment related* emotional burden.

091

Insulin Pumps

ATTD19-0057

PEDIATRIC ENDOCRINOLOGY FELLOWS' EDUCATION AND KNOWLEDGE ABOUT INSULIN PUMPS AND CONTINUOUS GLUCOSE MONITORS

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Studies show improved glycemic control in pediatric patients using insulin pumps and CGMs to manage type 1 diabetes (T1D). Despite the increasing use of these technologies, recent data show that the average A1c levels have increased in the United States.

Sixty pediatric endocrinology fellows in North America have been recruited to participate in an online educational curriculum about the use of insulin pumps and CGMs. Data reported are from a pre-test assessment. Despite consensus about the need for pediatric endocrinologists to understand these technologies, only 28% of fellows report having a formal curriculum at their institution. On a 5-point Likert scale (1: strongly disagree, 5: strongly agree), fellows report suboptimal confidence in their ability to manage patients using insulin pumps (3.4 ± 0.9) and CGMs (3.4 ± 0.9). The mean score on 20 multiple choice questions was 36 ± 10%; there were no significant differences according to year of training. Mean scores on questions addressing the following concepts were <20%: insulin on board, features of different CGM systems, infusion set selection, CGM calibration, managing insulin pump disconnections, CGM lag time.

Fellows' knowledge and education about the use of insulin pumps and CGMs for the management of T1D is suboptimal. Fellows' knowledge of these devices appears to be extrapolated from knowledge of fingerstick blood glucose monitoring and multiple daily injection therapy. An ongoing study aims to assess the impact of an online, case-based educational curriculum, Technology Knowledge Optimization in Type 1 Diabetes (TeKnO T1D), on fellows' knowledge of these technologies.

092

New Insulin Analogues

ATTD19-0157

INTRANASAL INSULIN EFFECTS COGNITION IN TYPE 2 DIABETES : A METANALYSIS

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Background: Type 2 Diabetes (T2DM) is a public health problem. T2DM can adversely affect cognition and increase dementia risk. This systematic review and metanalysis aimed to examine cognitive effect of Intranasal insulin in adults with T2DM.

Methods: A search of multiple electronic databases was conducted (e.g., Cochrane, Pubmed, Embase, Scopus) were used to locate articles written in English. The search strategy included terms for Type 2 diabetes, Adult onset Diabetes, Non Insulin dependent Diabetes, Diabetes Mellitus Type 2, Diabetes Type 2 complication etc. Articles that described intranasal insulin effect on cognition, memory or brain function were included. Two coders independently extracted data from all studies and both sought consultation services from expertise in the field of Community Medicine.).

Results: The full text of 70 studies were screened. After full text screening, four studies met all criteria. One was a protocol publication, One study was a conference abstract and two studies were randomized control trials experimental quantitative research designs. The studies demonstrated increased connectivity of hippocampus regions with regions (medial prefrontal cortex, inferior parietal cortex, posterior cingulate cortex) than those on placebo,. Functional connectivity between hippocampus and anterior cingulate cortex were associated with better Verbal Fluency Score. Intranasal Insulin modify functional connectivity among brain regions regulating memory and cognition compared to placebo.

Conclusions and Implications: Diabetes does lead to functional brain abnormalities. Intranasal insulin does lead improvement in the cognition and serves as a novel agent for Type 2 Diabetes but further research is warranted.

093

New Insulin Analogues

ATTD19-0292

THE BRIGHT RANDOMISED STUDY: SIMILAR GLYCAEMIC CONTROL AND LESS CONFIRMED HYPOGLYCAEMIA WITH GLA-300 VS IDEG-100 DURING THE INITIAL TITRATION PERIOD

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Background and Aims: BRIGHT demonstrated that insulin glargine 300 U/mL (Gla-300) was non-inferior to insulin degludec 100 U/mL (IDeg-100) for HbA_{1c} reduction, with comparable incidence and rates of hypoglycaemia over 24 weeks. This abstract focuses on the prespecified analyses of glycaemic control and hypoglycaemia during the titration period (0–12 weeks) – an important time for patients new to insulin, which may influence insulin persistence and adequate titration.

Method: This 24-week, multinational, multicentre, open-label, two-arm, parallel-group trial (NCT02738151) included insulin-naïve adults with T2DM uncontrolled on non-insulin antihyperglycaemic therapies. Participants were randomised 1:1 to Gla-300 or IDeg-100, administered once-daily during the evening, titrated to a fasting self-monitored plasma glucose (FSMPG) target of 4.4–5.6 mmol/L. Outcomes assessed included change in HbA_{1c}, FSMPG, and incidence and event rates of hypoglycaemia, during the titration, maintenance and full study periods.

Results: There was no significant difference ($p = 0.67$) between Gla-300 and IDeg-100 in HbA_{1c} change from baseline to week 12 (**Table**). Changes in FSMPG and insulin dose from baseline to week 12 (**Table**) and week 24 (data not shown) were similar with Gla-300 and IDeg-100. Gla-300 was associated with a lower incidence and event rate of confirmed hypoglycaemia (≤3.9 mmol/L) at any time (24 h), and a lower event rate at night (00:00–05:59 h), versus IDeg-100 during the initial 12-week titration period (**Table**).

Conclusion: During the initial 12 weeks of treatment in insulin-naïve people with T2DM, use of Gla-300 resulted in less anytime (24 h) hypoglycaemia than use of IDeg-100, without differences in glycaemic control.

Study sponsored by Sanofi: NCT02738151

Table: Efficacy, safety and insulin dose results for Gla-300 versus IDeg-100, during the initial 0–12 week titration period

	Gla-300	IDeg-100
Efficacy parameters (ITT population)	N=462	N=462
HbA_{1c}, %		
Baseline	8.72 ± 0.83	8.57 ± 0.80
Week 12	7.32 ± 0.83	7.23 ± 0.79
LS mean change from baseline to week 12 ± SE	−1.37 ± 0.04	−1.39 ± 0.04
LS mean difference (95% CI)	0.02 (−0.08 to 0.12)	
FSMPG, mmol/L		
Baseline	9.87 ± 2.25	9.53 ± 2.12
Week 12	6.41 ± 1.35	6.36 ± 1.36
LS mean change from baseline to week 12 ± SE	−3.26 ± 0.07	−3.25 ± 0.07
LS mean difference (95% CI)	−0.00 (−0.17 to 0.16)	
Safety parameters (safety population)	N=462	N=462
Hypoglycaemia at any time of day (24 h)		
Incidence of confirmed (≤3.9 mmol/L) or severe hypoglycaemia, n (%)	219 (47.4)	251 (54.3)
OR (95% CI)	0.74 (0.57 to 0.97) p=0.030	
Rate of confirmed (≤3.9 mmol/L) or severe hypoglycaemia, events (events/participant-year)	865 (8.08)	1120 (10.47)
RR (95% CI)	0.77 (0.62 to 0.96) p=0.023	
Nocturnal (00:00–05:59 h) hypoglycaemia		
Incidence of confirmed (≤3.9 mmol/L) or severe hypoglycaemia, n (%)	70 (15.2)	87 (18.8)
OR (95% CI)	0.77 (0.54 to 1.08) p=0.133	
Rate of confirmed (≤3.9 mmol/L) or severe hypoglycaemia, events (events/participant-year)	152 (1.42)	235 (2.20)
RR (95% CI)	0.65 (0.43 to 0.98) p=0.040	
Insulin dose, U/kg/day*		
Baseline	0.19 ± 0.04	0.12 ± 0.04
Week 12	0.48 ± 0.21	0.37 ± 0.20
LS mean change from baseline to week 12 ± SD	0.29 ± 0.20	0.26 ± 0.20

*Insulin dose was not a pre-specified endpoint and was analysed descriptively. Baseline and week 12 HbA_{1c}, FSMPG and insulin dose values are mean ± SD. p-values presented are nominal.
CI, confidence interval; ITT, intention-to-treat; LS, least-squares; OR, odds ratio; RR, rate ratio; SD, standard deviation; SE, standard error; FSMPG, fasting self-monitored plasma glucose

094

New Insulin Delivery Systems: Inhaled, Transderma, Implanted Devices

ATTD19-0338

DIABETES DURATION, BMI, AND HBA1C HAVE GREATER EFFECTS ON PULMONARY FUNCTION THAN INSULIN HUMAN INHALATION POWDER

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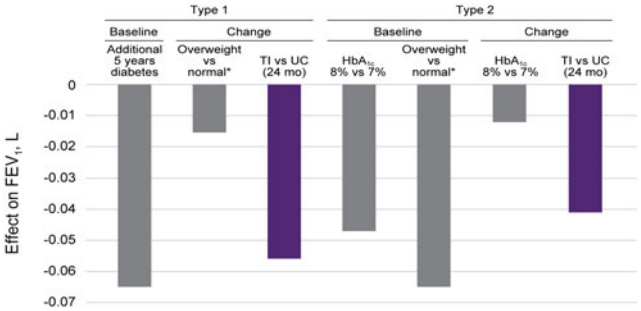
Background: Technosphere® insulin (TI), a rapidly absorbed inhaled insulin, may lead to improved patient compliance and outcomes. Small, rapidly developing, nonprogressive, and reversible decreases in pulmonary function (PF) are seen with TI treatment. However, diabetes-related factors, including BMI, duration of diabetes, and glucose control (HbA_{1c}), also affect PF.

Figure. Diabetes-related and TI-related effects on FEV_1.



BMI, body mass index; FEV_1, forced expiratory volume in 1 second; HbA_{1c}, glycosylated hemoglobin; TI, Technosphere® insulin; UC, usual care. *BMI 27.5 kg/m² vs 24.9 kg/m².

Method: To estimate contributions of these factors relative to the TI-related treatment effect, PF was correlated with baseline characteristics of patients with T1D (N = 446) and T2D (N = 1108) participating in a 2-year safety study (MKC-TI-030, NCT00308737).

Results: In the T1D cohort, diabetes duration negatively correlated with baseline FEV_1 (−13 mL/y), while BMI and HbA_{1c} were not significant factors. In the T2D cohort, both baseline BMI (−25 mL per kg/m^2) and HbA_{1c} (−47 mL per %HbA_{1c}) negatively correlated with baseline FEV_1, while duration of diabetes was not a significant factor. Over the 2-year study, mean FEV_1 decreased for patients receiving either usual care (injection therapy) or TI. Treatment with TI was associated with an additional decrease of approximately 56 mL in the T1D cohort and 41 mL in the T2D cohort. Diabetes-related factors also contributed to a decrease in FEV_1 over 2 years: baseline BMI correlated with an additional loss of 6 mL per kg/m^2 in T1D, while elevated HbA_{1c} increased the loss in FEV_1 by an additional 12 mL per %HbA_{1c} in T2D.

Conclusion: The effect of TI treatment on PF is comparable to effects due to diabetes-related factors (Figure). Unlike diabetes-related effects, however, the TI effect has been demonstrated to be reversible.

095

New Medications for Treatment of Diabetes

ATTD19-0137

ONE YEAR FOLLOW-UP OF PATIENTS WITH TYPE 1 AND TYPE 2 DIABETES TREATED WITH INSULIN GLARGINE U300 IN CLINICAL PRACTICE

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[2]University of Ulm, Institute of Epidemiology and Medical Biometry- ZIBMT, Ulm, Germany
[3]Children's Hospital, AUF DER BULT'', Diabetology- Endocrinology- Gastroenterology and Clinical Research, Hannover, Germany
[4]Klinikum Bayreuth GmbH, Clinic for Gastroenterology, Bayreuth, Germany
[5]Specialized Diabetes Practice, Medical Practice, Worms, Germany
[6]Diabetes Center Lindlar, Medical Practice, Lindlar, Germany

Background and aims: Insulin glargine U300 (Gla-300) is a new formulation of insulin glargine and is available in Germany and Austria since 2015. We investigated the clinical profile of Gla-300 in adult patients with type 1 (T1D) or type 2 diabetes (T2D) in the first year of treatment.

Methods: Adult (≥18 years) patients with T1D/T2D and treated with Gla-300 for at least 1 year included in the diabetes patient follow-up registry (DPV) or the diabetes care evaluation initiative (DIVE) were investigated. The clinical efficacy (HbA1c, BMI and total insulin dose per kg) and safety (proportion of ≥1 severe hypoglycaemia) of Gla-300 in the last six months prior to Gla-300 initiation (Q0) and in quarters 1–4 (Q1-Q4) were compared.

Results: A total of 476 patients with T1D and 1,157 patients with T2D were studied (median age 51.4 years and 65.4 years, respectively; diabetes duration 15.6 and years, respectively). During Gla-300-treatment mean HbA1c decreased from 8.0% to 7.8% in T1D and from 7.9% to 7.4% in T2D (unadj. $p < 0.001$). BMI increased in T1D (27.2 to 27.4 kg/m^2, $p = 0.039$), but did not change in T2D. Insulin dose increased in T1D (0.43 to 0.47 IU/kg, $p = 0.008$) and in T2D (0.34 to 0.37 IU/kg, $p < 0.001$). No significant difference in the proportion of ≥1 severe hypoglycaemia during Gla-300-therapy was found in T1D/T2D.

Conclusions: Results of real-world data match to those of prior randomized clinical trials and show that Gla-300 presents an effective and safe option for the treatment of patients with T1D and T2D.

Funding: Sanofi-Aventis.

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New Medications for Treatment of Diabetes

ATTD19-0198

BIOCHAPERONE GLUCAGON, A STABLE READY-TO-USE LIQUID GLUCAGON FORMULATION ENABLED BY BIOCHAPERONE TECHNOLOGY, IS WELL TOLERATED AND QUICKLY RESTORES EUGLYCEMIA AFTER INSULIN-INDUCED HYPOGLYCEMIA

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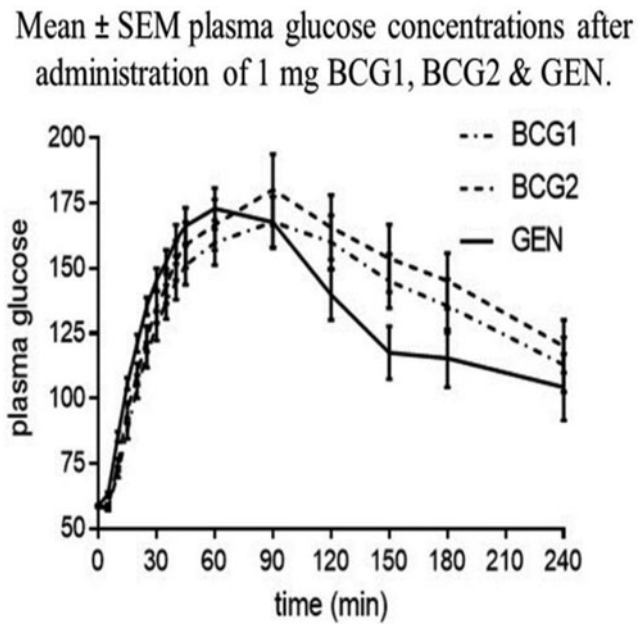
BioChaperone Glucagon (BCG) is a stable, ready-to-inject, aqueous formulation of human glucagon for hypoglycemia rescue therapy enabled by the BioChaperone technology. In this randomized, double-blind, three period, crossover phase 1 clinical trial, we investigated the safety and efficacy of two BCG formulations versus a commercially available rescue glucagon formulation (GlucaGen® HypoKit, GEN) in 27 participants with type 1 diabetes. Under hypoglycemic conditions (plasma glucose (PG) <60 mg/dL) induced by intravenous insulin infusion, participants received single subcutaneous doses of 1 mg of BCG1, BCG2 or GEN. After glucagon dosing, the intravenous infusion of insulin was maintained until the end of the 4-h procedure at a rate corresponding to 1- to 4-fold the usual basal insulin regimen of each participant. Both BCG formulations were safe and well



tolerated and the most frequent adverse event was mild nausea with all three treatments. Both BCGs quickly restored plasma glucose above 70 mg/dl after dosing (BCG1 11.5 ± 5.0 min; BCG2 10.0 ± 3.5 min; GEN 7.3 ± 1.8 min, $p < 0.001$ vs BCG1 & BCG2). Plasma glucose above 70 mg/dl was reached within 30 minutes by all but one patient with both BCGs and the mean plasma glucose increase at 15 minutes was 29 ± 17 mg/dl with BCG1, 36 ± 16 mg/dl with BCG2 and 47 ± 11 mg/dl with GEN ($p < 0.001$ vs BCG1 & BCG2). In conclusion, the BC technology allows the formulation of stable ready-to-use liquid formulations of human glucagon suited for rescue therapy of severe hypoglycemia.

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New Medications for Treatment of Diabetes

ATTD19-0286

PHASE 3 COMPARISON OF DRUG PREPARATION TIME AND THE SYMPTOMATIC RELIEF OF SEVERE HYPOGLYCEMIA IN A READY-TO-USE LIQUID GLUCAGON RESCUE PEN VERSUS GLUCAGON EMERGENCY KIT

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Objective: A novel ready-to-use stable liquid Glucagon Rescue Pen (GRP; Xeris Pharmaceuticals) auto-injector, was evaluated for relief of symptoms during rescue treatment of severe hypoglycemia.

Method: A Phase 3 randomized, controlled, single-blind, crossover clinical trial enrolled 81 adults with T1D to compare subcutaneous 1 mg doses of the GRP versus Glucagon Emergency Kit (GEK; Eli Lilly) to treat insulin-induced severe hypoglycemia. Drug preparation time by trained providers was recorded, and assessments of the overall sensation of hypoglycemia were performed at each treatment visit.

Result: Mean drug preparation time for GRP was significantly faster than GEK (27.3 ± 19.66 seconds, 97.2 ± 45.06 seconds, $p < 0.0001$). From decision to treat, subjects treated with GRP experienced significantly faster mean time to resolution of the overall feeling of hypoglycemia, compared to GEK (12.7 ± 6.45 minutes, 15.3 ± 8.01 minutes, $p = 0.02$). All subjects achieved successful plasma glucose recovery. The overall incidence of adverse events (AEs) was comparable in both groups; the most commonly reported AEs were mild to moderate nausea (GRP 36.8%, GEK 33.2%) and vomiting (GRP 26.3%, GEK 14.1%). No SAEs occurred related to GRP.

Conclusion: Prompt neurologic symptom relief is critical in the rescue from severe hypoglycemic emergencies. From decision to treat, GRP resulted in faster delivery of a full glucagon dose and achieved faster relief of the sensation of hypoglycemia during insulin-induced severe hypoglycemia. GRP achieved successful plasma glucose recovery in a reliable manner, was safe and well tolerated, and had an incidence of nausea and vomiting comparable to GEK. GRP is a viable alternative to currently available GEK.

098

New Medications for Treatment of Diabetes

ATTD19-0392

LIRAGLUTIDE-DEGLUDEC FIXED DOSE COMBINATION IMPROVES NASH/NAFLD IN PATIENTS WITH UNCONTROLLED TYPE II DIABETES MELLITUS

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Objective: Our previous studies have demonstrated that standard treatment of diabetes does not cause significant improvement in NAFLD. Therefore, the present study was conducted to evaluate the effects of Liraglutide-degludec fixed dose combination (FDC) 3.6mg/100 IU on NAFLD with elevated transaminases among patients with T2D. This combination has recently been available in our country.

Material and Methods: A total of 34 patients (male-13, female-21) with age group of 35–65 years, uncontrolled with oral anti diabetic drugs and basal insulin were included in the study. These patients had elevated transaminases and NAFLD. Liraglutide-degludec FDC was given along with other oral antidiabetic drugs and standard care. Selected clinical and demographic profile and liver fat content were recorded for all patients at both baseline and 24 weeks of treatment. The hepatic steatosis was assessed using transient elastography (Fibroscan) as CAP value and MR fat quantification. Age, BMI, diabetes duration, FPG, PPG, HbA1c, lipid profile, Microalbuminuria, RFT and LFT were also measured at baseline and every 3 months. All adverse events were recorded.

Results:

Parameters	Baseline	Week 24	Change
HbA1c (%)	8.6±0.9	7.2±0.6	-1.4%
Liver fat content (dB/m)	346.4±38.2	208.3±24	-138.1
Reversibility of transaminases	34/34	27/34	82%
Weight (kg)	84.3±8.6	79.1±6.7	-5.2

Conclusion:

1. Liraglutide-degludec FDC is effective for reducing hyperglycemia in uncontrolled diabetes
2. It also reduces hepatic steatosis and effectively cause reversal of elevated transaminases as well as weight reduction
3. We recommend liver histology study for efficacy of this FDC in NASH treatment in T2DM

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Other

ATTD19-0125

DIABETES ADVANCED NETWORK ACCESS (DANA) – CONNECTING CARE TEAMS AND TECHNOLOGY: PROVIDING AN INNOVATIVE TECHNOLOGY RESOURCE REMOVING BARRIERS TO CARE

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Background: Innovation is changing the way we manage, monitor and treat diabetes. New technologies are emerging daily and keeping up with the latest information is a challenge for any clinician.

With the rapid evolution of technology, the proliferation of patient-generated data, and the need to connect the care team with the latest technology, a resource was needed to help practitioners focus on what they do best—caring for their patients.

Methods: American Association of Diabetes Educators created an online platform that provides a central repository of diabetes technology.

In 2017, AADE surveyed members and found:

- 93% of educators interested in learning new technologies
- 91% would recommend technology to patients,
- 85% did not have a centralized resource to learn more

In response to this need, AADE developed DANA, a **robust, always-current destination where clinicians can:**

- Research and review the latest devices and mobile apps
- Access technology-focused continuing education and device training
- Participate in innovation-shaping research
- Search a repository of news and evidence-based research

Results: Launched in August 2018, DANA is changing the way educators work. A resource where members can learn about the latest technology, is assisting in the adoption and utilization of devices and apps in the clinical management of people with diabetes. Averaging 4500 users a month, it's becoming the go-to technology tool for clinicians.

Conclusion: DANA is helping clinicians lead using technology to achieve positive health outcomes. Case studies show DANA is receiving enthusiastic feedback. AADE plans to extend DANA with a robust phase II in 2019.

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Other

ATTD19-0274

PRECLINICAL VALIDATION OF A CELL ENCAPSULATION DEVICE TO TREAT TYPE 1 DIABETES

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The bioartificial pancreas MailPan® consists of a pouch made of semi-permeable membranes to encapsulate insulin-secreting cells. Membranes are designed to allow rapid diffusion of glucose, insulin, nutrients while rejecting IgG.

The selectivity of membranes was first validated *in vitro.* Safety was then assed in rats, primates and pigs. Ability of the device to prevent immunization of recipient against encapsulated cells was assessed in rats. Finally, function of the device filled with a rat beta cell line was assessed in a diabetic rat model.

Diffusion tests performed on membranes revealed a rapid passage of insulin, glucose and oxygen while no passage of IgG was observed. Implantation of MailPan® device in peritoneal cavity of 6 non-diabetic Lewis rats resulted in a transient increase of α-2-Macroglobulin (α2M) and Monocyte Chemoattractant Protein-1 (MCP-1), two weeks after implantation, then rapidly resolved. These data together with histological analyses after implantation in rat, pigs and primates showed that the device is very well accepted. Injection of allogeneic islets in the device did not result in a significant increase of plasmatic α2M and MCP-1, and no antibodies against donor Major Histocompatibility Complex were detected in the serum of recipients. In diabetic rats, MailPan® device filled with rat beta cells was able to normalize glycaemia, and restore glucose tolerance.

Taken together, these data demonstrate that MailPan® is one of the most promising solutions for cell therapy in type 1 diabetes treatment, and could also be translated to other cell therapy applications, which require an encapsulation device.

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ATTD19-0061

CONTRADICTORY C-PEPTIDE EFFECTS ON MICROVASCULAR AND MACROVASCULAR ENDOTHELIUM IN DM2

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Background: For one-stage microvessels, macrovessels assessment digital nailfold capillaroscopy with pulse tonometry were performed. Between C-peptide three grades patients with low (≤400 pmol/l-1st) normal (400–999.9-2nd) and highly-normal C-peptide (≥1000 pmol/l-3nd subgroup) levels vascular parameters in context of same glycemia were compared. Thus, 3 glycemic control groups were formed: with HbA1C<7% (N = 46), 7≤HbA1C<9% (N = 64) and HbA1C≥9% (N = 51).

Results: In HBA1C<7% C-peptide highly-normal level shows a capillaroprotective effect with arterial (p_2<0.005), venous segment expansion (p_2<0.005), capillary tortuosity decrease (p_2 = 0.02), but it has a negative effect on the arteries with endotelial dysfuntion (p_2 = 0.04), increased pulse wave velocity (p_2 = 0.05), pulse increase (P_2 = 0.03).

In 7%≤HbA1C<9% C-peptide highly-normal level reflected capillaroprotective effect with less extent then in HBA1C<7%. Capillary expansion with apex segment expansion (p_2<0.01), arterial segment expansion tendency (p = 0.06), and polymorphism (P_2 = 0.26) were revealed. Among patients of 3rd subgroup increased arterial stiffness, endothelial dysfunction, elevated BP were found.

In HbA1C≥9% C-peptide highly-normal level positive capillary effect wasn't found, on the contrary it affects negatively capillaries with tortuosity increase (p = 0.04), density decrease tendency (p = 0.5), remodeling coeffiient increase tendency (p_2 = 0.47). The negative capillary reaction to C-peptide ≥1000 pmol/l under HBA1C≥9% is probably associated with insulin resistance, glucose toxicity. Macrovascular parameters didn't differ significantly depending on C-peptide level.

Conclusion: Different reactions of microvascular and macrovascular endothelium to C-peptide highly-normal level in DM-2 were revealed: in capillaries - favorable changes in their expansion, tortuosity reduction, while in arteries - negative changes with endothelial dysfunction and increased stiffness, which may be associated with different microvascular and macrovascular endothelium insulin receptors sensitivity.

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ATTD19-0075

SOME PARAMETERS OF CARBONYL AND OXIDATIVE STRESS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND MACROANGIOPATHY OF THE LOWER EXTREMITIES

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Background and Aims: The complications are the main cause disability and mortality of patients with diabetes.Oxidative stress is considered important in the pathogenesis of vascular complications. The aim is to study of carbonyl and oxidative stress some parameters in patients with type 2 diabetes mellitus (T2DM) and macroangiopathy of the lower extremities.

Methods: 40 men with T2DM and macroangiopathy of the lower extremities, 20 men with T2DM without such complications and 30 (healthy men) - control group were involved in the study. Methods of high-performance liquid chromatography were used.

Results: The malonic dialdehyde content in the T2DM group without macroangiopathy was higher than in the control group (by 112%), and in the group with macroangiopathy of the lower extremities there was an increase by 30% in relation to the control and a decrease by 28% in relation to the group without complications. The development of macroangiopathy of the lower extremities in patients with T2DM is accompanied also by an intensification of carbonyl stress (an increase glyoxal (by 11 time) and methylglyoxal levels (by 13 times)) in relation to the control group. There were also changes in the antioxidant defense system in these patients.

Conclusion: The obtained results indicated on prevalence of carbonyl and oxidative stress in patients with type 2 diabetes with macroangiopathy of the lower extremities. The level of parameters of carbonyl and oxidative stress may be the criteria for the development of vascular complications in patients with type 2 diabetes mellitus and macroangiopathy of the lower extremities.

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ATTD19-0227

REMOTE MONITORING OF CGM DATA FOLLOWED BY TELE-CONSULTATIONS IN A PEDIATRIC TYPE 1 DIABETES POPULATION: CHOOSING THE RIGHT PATIENTS TO ACHIEVE VALUE BASED HEALTH-CARE

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Background and aims: Improvement of metabolic outcome must be balanced against the economic burden of CGM use. We wanted to characterize whether CGM use can be leveraged by tele-consultations.

Methods: CGM data from 47 T1DM patients (3–18 years) on Guardian Connect were automatically uploaded in the hospital files between April and October 2017. Bi-weekly tele-consultations were implemented. Patients were divided into a compliant group, following the insulin treatment changes, and an uncompliant group. HbA1C, time-in-hypo, days-in-hospital and QOL (DQOLY questionnaire) were measured in a cross-over study investigating 6 months before tele-consultations (T0), 3 and 6 months with tele-consultations (T1;T2), and 6 months without tele-consultations after a 6 months washout period (T3).

Results: Baseline HbA1C(±SD) for the total group was $7.7 \pm 1\%$ and did not change significantly; time-in-hypo decreased from $8 \pm 5\%$(T0) to $5 \pm 3\%$(T2) ($p = 0.002$) and increased to $6 \pm 4\%$(T3) ($p = 0.143$). HbA1C of patients with HbA1C > 7.5% at T0 decreased significantly from $8.3 \pm 0.6\%$ to $8 \pm 0.7\%$ at T1 ($p = 0.024$), to $8.1 \pm 1\%$ at T2 ($p = 0.176$) and increased to 8.3 ± 0.9 at T3 ($p = 0.495$). In compliant patients ($n = 8$) with baseline HbA1C >7.5%, HbA1C changed significantly from $8.1 \pm 0.5\%$(T0) to $7.6 \pm 0.4\%$(T1) ($p = 0.029$), $7.3 \pm 0.3\%$ at T2 ($p = 0.001$), and to $7.9 \pm 0.9\%$ at T3($p = 0.035$). Number of serious hypos in this group decreased from 9(T0) to 1(T2) and 1(T3); days-in-hospital (for diabetes) from 7(T0) to 0(T2 and T3). QOL did not change significantly.

Conclusions: A real benefit from tele-consultations in pediatric CGM patients was only seen in compliant patients with HbA1C above 7.5%. Targeted use of tele-consultations can increase the metabolic and economic benefit of CGM use.

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Advanced Medical Technologies to Be Used in Hospitals

ATTD19-0241

DEAPP – DIABETES EDUCATION APPLICATION - A NEW STRUCTURED EDUCATION PROGRAMME FOR NEWLY DIAGNOSED CHILDREN WITH TYPE 1 DIABETES

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Our programme delivers the full Type 1 Diabetes curriculum at diagnosis using a fun and exciting structured educational course via Flipped Learning. Children first learn about Type 1 Diabetes by downloading ''deapp'', an educational application, onto their own mobile devices. Following registration, patients can sequentially view the whole curriculum by watching video sessions.

The animated videos have been developed in collaboration with clinicians, product designers and educationalists, to deliver age and language appropriate content. Lesson plans cover a defined curriculum that runs alongside the application. These are matched to physical educational resources.

Diabetes health care professionals have had training on how to use the application and test patient's knowledge acquisition, thereby ensuring consistency of delivery. This process of training and education is a form of Flipped Learning. This is where the patient first learns the theoretical knowledge and is tested by the healthcare professional to check their application of that knowledge.

Since March 2017, 133 newly diagnosed patients from across ten sites have used deapp. Following completion of deapp education, these patients have been signed off as safe for discharge.

Deapp demonstrates the ability to deliver structured education to patients at diagnosis. The content is no different to previous education at diagnosis; however it is using a new mode of delivery via the Flipped Learning approach. Essential findings have shown that this education provides at least equivalent glycaemic control and patients reported measures as to previous education. Deapp is an easily accessible application that puts the fun back into learning.

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ATTD19-0484

AYTOMATIC NUTRIENT ESTIMATION FOR HOSPITALISED PATIENTS

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Background and Aims: Dietary assessment and appropriate nutrition management is of high importance for hospitalized patients, as it is associated with improved outcomes, reduced incidence of complications, and reduced length of stay. Although various approaches have been applied, they are non- or semi-automatic and rely on the expertise of the involved specialist. Scope of the present research is to introduce a fully automatic, portable system, able to real-time estimate the nutrient content of a patient's tray.

Method: The basic components of the system are: (i) an RGBD sensor, (ii) a food image analysis module based on AI, (iii) food image databases, and (iv) nutrient and recipe databases. In a typical scenario, the meal is placed on a table under the sensor before and after eating. The RGBD sensor captures colour images together with depth. Then, the captured images are automatically processed by the food image analysis module, which

Figure 1. Example of the system's output. (a) input of the colour image; (b) image result after the food image analysis – each food item is detected, segmented and recognized, while the respective volume is calculated; (c) output of the macronutrient and calorie content for each food item and the entire meal

utilizes the visual and nutritional databases to detect the food, calculate the consumed quantity and estimate the calorie and nutrient information.

Results: Preliminary results are presented in Figure 1.

Conclusion: The newly introduced and under development system shows promising results and intendsto be used for dietary assessment of hospitalized patients in an attempt to tackle malnutrition and support the nutrition management of diet-related diseases, such as diabetes, in the case of hospitalised patients.

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Artificial Pancreas

ATTD19-0039

A CONTROLLER FOR BLOOD GLUCOSE REGULATION BASED ON MODULATION OF INSULIN SENSITIVITY IN PEOPLE WITH TYPE I DIABETES

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Background: Despite new technology developed for diabetes management, glucose control remains suboptimal especially during meals. In recent years, bioelectronic medicine has shown promise for management of glucose fluctuations by controlling the insulin sensitivity (SI) through modulation of neural pathways. Within this context, in this work we present a proof-of-concept of the first closed-loop system that incorporates SI as an additional control variable for glucose regulation.

Method: The coordinated bi-hormonal bio-inspired controller (BiAP) for type 1 diabetes mellitus (T1DM) was extended by including a standard proportional-derivative (sPD) controller to determine the optimal SI from continuous blood glucose measurements. The tuning of the parameters of the resulting hybrid hormonal-insulin sensitivity glucose (InSiG) controller, and a comparison in performance with BiAP, were carried out on a virtual population of subjects with T1DM ($n=20$, 10 adults and 10 adolescents). A statistical analysis of the differences between controllers was performed using the parametric student paired t-test ($\alpha=0.01$).

Results: InSiG significantly increased the percentage of time glucose levels were within target (70–180 md/dL) to $99.4\pm1.0\%$ in adults and $96.4\pm4.6\%$ in adolescents ($p<0.01$), while not increasing hypoglycemia. In addition, the insulin and glucagon doses significantly decreased in adults and adolescents in comparison with the bi-hormonal BiAP ($p<0.01$).

Conclusions: The presented controller shows for the first time the potential of controlling glucose through modulation of SI. Moreover, these findings serve as motivation to design technology to adjust the insulin sensitivity of the people with diabetes through the nervous system, emphasising the future promise of bioelectronic medicine.

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Artificial Pancreas

ATTD19-0055

INTRAPERITONEAL AND SUBCUTANEOUS GLUCAGON DELIVERY IN PIGS: EFFECTS ON CIRCULATING GLUCAGON AND GLUCOSE LEVELS

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Glucagon has received renewed interest, and particularly in the development of a dual hormone artificial pancreas (AP). Most of the research investigates the double subcutaneous (SC) approach, i.e. both measuring glucose and delivering insulin in SC tissue. The slow dynamics of the SC tissue however, motivates for investigation of the intraperitoneal (IP) space both for glucose sensing and hormone delivery. The effect of IP glucagon delivery is poorly studied. The primary aim of this study was to compare the glucose dynamics after IP and SC glucagon delivery.

Ten anaesthetized, non-diabetic pigs (35–50 kg) were given three different glucagon boluses in randomized order. Boluses of 0.3 μg/kg and 0.6 μg/kg were given in the upper right part of the IP cavity and a bolus of 0.6 μg/kg was injected SC. In addition, 1 mg glucagon was given IP as the fourth and last bolus to test maximum glucose response. Blood samples were frequently drawn for glucose and glucagon analysis. Endogenous insulin and glucagon release were suppressed by repeated doses of somatostatin analogue.

Most of the glucagon boluses had a glucose increasing effect, but the preliminary analysis shows great variation in glucose responses:

The mean maximum effect on glucose was 1.66, 1.46 and 1.19 mmol/L for 0.6 μg/kg IP, 0.3 μg/kg IP and 0.6 μg/kg SC glucagon, respectively.

Mean time to maximum effect was 21.2, 28.8 and 15.5 min for 0.6 μg/kg IP, 0.3 μg/kg IP and 0.6 μg/kg SC, respectively.

Results of glucagon analysis, statistical analysis and further discussion will be presented.

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Artificial Pancreas

ATTD19-0111

LONG-TERM SAFETY AND TOLERABILITY OF DASIGLUCAGON, A STABLE-IN-SOLUTION GLUCAGON ANALOG

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Several groups are developing fully integrated dual-hormone artificial pancreas systems. These systems hold the potential to transform management of type 1 diabetes, but in order to be realized these systems require a stable-in-solution glucagon analog suitable for chronic use. Dasiglucagon is a novel glucagon analog stable in liquid formulation. The present studies evaluated safety and tolerability of chronically administered dasiglucagon.

Rats and dogs were dosed s.c. daily for 26 and 39 weeks, respectively, in 4 groups of 20 rats with 0 (vehicle), 0.5, 2, or 8 mg/kg/day; 4 groups of 4 beagle dogs with 0, 0.02, 0.1, or 0.3 mg/kg/day.

Chronic administration of dasiglucagon multiple times above relevant human doses was well tolerated. All findings were consistent with the known pharmacological effects of glucagon and showed full/partial recovery after 4-week, treatment-free periods. Glucose and insulin levels increased in all treated animals. In dogs, heart rate increased at 0.1 and 0.3 mg/kg/day. Liver and kidney weights increased at all dose levels in both species, and microscopic pathology demonstrated an increase in hepatocyte glycogen vacuolation and increased incidence of background lesions in the kidneys (progressive nephropathy in rats and hyaline/granular casts in dogs). Heart weights increased with no histopathological correlate.

The NOAEL (no observed adverse effect level) dose of 2 mg/kg/day in rats and 0.1 mg/kg/day in dogs represents exposure multiples (AUC) of 22 and 2 compared to anticipated human doses of up to 1 mg/day.

These findings support long-term human testing of dasiglucagon in dual-hormonal artificial pancreas systems.

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Artificial Pancreas

ATTD19-0113

A BREAKTHROUGH IN DIABETES TREATMENT REPLACING INSULIN

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Betalin Therapeutics is developing an Engineered Micro Pancreas (EMP) based on our proprietary technology of tissue-derived acellular micro-organ matrix technology, reducing or eliminating diabetes patients' dependence on insulin therapy. The United States, along with other growing countries such as China, have been affected by a dramatically increasing prevalence of diabetes. Today, the etiology of both type 1 and type 2 diabetes is thought to revolve around the dysfunction of β-cells, the insulin producing cells of the body. When β-cells are attacked either by chronic inflammation or autoimmunity, the loss of insulin production leads to increased blood glucose levels and eventually resulting in diabetes. Our product, EMP1 is a combination of a micro-organ matrix (MOM), implanted with ß cells mimicking the native human pancreatic insulin producing cell function and restoring insulin production in patients with Type 1 & 2 Diabetes Mellitus (T1D & T2D). The 3D micro-scaffold provides an essential supportive microenvironment for long-term survival and functioning of islet cells (in particular beta cells), thus ensuring long-term islet cells viability and insulin secretion. The EMP is implanted using a simple procedure, wherein the patient is provided with a local anaesthetic and the combined product is injected using a larger-gauge needle or implanted subcutaneously. The procedure, overall, does not require any more invasive surgery. Our previous results showed that EMPs are viable and secrete quantities of insulin per cell, similar to freshly isolated human islets in a glucose-regulated manner, for more than three months in vitro.

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Artificial Pancreas

ATTD19-0138

INTRAPERITONEAL INSULIN ADMINISTRATION IN PIGS: EFFECT ON CIRCULATING INSULIN AND GLUCOSE LEVELS

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Objective: Investigate different insulin boluses after intraperitoneal delivery, with respect to the dynamics of insulin level increase in blood and the effect on blood glucose level

Research design and methods: Eight anaesthetized, non-diabetic pigs (36–42.6 kg, Mean ± SD 39.5 ± 2.7) were given three different insulin boluses (2U, 5U or 10U) in the upper right part of the peritoneal cavity. The order of boluses for the last six pigs was randomized. Endogenous insulin and glucagon production were inhibited by repeated octreotide and pasireotide injections. The first pig was used to obtain information about necessary infusion rate of glucose to maintain stable glucose value throughout the experiments. The last seven pigs received a continuous glucose infusion (8 g/h). Blood samples were collected at least every 5 minutes. Exogenous and eventual detectable endogenous circulating insulin levels were measured with ELISA kits (Mercodia, Sweden). The limit of detection of the porcine insulin assay was 0.02 μg/L and of iso-insulin assay it was 0.13 μg/L.

Results: Octreotide and pasireotide had the wanted effect on insulin production, and endogenous insulin was not detectable (lower than 0.02 μg/L) during the experiments.

Decrease of blood glucose level was observed 20 minutes after all insulin boluses. Blood glucose level changed as expected: The 2U insulin bolus had the smallest blood glucose decreasing effect and the 10U insulin bolus had the largest glucose level decreasing effect.

Results of insulin analysis, statistical analysis and further discussion will be presented.

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Artificial Pancreas

ATTD19-0147

INFLUENCE OF PHYSICAL ACTIVITY (IPA): A NEW WAY TO QUANTIFY CUMULATIVE EFFECT OF SPORT ON INSULIN SENSITIVITY

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Objective: Physical activity (PA) commonly affects Compensation Ratio (CR in U/(g/L)), a surrogate of insulin sensitivity, but this effect is not quantified and disturbs the glycaemia regulation. A new variable, named Influence of Physical Activity (IPA) is proposed to explain the variability in insulin sensitivity. It should include the cumulative effect of PA.

Method: IPA is defined from PA events (3-level based intensity and duration) and, similarly to Insulin On Board, exponentially decreases with time. When possible (far from meals events), an event-specific evCR is estimated using insulin activity and glycaemia decrease. The relationship between evCR normalized by the current CGM (nCR), and corresponding IPA is studied.

Results: Diabeloop DBLG1 is an artificial pancreas designed for adults for which the closed-loop outpatient study containing Continuous Glucose Measurement (CGM), insulin infusion, meals and PA lasted 12 weeks (Id: NCT02987556). We focus on two subjects who regularly performed PA. The linear correlation between IPA and nCR for both patients was 0.54 ($p = 0.004$) and 0.62 ($p = 0.05$) respectively. This shows that the new IPA variable can significantly explain the variation of nCR.

Conclusion: In this preliminary work we have demonstrated the relevance of IPA and its correlation with nCR. Although based on a few events, this new variable IPA paves the way to quantify the impact of sustained PA on insulin sensitivity. This conclusion should be confirmed with more observations. In practice, this relationship could be used for a better diabetes management, in particular for sizing compensation bolus after PA or for hypoglycemia reduction.

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Artificial Pancreas

ATTD19-0211

DIWHY–MOTIVATIONS, BARRIERS AND RETENTION FACTORS OF DIY ARTIFICIAL PANCREAS USERS IN REAL WORLD USE

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Digital innovations in healthcare up until recently have typically followed a 'top-down' pathway, with manufacturers leading the design and production of technology-enabled solutions and patients involved only as users of the end-product. However, this is now being disrupted by the increasing influence and popularity of more 'bottom-up' and patient-led open source initiatives. A leading example is the growing movement of people with diabetes (PwD) who create their own ''do-it-yourself'' artificial pancreas systems (DIY APS) through remote-control of medical devices with an open source algorithm.

Little is known about why PwD leave traditional pathways and turn to DIY technology. This study aims to examine the motivations of current DIY APS users and to explore the barriers to, and facilitators of, building and maintaining such systems and how they might differ by socioeconomic status, ethnicity, gender and age. An online survey with 34 items will be distributed to participants recruited through the Facebook group ''Looped'' and Twitter pages of the ''DOC'' (Diabetes Online Community). Collected data will be transmitted to the REDCap database. Additionally, participants will be invited to reflect on their motivations behind DIY-looping, to share their individual patient journey, and to describe any changes they have experienced in their day-to-day lives through a series of open-ended questions.

As part of the EU-H2020 funded ''OPEN''-project, this study will provide a better understanding of the unmet needs of PwDs and current challenges to uptake, which will, in turn, facilitate dialogue and collaboration to strengthen the involvement of open source approaches in healthcare.

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Artificial Pancreas

ATTD19-0222

FUZZY CLUSTERING BASED SEASONAL STOCHASTIC LOCAL MODELING FRAMEWORK FOR GLUCOSE PREDICTION IN TYPE 1 DIABETES

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Objective: Stochastic seasonal models (SARIMA/SARIMAX) have shown improved glucose prediction compared to their non-seasonal counterparts. However, seasonal models need ''similar enough'' glycaemic responses to correctly identify their parameters. A fuzzy clustering based local modeling framework is presented to take full advantage of seasonality for improved glucose prediction.

Methods: Long-term simulated data (6 months for identification, and 6 months for validation) were generated and partitioned into a set of ''event-to-event'' time subseries, driven by meals and night period, to enforce seasonality. Identification data subset was clustered using a modified Fuzzy C-Means algorithm and a SARIMA local model was identified for each cluster. Glucose predictions were computed from weighted SARIMA local models (WLM-SARIMA) following the cluster structure. Finally, WLM-SARIMA and single model SARIMA forecasting capabilities were compared for different prediction horizons (PH) via the mean absolute percentage error (MAPE) by using validation data.

Results: SARIMA (2,0,2) $(1,0,1)_{99}$ achieved the following MAPEs (%): 4.05, 8.11, 15.23, 19.01, and 21.53 (for PH of 30, 60, 120, 180, and 240 minutes, respectively). Using the same model structure, the WLM-SARIMA approach MAPEs were significantly lower: 3.14, 6.37, 11.93, 14.10 and 15.45 ($p < 0.05$ for all PHs). WLM-SARIMA allowed to double the PH for a similar MAPE. Additionally, WLM-SARIMA MAPE showed a lower maximum MAPE and covariance than using the single SARIMA model (WLM-SARIMA 4-h PH [maximum MAPE/covariance]: 56.37 / 102.20; SARIMA 2-h PH: 81.22 / 110.73).

Conclusions: WLM-SARIMA framework improves single model SARIMA forecasting capabilities, and the longer the prediction horizon the higher the improvement.

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Artificial Pancreas

ATTD19-0233

DATA-DRIVEN ROBUST CONTROL FOR A CLOSED-LOOP ARTIFICIAL PANCREAS

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Background and Aims: Designing a fully closed-loop artificial pancreas (AP) that operates independently of meal announcements is challenging because blood glucose (BG) levels are significantly affected by unknown disturbances related to the patient behavior, namely, meals and physical activity. The purpose of this work is to study the application of data-driven models of patient behavior to account for such unknown disturbances in AP control.

Methods: We use a virtual patient based on the model of Jacobs et al. (2016), which extends the Hovorka model to account for the effect of exercise. We develop a robust model predictive controller (MPC) that derives the insulin therapy maximizing the worst-case performance with respect to so-called uncertainty sets, which capture the unknown future patient behavior. We learn uncertainty sets from data using the method of Bertsimas et al. (2018), which provides probabilistic guarantees that thus computed therapy accounts for all behaviors induced by the unknown data-generating distribution. We evaluate our data-driven robust controller in different in silico experiments, including one-day simulations with patient behavior learned from population-wide survey data (CDC NHANES).

Table 1: Comparison of the robust controller with a perfect controller (having complete information of state and future disturbances) and a non-robust variant. Reported are the time spent in hypoglycema, euglycemia, and hypoglycema, and the average minimum and maximum BG. The experiment considers meal behavior from three clusters (1-3) of the CDC NHANES database.

	t_{hypo}	t_{eugly}	t_{hyper}	$BG_{\min}$	$BG_{\max}$
1), Perfect	0%	100%	0%	6.37	8.92
1), Non-rob.	18.5%	80.97%	0.53%	2.89	9.64
1), Robust	2.02%	93.45%	4.52%	4.18	11.48
2), Perfect	0%	100%	0%	6.32	8.39
2), Non-rob.	21.59%	59.54%	18.87%	2.37	13.02
2), Robust	2.4%	94.2%	3.95%	5.16	11.02
3), Perfect	0%	100%	0%	6.3	8.55
3), Non-rob.	6.57%	61%	32.43%	3.43	14.44
3), Robust	1.11%	89.78%	9.1%	4.12	12.38

Results: In the experiments using CDC NHANES data, our data-driven insulin controller maintains, without announcements, euglycemia for 89.78% to 94.2% of the time, with 1.11% to 2.4% of the time in hypoglycemia.

Conclusions: Results show the promise of using predictive data-driven models of patient behavior to enhance AP control towards fully closed-loop insulin therapy.

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Artificial Pancreas

ATTD19-0275

COMPARISON OF PARAMETRIC LINEAR MODEL IDENTIFICATION TECHNIQUES FOR PREDICTION IN TYPE 1 DIABETES

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Objective: We considered the problem of predicting future values of glucose in Type 1 diabetes patients, exploiting information on injected insulin, carbohydrates intake and past glucose samples.

Derivation of individualized predictors is crucial to cope with the wide inter- and intra-subject variability: in this direction, we explored different parametric linear black-box identification techniques to derive patient-tailored predictors.

Research Design and Methods: Different parameterizations (i.e., ARX, ARMAX and BoxJenkins), and different automatic techniques to choose individual-specific orders (i.e., parsimony criteria, like AIC and BIC, and cross-validation) were considered. A model for each combination was identified using the mainstream technique in system identification, the Prediction Error Method, on 100 virtual subjects created using the UVA/Padova T1D Simulator.

3-hr COD	CV	AIC	BIC	p-value
ARX	41.3%	39.2%	30.0%	
ARMAX	43.3%	41.1%	38.5%	0.2
BJ	40.3%	43.8%	39.9%	
p-value		0.1		

In order to find the best model class and order selection criterion, we computed Coefficient of Determination (COD) at different prediction horizon, and compared the results using ANOVA.

Results: Similar performances were found for the 5-min prediction, both between model classes, and between order selection criteria (median COD = 99.3%, and, respectively, p-value = 0.5 and 0.3). Regarding the 3-hr prediction COD, the table below reports the median values for the different combinations, with the respective p-values.

Conclusions: No significant difference was found neither between model classes, nor between order selection criteria. However, the results suggest that we could use more complex parameterization (ARMAX or BJ) in order to model a complex system like the glucose-insulin one.

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ATTD19-0284

MODEL-BASED ASSESSMENT OF EXERCISE EFFECT ON INSULIN-INDEPENDENT AND INSULIN-DEPENDENT GLUCOSE UTILIZATION IN HEALTHY SUBJECTS

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Background and Aim: Exercise effects on whole body glucose utilization occur through insulin dependent (IDGU) and insulin independent (IIGU) mechanisms. However, accurate quantification of these processes by physiological models have not been conducted in humans.

Methods: We studied six healthy subjects (age = 28.2 ± 4.2 yr, BMI = 23.6 ± 1.0 kg/m^2) during, before and after a 60 min exercise session at 65% VO_2max on three occasions. Glucose turnover was measured with the isotope dilution clamp technique using [6,6-$^2H_2$]glucose. Visits were randomized to V_1: euglycemia-low insulin; V_2 euglycemia-high insulin and V_3: hyperglycemia-low insulin.

A battery of single-compartment kinetic models was tested, differing in the time course of exercise induced changes in model parameters: immediate vs delayed effect on IDGU and/or IIDU. Model selection was based on parsimony criteria.

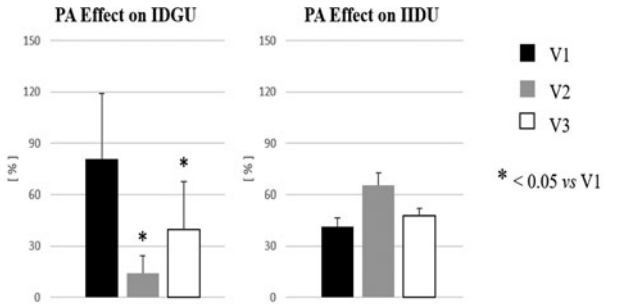

Fig. 1: Effect of physical activity on insulin-dependent (left) and -independent (right panel) glucose utilization measured as % increase from baseline.

Results: The best model assumes an exercise induced immediate effect on IIGU with a delayed effect on IDGU. The model predicted that exercise effect on IDGU was significantly higher in V1 vs. V2 or V3, while exercise effect on IIGU did not differ between visits (Figure 1).

Conclusion: Results show that, in healthy subjects, exercise acts both on IIGU and IDGU. However, while exercise effect on IIGU was independent of prevailing glucose and insulin concentrations, the action on IDGU was significantly reduced in hyperglycemic and hyperinsulinemic states.

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ATTD19-0325

THE IMPACT OF TECHNOLOGY ON INTIMACY AMONG ADULTS WITH T1D AND THEIR PARTNERS

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Background and Aims: Prior research examining relationship intimacy among persons with type 1 diabetes (PWD) typically focuses on sexual dysfunction that can occur in T1D; however, limited research examines the impact of diabetes technology on intimacy and relationships among PWD. The current study evaluated the expectations of PWD and their partners for how advances in technology may impact physical intimacy.

Methods: The INSPIRE study usedfocus groups and interviews to explore expectations for automated insulin delivery systems. The current analysis extracted data regarding the impact of technology on relationship intimacy among adults with T1D (n = 113) and their partners (n = 55).

Results: Thirty-five (30.9%) PWD and seven (12.7%) partners made references to intimacy, and two primary themes were identified: (1) vulnerability of PWD in romantic relationships and (2) challenges technology presents for physical intimacy. Participants expressed hope that new technology maydecrease vulnerability by increasing control over diabetes disclosure and lowering visibility of diabetes tasks. Participants expressed hope that regardless of new technology complexity, the systems would be small, unobtrusive, limit risk of injury during intimacy, and decrease interference during intimate moments. Surprisingly, participants also reported reduced fear about diabetes complications due to improved control.

Conclusions: PWD expressed hopes that new technology will improve relationship intimacy through flexibility in diabetes management, increased control regarding diabetes disclosure, improved technology, and smaller devices. Patient-reported outcomes should be incorporated in system development and provider discussions within clinic appointments because the impact of these systems on intimacy and relationships may influence technology uptake and continued use.

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Artificial Pancreas

ATTD19-0333

THE ROLE OF INFLAMMATION IN LIMITING EFFECTIVE CONTINUOUS SUBCUTANEOUS INSULIN INFUSION

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Background and Aims: Currently there is little known about the contribution of biological/tissue processes that leads to the loss of blood glucose regulation seen during **C**ontinuous **S**ubcutaneous **I**nsulin **I**nfusion (**CSII**). The aim of these studies is to demonstrate that inflammation at sites of insulin infusion contributes to the short lifespan of CSII *in vivo*.

Method: For these studies, we developed murine models of ''Open Loop'' (OL) CSII and a modified ''air pouch'' model (APM). The AMP allows infusion as well as lavage of cells and fluids at the CSII infusion site for subsequent analyses. The remaining air pouch tissue is analyzed by standard histopathology.

Results: Using APM and OP models our studies demonstrated that, 1) insulin excipients (diluents) induce infusion site inflammation in mice; 2) diluent induced inflammation compromised blood glucose regulation (BGR); 3) co-infusion of Humalog (insulin + diluent), saline or diluent with the addition of anti-inflammatory agents (dexamethasone or cromolyn) suppressed Humalog and diluent induced inflammation in diabetic mice as well as extended CSII to over 7 days. Additional studies using fluorescent insulin demonstrated insulin uptake by leukocyte and insulin degradation.

Conclusion: We demonstrated that insulin/diluent induces inflammation and inhibits insulin-induced regulation of blood glucose in diabetic mice. This further supports our hypothesis that one of the underlying reasons for CSII failure is the inflammatory reaction caused by insulin formulations and subcomponents. We also showed that CSII longevity is extended when mitigating the insulin induced tissue reaction using anti-inflammatory drugs.

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Artificial Pancreas

ATTD19-0337

SLOWED MEAL APPEARANCE MAY ENABLE HYBRID CLOSED LOOP SYSTEM IN TYPE 1 DIABETIC PATIENTS: IN SILICO RESULTS

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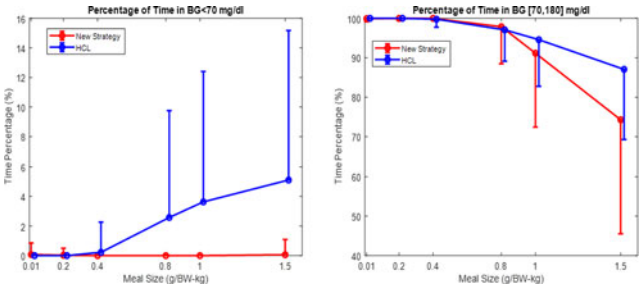
Background/objective: Several novel adjunctive treatments in type 1 diabetes (T1D) result in slowed and/or delayed postprandial glycemic rise (e.g. pramlintide, GLP1-RA, SGLT1). Their association with hybrid closed-loop (HCL) systems may free patients from carbohydrate counting, while maintaining adequate glycemic control.

Method: We combined the UVA HCL system with a new meal control module combining temporarily increased basal rate triggered by meal announcement (snack/regular/large size without carbohydrate counting) and body-weight dependent priming bolus triggered by glycemic rise. This new carbohydrate independent methodology was compared to standard HCL (using carbohydrate counting and carbohydrate:insulin ratios) using the UVA/Padova T1D simulator. Single meals of varying size were simulated in 100 virtual adults, from a variety of fasting glycemic states. Meals were slowed down to achieve half-appearance of 60min on average. Glycemic control was assessed by computing time spent between 70mg/dL and 180mg/dL and time spent below 70mg/dL over the prandial excursion.

Results: The new carbohydrate independent strategy achieved similar or better protection against hypoglycemia and similar glycemic control when compared with HCL, but for particularly large meal. For these, hypoglycemia exposure was significantly reduced, but at the cost of time spent in range; see Figure 1.



Conclusion: A new closed loop strategy, independent of prandial carbohydrates estimation, was shown in-silico to have similar performances and an improved safety profile when compared with standard HCL in case of mild prandial delays/slow down commensurate with available non-insulin adjuvants. Combining such methodology with automated meal detection and/or eating pattern recognition may enable fully automated closed loop systems.

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ATTD19-0365

COULD CLOSED-LOOP INSULIN DELIVERY BENEFIT INDIVIDUALS APPROACHING THE END OF LIFE? A CASE REPORT

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Glucose management for people with diabetes approaching the end of life can be very challenging due to variable oral intake, stress responses to severe illness and medications used for symptom relief. Healthcare professionals try to balance avoidance of symptomatic hypo- and hyperglycaemia with a minimally invasive approach to glucose monitoring and insulin administration.

During a randomised controlled trial comparing closed-loop insulin delivery with standard insulin therapy in hospitalised patients receiving enteral/parenteral nutrition, one participant required palliative care. The participant was a 79 year old female who presented following a large intracranial haemorrhage which was managed with an external ventricular drain. After obtaining consent for participation in the trial, closed-loop insulin delivery was commenced. Her clinical condition deteriorated during the study period and focus switched to palliation. Glucose control for the study period was safe with no glucose-related harm. Mean sensor glucose was 11.3 mmol/l (SD 4.3), the percentage of time in target glucose range 6–15 mmol/l was 70.5% and time in hypoglycaemia <3.9 mmol/l was 2.0%.

Closed-loop systems may provide a safer and less burdensome approach to glucose management in individuals towards the end of life. Factory-calibrated real-time continuous glucose sensors obviate the need for finger-stick glucose measurements, and insulin pump therapy is less intrusive than frequent insulin injections. Closed-loop delivers insulin in a glucose-responsive manner, accommodating highly variable day-to-day insulin requirements, and allows for personalised glucose targets. Acceptability of this technology to patients, family members and healthcare professionals needs to be determined.

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Artificial Pancreas

ATTD19-0406

CLOSED-LOOP INSULIN DELIVERY TO MANAGE INPATIENT NUTRITIONAL SUPPORT: A RANDOMISED CONTROLLED TRIAL

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Glucose management is challenging in patients requiring enteral/parenteral nutrition in hospital with frequent adjustments and interruptions of nutrition, in addition to the effects of acute illness.

Fully-automated closed-loop (CL) insulin delivery was evaluated in non-critical care patients receiving enteral/parenteral nutrition. In a randomised controlled trial, 43 patients received closed-loop (n = 21) or conventional insulin therapy with masked continuous glucose monitoring (n = 22) for up to 15 days. Study groups were comparable in age (66(14) vs. 69(10)years; CL v control), HbA1c (56(17) vs. 57(19)mmol/mol) and pre-study insulin dose (0.6(0.4) vs. 0.6(0.3)units/kg).

The proportion of time when sensor glucose was in target range 5.6-10.0mmol/l was 32.0 percentage points ($p < 0.001$; primary endpoint) greater during CL compared to control. Mean sensor glucose was 2.9mmol/l lower during CL compared to control ($p = 0.001$). CL significantly decreased time above target by 32.6 percentage points ($p < 0.001$), while the proportion of time below 3.0mmol/l was comparable between groups ($p = 0.37$). Total daily insulin and carbohydrate intake were comparable between groups (ns). No severe hypo-/hyperglycaemia with ketonaemia occurred in either group.

CL-insulin delivery is a promising tool to improve glycaemia during nutrition support in hospital.

	Closed-loop (n=21)	Control (n=22)	P
Time spent at sensor glucose level (%)			
5.6 to 10.0 mmol/l	68.4±15.4	36.4±26.6	<0.001
>10.0 mmol/l	22.2±15.7	54.8±29.7	<0.001
<5.6 mmol/l	9.3±6.3	8.7±10.3	0.82
<3.0 mmol/l	0.0 (0.0-0.2)	0.0 (0.0–0.8)	0.37
Mean sensor glucose (mmol/l)	8.5±1.2	11.4±3.4	0.001
SD sensor glucose (mmol/l)	2.3±0.8	3.4±1.4	0.003
Total daily insulin (units)	54.1 (26.5-84.5)	40.3 (28.8-52.7)	0.38

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Artificial Pancreas

ATTD19-0455

KALMAN FILTER-BASED NOVEL METHODOLOGY TO ASSESS INSULIN PUMP PRECISION FOR ARTIFICIAL PANCREAS EFFICIENCY

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Introduction: Insulin pump is nowadays one of the trendiest treatment for type 1 diabetes and is about to become artificial pancreas (AP) major component.

Insulin pump accuracy and performances are essentials and have not been so much studied so far, especially in a context of a closed-loop system. Gold-standard assessment method appears limited.

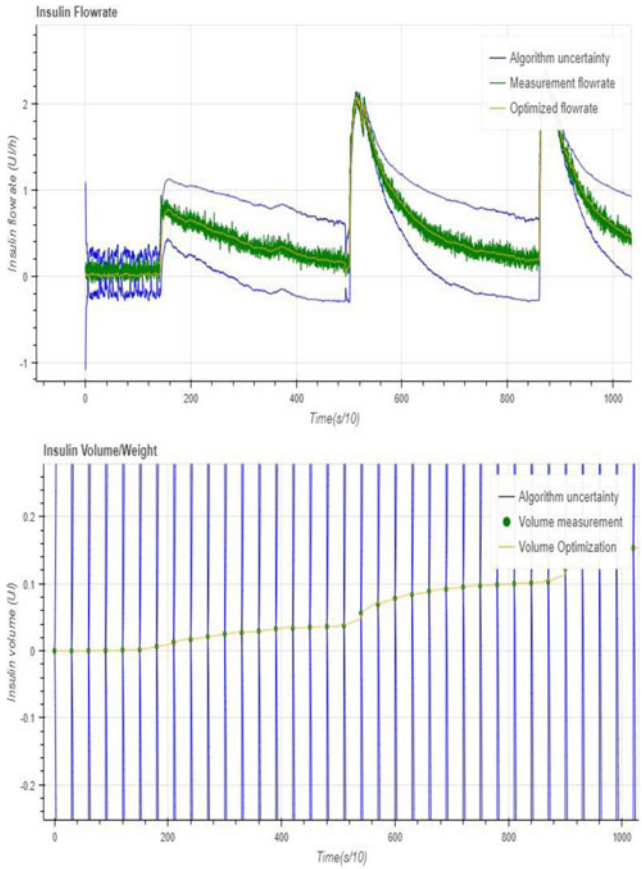
Methods: A leading edge assessment method based on a double measurement - direct mass flow meter and a micro-gravimetric bench test - combined with a bayesian-based algorithm optimizing the measurements (ie: Kalman filter) is presented here.

It advantages and performances are illustrated while assessing two insulin pumps from the market at 0.1UI/h and 0.5UI/h basal rate.

Results: The new proposed methodology offers a double reading - volume and flow rate - with a much more timewise precise measurement (from 0.03Hz to 10Hz). Direct instantaneous flow rate is displayed for the first time.

Then, measurement accuracy is considerably improved: pediatric basal rate is read with a 1.2%error for 15.3%error before.

Pumps are unequal in terms of precision, specifically for smaller basal rate:



Pump#1 (0.5UI/h): MARD = 3.2%, Pump#1(0.1UI/h): MARD = 13.3% (p = 0.02)

Pump#2 (0.5UI/h): MARD = 8.7%, Pompe#2(0.1UI/h): MARD = 23.6% (p < 10-3)

Conclusion: This innovative method to assess insulin pump administration highlights an imprecision of insulin delivery, especially for lowest basal rate as used in pediatric.

An accurate delivering error identification might feed AP control algorithm.

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Artificial Pancreas

ATTD19-0469

EDGE COMPUTING FOR PERSONALIZED ADAPTIVE ARTIFICIAL PANCREAS

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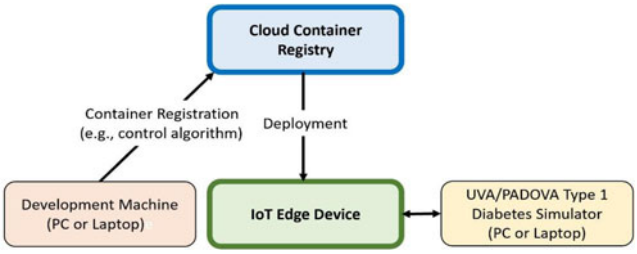
A fully automated artificial pancreas must be robust to the effects of various disturbances such as meals, exercise, stress, and sleep on blood glucose levels. Since these disturbances and the patient body may dynamically change over time, a personalized adaptive artificial pancreas approach is desired. This approach should not only adapt its control algorithm (e.g., PID or adaptive MPC) on an individual basis but also flexibly integrate other components such as meal detection, performance assessment, and fault detection as they become available. However, the adaptive and flexible nature is quite challenging to achieve using conventional embedded system approaches due to their limited capability and flexibility. IoT (Internet of Things) edge computing is a technology that has the potential to address this issue by extending the power of cloud computing to local (edge) devices such as single-board computers. Container-enabled edge computing makes it possible for local devices to deploy multiple containers from cloud repositories as often as needed. These containers can interact with each other within the device while individual container is executing a specific function such as a control algorithm. Although edge computing is cloud-enabled, edge devices can run even when they are offline or have intermittent connectivity to the cloud. Here, a proof-of-concept edge computing for personalized adaptive artificial pancreas is presented. A control algorithm wrapped within a container is pulled from the cloud to a local device and used to interact with the UVA/PADOVA Type 1 Diabetes Simulator. Critical issues such as security and reliability are also discussed.



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Blood Glucose Monitoring and Glycemic Control in the Hospitals

ATTD19-0023

REMOTE MONITORING FOR THE DIABETES MELLITUS TYPE 1 AS AN EFFECTIVE TOOL TO IMPROVE DISEASE COMPENSATION

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The aim: To evaluate the clinical and metabolic efficiency of remote monitoring of the children with diabetes mellitus type 1.

Materials and Methods: The study included 80 patients with diabetes mellitus type 1 receiving pump insulin therapy, aged 8-18 years, who were divided into 2 groups: 1 - patients with a remote monitoring and 2 - patients with the standart monitoring (40/40). The first group patients remotely transmitted data on self-monitoring, insulin therapy to the doctor for recommendations, using the program CareLink iPro-2, Guardian. Patients from the second group were visiting a doctor at their place of residence. All patients done analysis of HbA1c. Using the EasyGV calculator, the following indexes were determined: SD, CONGA, LBGI, HBGI, MAGE, M-value. The statistical processing of the results was carried out using the IBM SPSS Statistics 20.0.0 program. The significance of the differences was evaluated according to the Mann-Whitney U test. Significant differences were considered when $p < 0.05$.

Results: HbA1c had a significant decrease in the measurements in group 1 compared to group 2 ($\chi^2 = -0.450$, $p = 0.014$). Since HbA1c does not always reliably reflect the level of compensation, an analysis of the variability parameters, which was lower in group 1 than in the 2: SD ($\chi^2 = 0.022$, $p = 0.022$), CONGA ($\chi^2 = -0{,}853$, $p = 0.001$), J-index ($\chi^2 = -0.504$, $p = 0.005$), LBGI ($\chi^2 = -0{,}451$, $p = 0.014$), HBGI ($\chi^2 = -0.053$, $p = 0.003$), MAGE ($\chi^2 = -0.480$, $p = 0.008$), M value ($\chi^2 = -0.593$, $p = 0.001$).

Conclusions: Remote monitoring of patients with diabetes mellitus type 1 is an effective method of observation and leads to a decrease in the variability of glycemia and improvement of disease compensation.

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Blood Glucose Monitoring and Glycemic Control in the Hospitals

ATTD19-0026

THE PREVALENCE OF COMPLICATIONS IN TYPE 2 DIABETICS IN DIABETES CENTERS IN DUBAI.

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Background: Diabetes complications have been increasingly prevalent among type 2 diabetics during the past decades causing high rates of morbidity and mortality. Measures of the prevalence of diabetes complications will lead to preventive decisions and planning of health care.

Objective: To assess the prevalence rates of complications in Type 2 diabetics in two Diabetes Centers in Dubai.

Methodology: A cross-sectional descriptive analytical study conducted among type 2 diabetics attending diabetes centers in Dubai. Data was collected form secondary source using patient's records from two diabetes centers involved in the study. Random sampling technique was used to collect 150 patients proportionally allocated according to the total patients (4700 attending patients) available in the two diabetes centers.

Results: The study showed that the most dominant prevalence type of complications: Hyperlipidemia (84%), Neuropathy (34%), Dyslipidemia (32%),

Retinopathy (28%), Lethargy (21.3%), and Nephropathy (16.7%). The associations made between three variables each separately (Date of First Visit,

HbA1c, and Fasting Blood Glucose) with the prevalence type of complications, showed significant differences in some types: Dyslipidemia, Hyperlipidemia, Neuropathy, Retinopathy, and Joint & Bone pain.

Conclusion: There is a reasonable correlation between different variables and the prevalence of complications among the diabetic population, thus studies should always follow up on this issue in order to have clear associations to prevent complications from occurring in the first place.

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Blood Glucose Monitoring and Glycemic Control in the Hospitals

ATTD19-0030

INVESTIGATION OF TITRATION METHOD IN BASAL INSULIN THERAPY WITH VILDAGLIPTIN + METFORMIN USING CONTINUOUS GLUCOSE MONITOR: RANDOMIZED CROSSOVER STUDY

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We investigated whether previous administration of metformin or insulin in increased dose for intervention ('Insulin Increase') improves glycemic control earlier in patients treated with long-acting insulin and vildagliptin, who are hospitalized for glycemic control (PLVHG).

This study was conducted during hospitalization. Thirty patients with type 2 diabetes treated with long-acting insulin and vildagliptin 100 mg (Vildagliptin100) were randomly classified into two groups. After hospitalization, the patients' fasting plasma glucose levels were stabilized by insulin glargine 300 U/mL (Glargine300), and then they wore a continuous glucose monitoring device (FreeStyle Libre Pro) (day 1). Vildagliptin100 were continued during the research period. Group1: (a)Patients received metformin 500 mg (Metformin500) from days 3 to 7. (b)The dose of Glargine300 was increased according to an algorithm on day 5 and was then maintained [(a):metformin, (b):insulin increase. (a), next, (b):MI]. Next, metformin was washed out and the Glargine300 dose was maintained on days 8 and 9. (b)Then, Glargine300 was increased according to the algorithm on day 10 and was then maintained until day 14. (a) Patients received Metformin500 from days 12 to 14 [(b), next, (a):IM]. Group2: Vice versa.

A 15% reduction was significantly achieved earlier (mean glucose level and standard deviation [24-h, 0:00–8:00, and

	Metformin, next, insuline increase	Insuline increase, next, metformin	p1: log-rank test p2: Wilcoxon signed-rank test
A 15% reduction in the number of days (15% reduction days), n [mean glucose level (24-h)]	2.0 [1.3-2.7]	4.0 [3.4-4.6]	p_1=0.0002
15% reduction days, n [mean glucose level (0:00-8:00)]	2.0 [1.4-2.6]	4.0 [3.1-4.9]	p_1=0.0003
15% reduction days, n [mean glucose level (8:00-24:00)]	2.0 [1.5-2.5]	4.0 [3.4-4.6]	p_1<0.0001
15% reduction days, n [standard deviation (SD) (24-h)]	2.0 [1.7-2.3]	4.0 [3.1-4.9]	p_1=0.0002
15% reduction days, n [SD (0:00-8:00)]	1.0 [1.0-1.5]	3.0 [2.6-3.4]	p_1=0.004
15% reduction days, n [SD (8:00-24:00)]	1.0 [1.0-1.4]	4.0 [3.3-4.7]	p_1=0.0004
Glycemic variability percentage, % (from the day before the start of intervention until the day when a 15% decrease [mean glucose level (24-h)] is achieved)	20.9 (16.2-25.0)	19.6 (15.3-24.6)	p_2=0.5
Basal insulin dose (before increase), U/day	8.0 (6.0-19.5)	10.0 (4.5-17.5)	p_2=0.57
Basal insulin dose (after increase), U/day	11.0 (9.3-22.5)	12.5 (7.3-18.5)	p_2=0.11
Basal insulin in increased dose, U/day	2.5 (2.0-4.0)	2.5 (1.0-3.0)	p_2=0.23

The early combination use of metformin, rather than previous 'Insulin Increase', reduces glucose levels earlier without deterioration in intermediate-term glycemic variability and improves glycemic diurnal variation earlier in PLVHG.

	Vildagliptin, next, metformin increase	Metformin increase, next, vildagliptin	p1: log-rank test p2: Wilcoxon signed-rank test
A 15% reduction in the number of days (15% reduction days), n [mean glucose level (24-h)]	2.0 [1.4-2.6]	4.0 [3.2-4.8]	p_1=0.02
15% reduction days, n [mean glucose level (0:00-8:00)]	3.0 [2.0-4.0]	5.0 [4.1-5.0]	p_1=0.048
15% reduction days, n [mean glucose level (8:00-24:00)]	2.0 [1.5-2.5]	3.0 [2.1-3.9]	p_1=0.048
15% reduction days, n [standard deviation (SD) (24-h)]	1.0 [1.0-1.5]	3.0 [2.4-3.6]	p_1=0.001
15% reduction days, n [SD (0:00-8:00)]	1.0 [1.0-1.5]	4.0 [1.4-5.0]	p_1=0.003
15% reduction days, n [SD (8:00-24:00)]	1.0 [1.0-1.4]	3.0 [2.1-3.9]	p_1=0.005
Glycemic variability percentage, % (from the day before the start of intervention until the day when a 15% decrease [mean glucose level (24-h)] is achieved)	16.0 (12.6-20.8)	17.0 (14.2-21.9)	p_2=0.04

The early combination use of vildagliptin, rather than previous metformin in increased dose, reduces glucose levels and diurnal variation earlier and improves intermediate-term glycemic variability in BBIM in PHG.

8:00–24:00]) in patients on MI than in those on IM. Glycemic variability percentage wasn't significantly different between patients on MI and those on IM (table).

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Blood Glucose Monitoring and Glycemic Control in the Hospitals

ATTD19-0031

EARLY COMBINATION EFFICACY OF VILDAGLIPTIN IN BASAL-BOLUS INSULIN THERAPY WITH METFORMIN: RANDOMIZED CROSSOVER STUDY

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We investigated an early combination efficacy of vildagliptin in basal-bolus insulin therapy with metformin (BBIM) in patients hospitalized for glycemic control (PHG).

This study was conducted during hospitalization. Thirty patients with type 2 diabetes treated with basal-bolus insulin (BBI) regimens (insulin glargine 300 U/mL [Glargine300]+glulisine)+metformin 500 mg (Metformin500) were randomly classified into two groups. After hospitalization, the patients' fasting plasma glucose levels were stabilized by BBI (Glargine300 dose : total amount dose of glulisine [per day] = 2 : 3), and then they wore a continuous glucose monitoring device (FreeStyle Libre Pro) (day 1). Metformin500 and the dose and rate of BBI were maintained during the research period. Group1: (a)Patients received vildagliptin 100 mg (Vildagliptin100) from days 3 to 7. (b)The dose of metformin (Dmetformin) was increased (500 → 1000 mg) from days 5 to 7 [(a):vildagliptin, (b):metformin increase. (a), next, (b):VM]. Next, vildagliptin was washed out and Dmetformin was decreased (1000 → 500 mg) on days 8 and 9. (b)Then, Dmetformin was increased (500 → 1000 mg) from days 10 to 14. (a)Patients received Vildagliptin100 from days 12 to 14 [(b), Next, (a):IM]. Group2: Vice versa.

A 15% reduction was significantly achieved earlier (mean glucose level and standard deviation [24-h, 0:00–8:00, and 8:00–24:00]) in patients on VM than in those on MV. Glycemic variability percentage was significantly lower in patients on VM than in those on MV.

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Blood Glucose Monitoring and Glycemic Control in the Hospitals

ATTD19-0034

THE ASSOCIATION OF HYPOGLYCEMIA WITH ENDOCRINE PATHOLOGY

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Background: Hypoglycemia is one of the most common metabolic problems in neonatal medicine. The most frequent causes of hypoglycemia in neonatal intensive care units are related to non- endocrine factors. Stress, prematurity and infections

are some examples. Endocrinology causes such as neonatal hyperinsulinemia and panhypopituiarism are not as common.

Aim: To review the association between neonatal hypoglycemia and endocrine pathology.

Method: A retrospective review of billing report from one high volume, University-based neonatal intensive care unit (NICU) from January 2016 through December 2016 was conducted. Billing reports were analyzed using ICD 10 codes for hypoglycemia or neonatal hypoglycemia as a primary diagnosis and its association with hyperinsulinism, adrenal insufficiency, growth hormone deficiency and hypopituitarism as a co-diagnoses.

Result: Out of a total of 2890 cases of hypoglycemia, only 140 (4.8%) of the total were due to endocrine pathology. Of the hypoglycemic patients with underlying endocrine causes, the majority, and 77 (55%) had a diagnosis of hyperinsulinism. Forty-six patients (32.9%) had adrenal insufficiency while 17 (12.1%) had either growth hormone deficiency, hypopituitarism or panhypopituirarism.

Conclusion: Endocrine causes of neonatal hypoglycemia in the NICU were rare. Endocrine testing should be reserved for cases that have high clinical suspicion for growth hormone deficiency (micropenis, mid-facial line defect), adrenal insufficiency (abnormal electrolytes) or severe cases that do not get better over time (hyperinsulinism). All other etiologies of neonatal hypoglycemia including prematurity, stress, infections, feeding patterns, growth restriction and large for gestation should be considered first prior to obtaining complicated and expensive hypoglycemia critical samples work up.

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Blood Glucose Monitoring and Glycemic Control in the Hospitals

ATTD19-0058

HYPOGLYCEMIA IN DIABETES ASSESSED WITH CONTINUOUS GLUCOSE MONITORING IN A SHORT-TERM LONGITUDINAL STUDY

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Background and aims: Hypoglycemia is usually the undetected pitfall and obstacle in diabetes treatment and control and increases the risk for severe complication in diabetes. The aim of this study was assess continuous (interstitial) and intermittent (capillary) glucose in detecting and treating hypoglycemia during a three-months study in persons with diabetes.

Methods: 55 persons with type 1 diabetes (T1D,24) and type 2 diabetes (T2D,31) were investigated by blinded continuous glucose monitoring (CGM) for three days,while testing capillary glycemia four times a day. 21 persons (13 T1D,8 T2D) performed a second monitoring visit after three months. Parameters: percentage of CGM glucose <70 mg/dl (%CGMG <70), number of CGM hypoglycemic episodes (periods with at least one interstitial glucose value <70 mg/dl), and number of known hypoglycemic episodes (on glucose meter and/or symptomatic), mean amplitude of glucose excursions (MAGE).

Results and discussion: %CGMG <70 were 3.25% for the whole group, 5.55% for T1D, 1.47% for T2D. CGM hypoglycemic episodes averaged 2.07 for the entire group, 3.42 for T1D, 1.03 T2D. Known hypoglycemic episodes averaged 1.02 for the entire group, 2.04 for T1D, 0.23 for T2D. CGM hypoglycemic episodes (total and diurnal) were significantly more frequent than known hypoglycemic episodes. % CGMG <70, CGM hypoglycemic episodes and known hypoglycemic episodes were significantly higher in T1D. Known hypoglycemic episodes, but not CGM hypoglycemic episodes,were more frequent in insulin treated T2D. CGM hypoglycemic episodes and known hypoglycemic episodes were directly correlated with glucose variability (MAGE). Both CGM hypoglycemic episodes and known hypoglycemic episodes decreased in T1D and increased in T2D at second monitoring visit.

Conclusions: CGM proved to be an essential tool in detecting asymptomatic hypoglycemia in diabetes persons. It is important to take appropriate therapeutic measures in order to reduce and not increase hypoglycemic events in diabetes.

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Blood Glucose Monitoring and Glycemic Control in the Hospitals

ATTD19-0063

TO PARTICIPATE IN AN IMPROVEMENT COLLABORATIVE IN A NEIGHBORING COUNTRY – EXCELLENT RESULTS IN METABOLIC CONTROL OF PEDIATRIC TYPE 1 DIABETIC PATIENTS

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Many pediatric diabetes centers fail to reach HbA1C target levels. In Sweden data from a national pediatric diabetes quality registry, SWEDIABKIDS, was used to analyze factors that affect the diabetes control. Centers with better metabolic outcome showed higher compliance with guidelines, aimed at a lower HbA1c, teams were devoted, and had a positive attitude. Based on these findings a quality improvement collaborative (IQ) was conducted in Sweden 2011. The IQ had duration of 18 months, including learning-sessions with lectures on improvement methods, teamwork, and sharing experiences. Between the learning sessions, the teams identified improvement areas at their centers, and started interventions. Since the start of IQ mean HbA1c in swedish pediatric T1D patients has decresed from 62, 6 mmol/mol to 56, 8 mmol/mol. Almost all swedish pediatric diabetic centers have participated to one of the three IQs.

Our pediatric diabetes team from Helsinki University Hospital, Jorvi, participated to IQ3 (2014–2016) as a first team from another country. We are the second largest pediatric diabetes center in Finland, taking care of approximately 400 children with T1D. Before the IQ3 start mean Hba1c in Jorvi pediatric diabetes population was 64 mmol/mol, and only 27 % of the patients reached Hba1c target (< 58 mmol/mol). As IQ3 ended, mean HbA1c was 62 mmol/mol, and 34 % reached target. The

improvement work has continued, and currently mean HbA1c is 57.5 mmol/mol and 55% of the patients reach HbA1c target.

To participate in a quality improvement collaborative facilitates pediatric teams to improve local care, even over borders.

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Blood Glucose Monitoring and Glycemic Control in the Hospitals

ATTD19-0073

THE EFFECT OF MOTIVATIONAL INTERVIEW AND INTENSIVE EDUCATION ON HBA1C VALUES AND GLUCOSE VARIABILITY IN POORLY CONTROLLED TEENS WITH TYPE 1 DIABETES

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Introduction: Poor glycemic control during adolescence markedly increases the incidence of micro- or macrovascular complications during subsequent years. Despite novel technologies for diabetes treatment, poor metabolic control is a common problem during adolescence. Our aim was to study, if Motivational interview (MI), used by diabetes doctor, trained for use of MI, combined with standard education helps adolescence to improve their glucose control.

Materials and Methods: This randomized, controlled, follow-up study was conducted in 49 T1D patients with poor diabetes control, aged 13–17 years, 50 % males, for 1 year. Patients came to diabetes outpatient clinic every 3 months, and in every visit MI was used, in control group visits were done as before. CGM was conducted in 0, 6 and 12 months.

Results: The glucose control in MI and control groups are shown in table 1.

Table 1. The glucose control in MI and control groups

	0 months			6 months			12 months		
	MI	Control	P	MI	Control	P	MI	Control	P
HbA1c (mmol/mol)	87,5	84,3	NS	85,0	85,8	NS	84,6	82,5	NS
Mean glucose (mmol/l)	12,1	11,4	NS	13,0	11,9	NS	12,7	12,4	NS
SD (mmol/l)	4,8	5,0	NS	4,4	4,7	NS	4,7	4,5	NS
CV (%)	40,1	45,1	NS	35,8	39,6	NS	38,4	37,7	NS
TIR (%)	34,8	36,4	NS	38,1	36,3	NS	31,8	35,8	NS
Hypoglycaemias (%)	3,8	6,6	NS	2,8	2,6	NS	4,4	4,2	NS

Mean glucose = CGM mean, SD = standard deviation, CV= Coefficiency variation, TIR= Time in range (3.9-10 mmol/l), H= Time in hypoglycaemia (<3,9 mmol/l)

Conclusion: Though few patients in the Motivational interview group clearly improved their glucose balance during the study, statistically significant difference was not found between groups during a one year follow up. It is interesting to see if the difference is seen during longer follow-up.

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Blood Glucose Monitoring and Glycemic Control in the Hospitals

ATTD19-0146

GLYCEMIC OUTCOMES IN INPATIENT WITH DIABETES FROM A LARGE UNIVERSITY HOSPITAL

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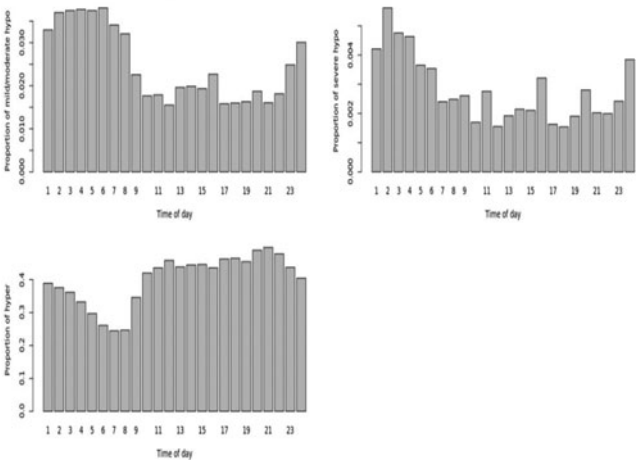
Introduction: We analysed data obtained from inpatients with diabetes admitted to a large university hospital.

Methods: We retrospectively assessed both laboratory and point-of-care blood glucose values in inpatients at Oxford University Hospitals. Based on the blood glucose values, the inpatients were grouped into normal glycaemia (4.0–10mmol/l), hyperglycaemia (>10mmol/l), mild to moderate hypoglycaemia (2.3–3.9mmol/l) and severe hypoglycaemia (<2.3 mmol/l). Mortality rates were compared between the groups with and without hypoglycaemia. We assessed time of day distribution of the hypoglycaemic and hyperglycaemic values.

Results: We analysed data obtained from 21, 463 inpatients with diabetes [11,960 males, age 69 (19) years, mean(SD)] who underwent 47,418 admissions between year 2014 and 2018. We analysed 830,631 blood glucose values with a mean (SD) of 10.1 (4.8) mmol/l. The proportion of hyperglycaemic values was 40.0% and these were observed in 78% of patients. The proportion of mild to moderate hypoglycaemic values was 2.4% (in 25% of patients) and the proportion of severe hypoglycaemic values was 0.25% (in 5% of patients). A high proportion of hypoglycaemic values were between 23h00 to 08h00 and hyperglycaemic values were between 09h00 to 00h00 (Figure 1). Compared to the group of inpatients without any hypoglycaemic values, the mortality rate was higher in groups with mild to moderate hypoglycaemia (odds ratio 1.9, 95% confidence interval [1.7, 2.0]) and severe hypoglycaemia (odds ratio 2.5, 95% confidence interval [2.2, 2.9]).

Figure 1. Time of day distribution of the proportions of hypoglycaemic and hyperglycaemic values.



Conclusion: Analysis of glycaemic control in inpatients with diabetes demonstrates a high prevalence of hyperglycaemia and hypoglycaemia. Patients who experience hypoglycaemia are associated with a higher mortality rate.

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Blood Glucose Monitoring and Glycemic Control in the Hospitals

ATTD19-0190

EFFECT OF DULAGLUTIDE VERSUS LIRAGLUTIDE ON GLUCOSE VARIABILITY AND OXIDATIVE STRESS AND ENDOTHELIAL FUNCTION IN TYPE 2 DIABETES PATIENTS

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Background: We aimed to evaluate evaluate the efficacy of dulaglutide versus liraglutide on oxidative stress and endothelial function in type 2 diabetes patients.

Methods: Twenty-two patients with type 2 diabetes who treated with liraglutide for at least 24 weeks were randomized to either continue liraglutide or receive dulaglutide for 12 weeks. Primary endpoints were changes in diacron-reactive oxygen metabolites (d-ROMs) test as a marker of oxidative stress and the endothelial function by reactive hyperaemia index (RHI: EndoPAT® system). Secondary endpoints were changes in body weight, glucose variability, diabetes treatment satisfaction questionnaire status scores (DTSQs) and eating behavior.

Results: There were no significant differences in changes of d-ROMs and logarithmic-scaled RHI (L-RHI) between the two groups after 24 weeks of treatment. However, compared with liraglutide, treatment of dulaglutide significantly improved in the mean glucose levels, mean amplitude of glycemic excursions. Convenience of DTSQs improved in the dulaglutide group. No statistically significant change in fasting plasma glucose, hemoglobin A1c and body weight was observed between two groups.

Conclusions: The present study suggest that once-weekly dulaglutide is similar to once-daily liraglutide for oxidative stress and the endothelial function. In addition, switching from liraglutide to dulaglutide improved convenience by decreasing in the number of injections without deteriorating glucose metabolism.

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Blood Glucose Monitoring and Glycemic Control in the Hospitals

ATTD19-0257

DIGITAL DIABETES MANAGEMENT TOOL FOR MONITORING AND COUNSELLING OF PATIENTS TREATED AT APOLLO SUGAR DIABETES CLINIC ACROSS INDIA

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Background and Aim: To evaluate the advantages of health interactions(HI) on self-monitoring of blood glucose(SMBG) in diabetes patients through Apollo Sugar Mobile App.

Methods: Apollo Sugar app (ASapp) is the brain child of Apollo Sugar Clinics, which is developed to serve and engage diabetes patients beyond clinic visits. ASapp captures HI's, SMBG, prescription and diet, and patient's queries with 24/7 sugar buddy. HI's were categorized based on diet, insulin, medication, SMBG, hypoglycemia, blood glucose (BG), and exercise. Diabetes educate on the advantages of ASapp and encourage to interact. Descriptive statistics was applied to analyse the data.

Results: From a total of 883 patients, 17000 HI's were captured, of which only 6600 were meaningful on diet (29%), exercise (5%), medication (10%), insulin (5%), hypoglycaemia (3%), SMBG (24%) and diabetes education (20%). Among these 333 (38%) patients were regularly monitoring SMBG. 70% of the patients recorded SMBG >2times/week and 30% atleast once/week. Nearly 42% of patients have achieved Pre-meal (70–130 mg/dL) and 74% achieved post-meal (<180 mg/dL) BG and 9% of patients recorded hypoglycaemic BG. At start the pre-meal and post-meal SMBG were 176mg/dl and 179mg/dl, and reduced to 155mg/dl and 160mg/dL, respectively in an average of 3 months. At baseline mean HbA1c was 8.6% and at follow up HbA1c reduced to 8.1% with a mean reduction of 0.4%

Conclusions: The current analysis indicates that patients' interactions with health coach through an Apollo Sugar app is an advanced method of behavioural and clinical care, to achieve long term continuity of care for change in outcomes of hard end points.

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Blood Glucose Monitoring and Glycemic Control in the Hospitals

ATTD19-0364

ASSESSING THE BENEFITS OF A PAINLESS LANCING DEVICE IN A SUBSET OF PATIENTS FEARFUL OF FINGER PRICKING

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Parameters Assessed	Genteel Lancing Device	Conventional Lancing Device	p value	Effect size r
Painscore*	5.00±0.00	1.78±0.43	<0.0001	0.66
SMBG testing frequency **	0.66±0.23	0.28±0.16	0.0002	0.602

* To the question 'is pain a limiting factor for regular SMBG monitoring', subjects graded from 1 to 5 (1='very painful and a very strong limiting factor for performing SMBG,' 5='not at all a limiting factor')

** [SMBG frequency (Genteel vs. Conventional)]/Total number of SMBG performed

Self-monitoring of blood glucose (SMBG) has been recommended by the American Diabetes Association as the gold standard of glucose monitoring. There are a few patients including children and adults who are fearful of finger pricking, due to either real pain or needle phobia. Pricking the fingertips for glucose monitoring is in fact, more painful than the insulin shots, the latter being virtually painless with the new slender tiny needles. Genteel® is a novel vacuum-based lancing device that claims to be relatively painless by decreasing the depth of lancet penetration and thus decreasing the nociceptive stimuli while lancing. A randomized crossover trial was conducted over 6 months, comparing Genteel® versus conventional lancing device. Study subjects: T1DM and T2DM patients on multiple daily insulin injections and fearful about finger pricking for glucose monitoring; n = 15, age 39.27 ± 18.41y, 40% males, 52.33% T2DM. Subjects reported significantly lower pain scores using Genteel® ($p < 0.0001$), and also higher SMBG testing frequency ($p = 0.0002$). The difference in pain scores with Genteel® was also significant when compared with the subject's initial perceived pain score prior to randomization ($p < 0.0001$). Effect size 'r' was determined to be 0.660 (pain score) and 0.602 (SMBG frequency), suggestive of a large effect size difference between the 2 groups. We, therefore, conclude the utility of Genteel as a relatively painless lancing device for all ages with fear of pricking and could be a good alternative to the traditional ones. Structured SMBG will invariably improve the glycemic control and long-term outcomes.

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Blood Glucose Monitoring and Glycemic Control in the Hospitals

ATTD19-0397

GLYCATED ALBUMIN AS A GLYCAEMIC MARKER IN PATIENTS WITH ADVANCED CHRONIC KIDNEY DISEASE AND ANEMIA: A PRELIMINARY REPORT

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Background: Glycemic homeostasis in diabetic chronic kidney disease (CKD) is usually monitored by HbA1c. Glyctaed Albumin (GA) has recently suggested as a preferred glycemic marker in subjects with CKD with respect to HbA1c for its shorter half-life and its independence from the altered erythrocytes turnover. The aim of this study was to evaluate the relationship between GA and glycemic measures in subjects with advanced CKD (stage 3 to 5) in relation to anemia.

Methods: eighty-one subjects with eGFR <30 ml/min per $1.73m^2$ were included in the study. Laboratory test results and tog complete medical history were collected at the enrollment. GA was measured on plasma-EDTA by quantILab® Glycated Albumin (Instrumentation Laboratory, A Werfen Company).

Results: the study included 81 subjects, 46 (57%) males, 45 (55%) diabetics. HbA1c was correlated with Hb ($r = 0.39$; $p = 0.0003$), and no significant correlation was detected between plasma GA and serum albumin ($p = 0.82$). A significant association between FPG and GA ($r^2 = 0.41$; $p < 0.0001$), and between FPG and HbA1c ($r^2 = 0.42$; $p < 0.0001$) was detected in the whole study population. Patients with moderate/severe anemia had lower HbA1c than patients with no anemia, while both FPG and GA were comparable between the two groups. Multivariate regression analysis showed that GA was the strogest predictor of FPG in patients with moderate/severe anemia while HbA1c didn't ($r^2 = 0.55$; $p < 0.0001$ for the model).

Conclusions: GA is significantly associated to FPG in patients with advanced CKD and anemia and it can be considered an useful test to control glycemic status in this setting.

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Blood Glucose Monitoring and Glycemic Control in the Hospitals

ATTD19-0447

EFFECTS OF METFORMIN OR ACARBOSE AS ADD-ON TO INSULIN THERAPY ON GLYCEMIC VARIABILITY IN TYPE 2 DIABETES

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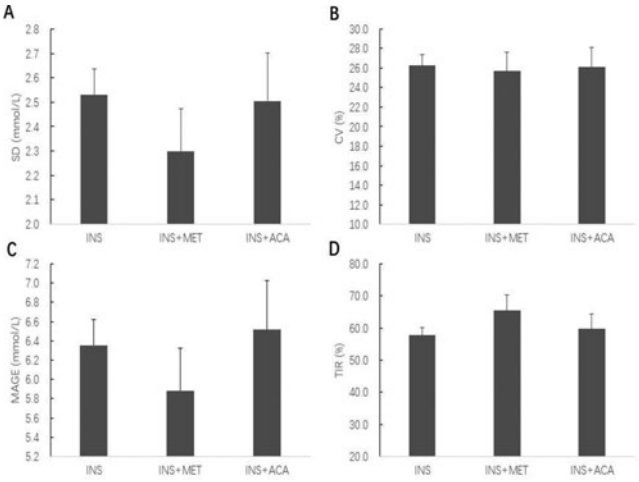
Aims: Glycmeic variability (GV) has been suggested to contribute to the development of chronic diabetic complications. The aim of the study was to investigate the effects of metformin or acarbose as add-on to insulin therapy on GV in type 2 diabetes.

Methods: 914 patients with type 2 diabetes were cross-sectionally surveyed. Study patients were stratified into: 1) insulin alone (INS group, n = 575); 2) insulin with metformin (INS+MET group, n = 175) ; and 3) insulin with acarbose (INS+ACA group, n = 164). All participants underwent continuous glucose monitoring (CGM) for 72 h, and 3 metrics of GV including standard deviation (SD), coefficient of variation (CV), and mean amplitude of glycaemic excursions (MAGE) were calculated. Besides, time in range (TIR [3.9-10mmol/L]) was also assessed.

Results: Although HbA1c were comparable between the 3 groups ($P = 0.529$), there were significant differences in SD ($P = 0.011$) and TIR ($P < 0.001$) but not in CV or MAGE (both $P > 0.05$) among the 3 treatment groups. Patients with INS+MET exhibited significant lower SD and higher TIR than those with INS or INS+ACA (all $P < 0.05$ after Bonferroni correction). Multiple regression analysis revealed that, after adjustment of age, diabetes duration, body mass index, HbA1c and fasting C-peptide, INS+MET (vs. INS) was significantly associated with SD ($P = 0.031$) and TIR ($P < 0.001$), but not CV ($P = 0.740$) or MAGE ($P = 0.117$). In addition, HbA1c and fasting C-peptide were found to be consistently linked to all the GV metrics and TIR.



Conclusions: INS+MET seems to be associated with more stable glucose control compared with INS and INS+ACA.

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Clinical Decision Support Systems - Advisors

ATTD19-0013

THE RELATIONSHIP BETWEEN INSULIN THERAPY AND CARDIOVASCULAR DISEASE IN PATIENTS WITH TYPE 2 DIABETES

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Aim: The aim of this study is exploring the relationship between insulin therapy and cardiovascular disease by controlling on potential confounders using Bayesian and Doubly Robust propensity score approaches.

Method: In this study, data from an observational study of 458 diabetic type2 patients of the endocrine research center at Iran University of Medical Sciences (2008–2011) in Tehran, Iran were used. Cardiovascular events, type of diabetes treatment (insulin therapy compared to oral drug) and cardiovascular risk factors were assessed. Then using Bayesian and Doubly Robust propensity score methods, the relationship between insulin therapy and cardiovascular disease considering possible confounders, were investigated.

Result: Totally, 312 (68.1%) patients were insulin naïve and 146 (31.9%) patients were insulin user. The crude odds ratio and its 95% interval estimates for type of treatment (insulin therapy compared to oral drug) and cardiovascular events was 1.873 (1.061, 3.306). The adjusted odds ratio and its 95% interval estimates using Bayesian propensity score method and Doubly Robust propensity score method were 1.937 (0.993, 3.766) and 1.230 (0.662, 2.280), respectively. Moreover the relative risk considering Doubly Robust propensity score was calculated 1.199 (0.695, 2.070).

Conclusions: There was a significant difference between crude incidence of CVD in insulin and oral drug users but, after controlling possible confounders based on both Bayesian and doubly robust scores, we did not find any relationship between insulin therapy and cardiovascular disease in patients with type 2 diabetes. According to our findings, the Bayesian effect of association was stronger than the doubly robust method, but the conclusions were consistent.

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Clinical Decision Support Systems - Advisors

ATTD19-0037

EVALUATION OF ACCESS OF CARE IN PEDIATRIC DIABETES

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Introduction: Patient with diabetes ideally require an integrated team including a pediatric endocrinologist, diabetes educator familiar with children, dietitian, social worker, and psychologist. The limited number of such teams can cause scarce appointments, high cost, and limited choices. The global increased of diabetes does not parallel an increased availability of specialty team. This has made access to pediatric diabetes care more challenging.

Objective: To evaluate access to pediatric endocrinology care as well as the ability to make a choice in seeking this care.

Method: Guardians who brought a child with diabetes were asked to fill a survey during clinic visit. Survey approved by The Institutional Review Board. We asked whether the physician seen was selected by the family, if the visit was for a second opinion, and what distance they had to drive.

Results: Eighty three percent report having a choice to select a pediatric endocrinologist, while 17% report was dictated by insurance. Miles driven were, <10 (3%), 10–25(23%), 26–50 (47 %) and >50 (27%). Although 66% felt that distance was not a major factor in keeping follow up appointments.

Conclusion: In our survey, majority of patient needed to travel far distance, leading to significant amount of time spend to get health care, put in perspective of the family potential lost wages, missed work/school, additional cost, and missing visits. Large distance to reach a heath care provider place patients with diabetes at greater disadvantage and disparities. Further research is need to evaluate the impact of insurer dictated provider.

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Clinical Decision Support Systems - Advisors

ATTD19-0051

INSURANCE AND DIABETES CARE

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Background: Evaluating the delivery of medical care cannot be done promptly without analysis of the role of insurance

companies since they have a major role in the establishment of diabetes care starting from contracting with health care systems, providing insulin, medication, and diabetes supplies and allowing prompt referrals to other ancillary health care providers.

Method: The objective of the study is to get feedback evaluation from families about their insurance companies regarding diabetes care.

We surveyed **100** families with diabetic children in our practice, seeking their opinions about the delivery of diabetes care.

In a **confidential questionnaire**, we asked about family experiences related to satisfaction with their insurance companies in providing diabetes supplies, medications and health provider coverage.

Results: 75% of families had commercial insurance while **25%** had government supported one.

90% of families felt that they **had a choice** in finding the right physician to seek diabetes care.

50% of families were **not** satisfied with their insurance providers' coverage, **48%** were satisfied and **2%** were neutral

Conclusion: Diabetes management is one of the main current public health issues. Diabetes-related health expenditures were estimated to be at least $673 billion in 2015. The economic burden is considered very complex due to the chronic nature of this diagnosis.

Outcomes and adherence to diabetes treatment depend on insurance status. Patients with insurance were most likely to get (HbA1c) testing, foot and eye exams, diabetes education, and influenza immunization. The fear of out-of-pocket costs could lead to poor access to health care and poor utilization of diabetes care.

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Clinical Decision Support Systems - Advisors

ATTD19-0052

COMPARING DEEP-LEARNING METHODS WITH BOW FOR AUTOMATED CHC IN SELF-MANAGEMENT OF DIABETES

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Introduction: Carbohydrate counting (CHC), an established approach in type 1 diabetes, currently depends on patient perception. Researchers look for approaches to automate CHC by capturing food images with the help of the smartphone camera and then processing them to extract CHC. Alternative algorithms for the food recognition part include Deep Learning (DL), based in Convolution Neural Networks (CNNs) and Bag-of-Words (BoW) approach.

Aim: Compare runtimes and quality of state-of-art DL and BoW approaches to recognize food dishes.

Approaches: DL methods Googlenet, Inception-V3 and Resnet-101. Bag-of-Words of SURF features (BoW).

Metrics: (A) = Food Recognition Accuracy on each of 256 classes of food in UEC Food 256, using at least 10000 food images, 70% train, 30% test; (R) = Runtime. (Q,R) = Quality and Runtime.

Results: Training Runtimes (Rtrain): DL approaches with GPUs - Googlenet (6105 mins), Inception-V3 (5290 mins), Resnet-101 (7678 mins); Other approaches without GPUs - BoW (48.4 mins). **Classification Times (Rclass)**: Googlenet (0.138 secs), Inception-V3 (0.655 secs), Resnet-101 (0.27 secs); BoW (10 secs). **Accuracy (A)** Googlenet (mean = 56%, stdev = 24%, p10 = 20%, p90 = 83%), Inception-V3 (mean = 67%, stdev = 23%, p10 = 30%, p90 = 91%), Resnet-101 (mean = 71%, stdev = 22%, p10 = 36%, p90 = 91%), BoW (52%).

Conclusions: DL approaches achieve superior accuracy, are slow training but fast classifying. However, they also require powerful servers plus GPUs to work, and further work is needed to individualize food items and CHC.

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Clinical Decision Support Systems - Advisors

ATTD19-0053

COMPARING DEEP-LEARNING WITH HVS FOR AUTOMATED CHC IN SELF-MANAGEMENT OF DIABETES

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Introduction: Carbohydrate counting (CHC) is an established approach in type 1 diabetes, currently depending on patient perception. Automated CHC aims at estimating the value automatically. It requires capturing food images with a smartphone camera and applying food and food volume recognition algorithms.

Aim: Compare quality of state-of-art Deep Learning (DL) approaches based on Convolution Neural Networks (CNNs) to the capacity of the Human Visual System (HVS) in recognition of food dishes.

Approaches: DL: CNNs Googlenet, Inception-V3 and Resnet-101 on public food database (UEC Food 256); HVS: Survey on 30 individuals with training and testing phase on 15 classes of same database chosen to represent equally-separated DL percentiles of accuracy.

Metrics: (A) = Food Recognition Accuracy of DL on the classes of food in UEC Food 256, with 31000 food images, 80% train, 20% test, versus accuracy of HVS based on designed survey;

Results: Accuracy over all foods (A) Googlenet (mean = 56%, stdev = 24%, p10 = 20%, p90 = 83%), Inception-V3 (mean = 67%, stdev = 23%, p10 = 30%, p90 = 91%), Resnet-101 (mean = 71%, stdev = 22%, p10 = 36%, p90 = 91%). HVS (mean = 80.7%, stdev = 19%, p10 = 47%, p90 = 100%).

Conclusions: Deep learning approaches are the state-of-the-art approach for food recognition. They are quite accurate. We compared with HVS, still better in these experiments. Further challenges: improve DL approaches and region-based DL approaches, add semantics that might

improve accuracy to match or overcome that of HVS; add other parts to do CHC.

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Clinical Decision Support Systems - Advisors

ATTD19-0065

WHEN CHILDCARE ISN'T SWEET: CHALLENGES FOR VERY YOUNG CHILDREN WITH TYPE 1 DIABETES

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Objectives: Type 1 diabetes (T1D) can impact childcare options for parents of young children. The purpose of this study was to characterize diabetes care by childcare attendance status among young children in the T1D Exchange Clinic Registry.

Methods: A questionnaire was emailed to 219 parents/guardians of participants 1–6 years old, garnering a 32% response rate. Data from 71 children (mean age 5 years, mean age at diagnosis 2 years, 58% male, 93% non-Hispanic white, 80% pump users, 70% CGM users, 76% privately insured) were analyzed.

Results: Nearly 50% reported childcare attendance with median attendance of 15 hours/week. HbA1c ($p = 0.76$) and frequency of SMBG ($p = 0.44$) did not differ by childcare attendance. One third of respondents were denied childcare attendance due to T1D. At childcare, a staff member was solely responsible to check blood glucose in 51% and administer insulin in 34% of cases; otherwise, family members performed these tasks. While glucagon rescue kits were available for all childcare attendees, only 49% had a staff member identified to administer it. Among non-attendees, 70% reported T1D was a factor in having the child remain home. More than one-third of those surveyed experienced changes in parental employment status post-diagnosis, with 35% reporting a reduction in hours worked and 27% leaving the workforce.

	Childcare Attendees (n=35)	Non-Attendees (n=36)
Median (IQR) HbA1c	7.9% (7.4%, 8.2%)	7.4% (7.1%, 8.3%)
Mean ± StD SMBG	6.3 ± 2.5	6.5 ± 2.1
% using CGM	69%	71%
% using insulin pump therapy	79%	81%

Conclusions: T1D in young children potentially limits childcare options and influences parental employment status. Since much of the burden of diabetes management is still undertaken by family caregivers, even when the child attends childcare, advocacy to address this issue is needed.

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Clinical Decision Support Systems - Advisors

ATTD19-0066

IMPACT OF GLUCOSE ANALYTIC ERROR ON RISK OF MISCLASSIFICATION OF PATIENTS USING AMERICAN DIABETES ASSOCIATION DIAGNOSTIC CRITERIA

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Background & Aims: Current American Diabetes Association (ADA) guidelines state a fasting plasma glucose (FPG) ≥126 mg/dL (7.0 mmol/L) is diagnostic of diabetes, 100–126 mg/dL (5.6–7.0 mmol/L) pre-diabetes and <100 mg/dL (5.6 mmol/L) as healthy. The objective was to evaluate the impact of analytic error of glucose measurement and biological variation on misclassification of healthy, pre-diabetic and diabetic patients.

Methods: NHANES 2015 FPG dataset was used as a population sample ($n = 2972$) for simulation studies: prevalence of 13.1% diabetics by FPG. FPG results were categorized using ADA criteria. FPG concentrations were then modified in a statistical model by addition of bias, imprecision and biological variation. The fraction of modified FPG results misclassified between ADA healthy, pre-diabetic and diabetic groups was assessed.

Results: The fractions of FPG results misclassified as functions of bias and precision were determined. Representative results were: (A) Biologic variation of FPG alone misclassified: 15% of Healthy values as Pre-diabetics, 20% of Pre-diabetics as Healthy, 3 % of Pre-diabetics as Diabetic, and 4% of Diabetic as Pre-diabetics. (B) Addition of 2% precision and –5% bias misclassified: 44% of Pre-diabetics as Healthy and 11% of Diabetics as Pre-diabetics and 11% of Diabetics as Pre-diabetic. (C) Addition of 2% precision and +5% bias misclassified: 36% of Healthy patients as Pre-diabetics, 11% of Pre-diabetics as Diabetic and 11% of Pre-diabetics as Healthy.

Conclusions: This simulation model demonstrated significant risk of misclassification errors of diabetics, pre-diabetics and healthy patients due to bias of FPG methods and demonstrated minor influence of precision.

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Clinical Decision Support Systems - Advisors

ATTD19-0067

IMPACT OF HBA1C ANALYTIC ERROR ON CLASSIFICATION OF PATIENTS USING AMERICAN DIABETES ASSOCIATION DIAGNOSTIC CRITERIA

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Background & Aims: While HbA1c methods have improved, commercial methods continue to have ±5%bias (e.g. For a target of 53.5 mmol/mol: 50.8 to 56.2; For a target of 7.0%: 6.65 to 7.35%) in proficiency testing programs. The aim of this study was to evaluate the influence of HbA1c analytical error on misclassification of patients using diagnostic criteria outlined by the American Diabetes Association (ADA).

Methods: NHANES 2015 HbA1c dataset was used as a population sample (n = 6326) for simulation studies: prevalence of 11.0% diabetics by HbA1c. HbA1c results were categorized using ADA criteria as healthy, pre-diabetic or diabetic. HbA1c concentrations were then modified in a statistical model by addition of bias, imprecision and biological variation. The fraction of modified HbA1c results misclassified between ADA healthy, pre-diabetic and diabetic groups was assessed.

Results: The fractions of HbA1c results misclassified as functions of bias and precision were determined. Representative results were: (A) Biologic variation of HbA1c alone misclassified: 7% of Healthy values as Pre-diabetics, 15% of Pre-diabetics as Healthy, 1 % of Pre-diabetics as Diabetic, and 2% of Diabetic as Pre-diabetics. (B) Addition of 2% precision and -5% bias misclassified: 62% of Pre-diabetics as Healthy and 16% of Diabetics as Pre-diabetics. (C) Addition of 2% precision and +5% bias misclassified: 25% of Healthy patients as Pre-diabetics and 17% of Pre-diabetics as Diabetic.

Conclusions: This simulation model demonstrated significant risk of misclassification errors of diabetics, pre-diabetics and healthy patients due to bias of HbA1c methods and demonstrated minor influence of precision.

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Clinical Decision Support Systems - Advisors

ATTD19-0077

MICROBIOLOGICAL MONITORING OF URINE IN PATIENTS WITH DIABETES MELLITUS

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Background and Aims: Various factors may contribute to the enhanced risk of urinary tract infections in patients with diabetes mellitus (DM). The **aim** of this study is to monitor the microbial profile of urine in patients with DM to optimize therapeutic measures.

Method: 76 patients with DM from 18 to 78 years old were included in the study: 31 of them with type 1 diabetes mellitus (T1DM) (40.79%) and 45 (59.21%) – with type 2 diabetes mellitus (T2DM). The mean value of glycosylated hemoglobin A1C was 10.01 ± 2.96% for T1DM, 9.38 ± 2.01% for T2DM; glycosuria −31.04 ± 24.48 and 26.87 ± 19.02 mmol/L, respectively. The isolated strains of microorganisms were identified using the MICROLATEST test system.

Results: In 89.47% of cases, 86 strains of opportunistic microorganisms (OM) were isolated. The share of Gram-positive microflora was 65.64%, Gram-negative microflora - 27.91%, Candida (6.45%). The most frequent pathogens were *Staphylococcus spp.* - 48.38%, among which *S. aureus* was dominated (16.13%). The share of *S. ureolyticus* was 6.45%, *S.epidermidis* and *S. haemolyticus* were isolated at 12.9%. Often, *Streptococcus spp.* (*S. agalactiae*, 3.23%) and *Enterococcus spp.* (*E. faecalis, E. faecium,* 29.03% of the total). Among Gram-negative microflora - E. coli (12.9%) was dominanted. *Coagulase-Negative Staphylococci* (32.25%) and *Enterococci* (29.03%) in T1DM were dominated, *Enterobacteriaceae* were prevailing in T2DM (*E. coli* often was isolated (34.55%). During the urine test, *Candida* were isolated, that were potential pathogens in patients with diabetes.

Conclusion: Monitoring the microbial profile of urine using modern bacteriological methods makes it possible to optimize therapeutic measures for urinary tract infections in diabetic patients.

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Clinical Decision Support Systems - Advisors

ATTD19-0093

TECHNOLOGY UTILIZATION OF PATIENT PORTALS IN A PEDIATRIC CLINIC: A PILOT SCREENING REVIEW

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Background: The availability of electronic system such as patient portals have allowed patients and parents of children to retrieve updated health information electronically anywhere and anytime.

Some systems may allow patients and parents submitting appointment requests, receive reminders of upcoming appointments, request prescription refills and communicate securely with physicians.

Aim: To screen parents about their knowledge of an existing patient portal system then evaluate the utilization rate after the screen.

Methods: Parents were asked to fill a survey during a regular pediatric endocrinology clinic visit which included three questions regarding awareness of the portal system, whether if they are currently utilizing and their willingness to utilize it in the future. The utilization rate of patient portal was evaluated in a one- year period before and after the screen.

Results: Out of the 151 questionnaires obtained, only 34% of our population studied knew about the Patient Portal System. When asked if enrolled in the Patient Portal System, 33% of them were enrolled. The majority of people, 70%, wanted to know more about the Patient Portal System. Information regarding the Patient Portal System was given to them.

The utilization rate went up 12% between 2016 and 2017.

Discussion: Patient portals have been reported to have many benefits including improved doctor-patient communication, increased patient satisfaction and increased patient investment in their own care. One obvious barrier to the usage of patient portals is ignorance of its existence. Educating people about the portal can make patients more likely to use these platforms and possibly have better clinical outcomes.

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Clinical Decision Support Systems - Advisors

ATTD19-0129

THE IMPACT OF ACCURATE CARBOHYDRATE COUNTING ON PATIENT'S GLYCEMIC TARGETS

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Background and Aims: Preprandial insulin bolus is adjusted taking into account the carbohydrate content of each meal, the patient's glycemic targets (G_{Hyper}, $G_{T\ and}$ G_{Hypo}), the insulin sensitivity factor (ISF), and the insulin-to-carb ratio (ICR) throughout the day. Evidence suggests that accurate carbohydrate counting may have positive effects not only on reducing glycosylated hemoglobin concentration but also on decreasing the incidence of hypoglycemic episodes. Therefore, the efficacy of carbohydrate counting depends not only on the ability of each patient accurately estimate the carbohydrate content of each meal but also on each patient glycemic targets.

Method: This study proposes a new analytic method that uses personalized data (i.e., the insulin-to-carb ratio, the insulin sensitivity factor, and the glycemic targets of each patient) to find the maximum absolute error (ΔCHO_{max}) that each patient can commit while estimating the carbohydrate content of each meal in order to avoid hypoglycemic and hyperglycemic events, i.e.:

$$\Delta CHO_{max} = ICR/ISF \times \min\left\{G_{Hyper} - G_T, G_T - G_{Hypo}\right\}.$$

Results: Within the UVA/Padova T1 Diabetes Metabolic Simulation platform (T1DMS v3.2, 2013), we found that increments of about 20 mg/dL in $\min\{G_{Hyper} - G_T, G_T - G_{Hypo}\}$ result in increments of at least 5 g in ΔCHO_{max}, which may result in a substantial reduction of hypoglycemic episodes.

Conclusion: The proposed method allows patients with T1DM diabetes to be more confident when using carbohydrate counting, as their glycemic targets can be fitted according to their ability to accurately estimate the carbohydrate content of each meal and, therefore, reduce the risk of hypoglycemic events.

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Clinical Decision Support Systems - Advisors

ATTD19-0139

HOW TO IMPROVE HEALTHCARE MANAGEMENT IN LAB MEDICINE USING SYSTEMATIC BIG DATA ANALYTICS AN EXAMPLE OF DIABETIC PATIENT CARE IMPROVEMENT IN FRENCH LABORATORIES

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To improve diabetes care management, we used a big data analysis to show how the HbA1c prescriptions can be improved. In our study, data from more than 110000 patients (more than 200000 HbA1c tests) was analysed.

An examination of the population tested with HbA1c shows an average age of more than 65 years although the recommendation is 45. That means that HbA1c in our laboratories is requested mostly for monitoring according to French recommendations.

Is it possible to give more value to the diagnostic by using it for screening purposes ?

The average result for HbA1c value was pathological: 6,6 % (NGSP). WHO and ADA define an HbA1c cut-off criteria for type 2 diabetes diagnosis as 6.5%; 45–56% of pathological results (HbA1c ≥6,5%) and 20–26% of low risk ones (HbA1c < 5,7%). Approximately 30% of the results were in the grey zone (HbA1c 5,7–6,4%), which were recognized by endocrinologists as ''pre-diabetic'' results.

We found that only 13% of diabetic patients undergo 4 tests per year, which is mostly recommended for diabetes monitoring.

Due to interaction with prescribers discussing this data we achieved:

- Among screening patients, we found up to 10% of pathological results and approximately 35% of (''pre-diabetic'')
- Special reports were created to assist physicians to improve the monitoring of diabetic patients
- An increase of the HbA1c testing mostly by using it for diabetes screening

Conclusion: Big data analysis approach allows us to improve diabetes management care by monitoring diabetic patients through efficient diabetes screenings.

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Clinical Decision Support Systems - Advisors

ATTD19-0191

A PERSONALIZED MEAL GRADING SYSTEM USING PROFESSIONAL CGM (IPRO2) WITH THE FOODPRINT BY NUTRINO

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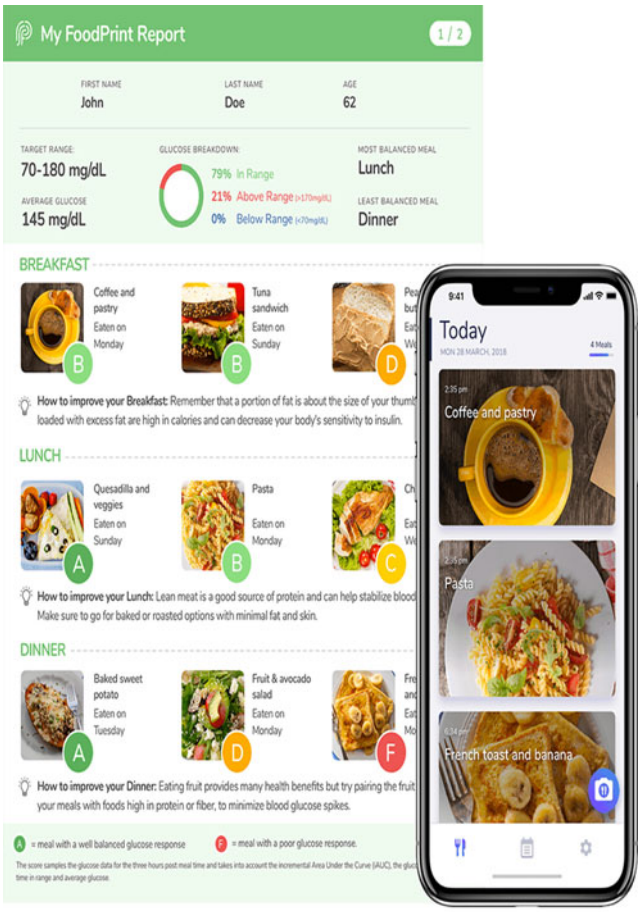
Background: The iPro2™ professional continuous glucose monitoring (CGM) system collects masked sensor glucose (SG) data for retrospective analysis through CareLink™ software. Meals, activity, and medication are entered via a smartphone app and integrated with the CGM tracings in the CareLink™ report. The iPro2™ CGM system now incorporates the FoodPrint™ report developed by Nutrino. Smartphone photographs are used to provide an association between the meal and glycemic excursion.

Methods: FoodPrint™ grading uses a proprietary, non-linear algorithm to score a set of meals for each patient from A through F. The patient is his/her own control allowing for the possibility that similar meals may result in different grades between patients.

Results: The relationship of the grade assigned by the FoodPrint™ report of 1248 meals in 117 patients with diabetes to the peak post-prandial glucose rise was analyzed (Table). The meal grade and mean glycemic excursions are well-correlated. The



FoodPrint

FoodPrint Grade	Number of Meals	% of Meals	Mean (+/- SD) Glucose Excursion (mg/dL)
A	332	26.6	11.3 +/- 15.3
B	293	23.5	22.0 +/- 22.9
C	266	21.3	38.8 +/- 33.7
D	195	15.6	50.8 +/- 44.1
F	162	13.0	71.5 +/- 59.7

high SD's reflect the wide inter-personal glucose responses to a set of meals for each patient.

Conclusions: The combination of CareLink™ reports and FoodPrint™ grading allows: a) patient-tailored nutritional advice; b) patient self-learning; and c) better informed medication changes. We believe this type of information into patients' CGM assessments can help achieve both patient engagement and more personalized therapy.

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Clinical Decision Support Systems - Advisors

ATTD19-0202

DECREASED ACCURACY OF THE FREESTYLE® LIBRE GLUCOMETER DURING ENDURANCE EXERCISE IN PEOPLE WITH TYPE 1 DIABETES: HYPOGLYCAEMIA IS THE WEAK SPOT

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Background and Aims: An increasing number of subjects with type 1 diabetes (T1D) are using the FreeStyle® Libre glucometer (Abbott, Diabetes Care, Alameda, USA) (FLGM) to monitor their glucose levels during exercise. However, data on FLGM performance during exercise is limited. The aim of this study was to evaluate the accuracy of the FLGM compared with Biosen C-line, (EKF diagnostic GmbH, Barleben, Germany) using capillary blood glucose in people with T1D performing moderate-intensity endurance exercise.

Methods: Nine participants with T1D (4 females, age 32.1 ± 9.0 years, BMI $25.4 \pm 3.6\,kg/m^2$, HbA_{1c} $7.2 \pm 0.6\%$ [$55 \pm 7\,mmol \cdot mol^{-1}$]) exercised on a cycle ergometer for 55 min at a moderate intensity for five consecutive days at the clinical research facility. During exercise, reference capillary blood glucose values obtained from the earlobe (20 μl) were compared to capillary blood glucose values obtained from fingertip (0.6 μl), analysed via FLGM. Accuracy of the FLGM during exercise was then evaluated by means of median absolute relative difference (MARD), Clarke error grid and Bland-Altman analysis for overall glucose levels and stratified for pre-specified glycaemic ranges.

Results: 495 blood glucose values were available to assess the FLGM accuracy. The overall MARD across glycaemic ranges at rest was 13.5% (interquartile range 7.3–17.6%), while the overall MARD during exercise was 12.7% (7.8–16.7%), 23.6% (12.3–32.8%) during hypoglycaemia, 12.8% (7.9–16.8%) during euglycaemia and 9.3% (6.0–12.3%) during hyperglycaemia.

Conclusion: The FLGM showed in general decreased accuracy during exercise and in particular during hypoglycaemia. Consequently, absolute glucose values given by the FLGM should be interpreted cautiously around exercise.

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Clinical Decision Support Systems - Advisors

ATTD19-0206

HOW DOES INPATIENT DIABETES MANAGEMENT AFFECT DISCHARGE SUGGESTIONS?

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Introduction: Type 2 diabetes treatment in hospitalized patients is often insufficient, expensive and laborious for medical staff. Decision support systems may play a crucial role in the improvement of inpatient glycemic control. The transition

process at hospitalization and hospital discharge is little characterized so far.

Methods: In this retrospective analysis we assessed all diabetes cases hospitalized and managed with GlucoTab®, a diabetes management system including the option for algorithm-driven basal-bolus insulin therapy, on an endocrinology ward of a tertiary center from October 2016 to November 2017.

Results: In 157 cases we evaluated insulin therapy before, during and after hospitalization according to allocated treatment: one group received physician-driven treatment (standard care: n = 79, 29.1% female, age 73.0 ± 11.8 years, HbA1c 63 ± 19 mmol/mol, creatinine 1.4 ± 0.8 mg/dl), one group algorithm-driven basal-bolus insulin therapy (algorithm group: n = 50, 32% female, age 69.0 ± 11.1 years, HbA1c 82 ± 28 mmol/mol, creatinine 1.5 ± 1.2 mg/dl) and one group received both treatments (mixed group, n = 28 42.9% female, age 73 ± 11.2 years, HbA1c 68.6 ± 19.0 mmol/mol, creatinine 1.48 ± 0.86 mg/dl). Post-discharge insulin therapy was suggested in 69.6% (standard care group), 86% (algorithm group) and 92.9% (mixed group). Subsequent basal-bolus insulin therapy was suggested in 72% (algorithm group), 19% (standard care group) and 39.3% (mixed group).

Conclusion: Inpatient algorithm-driven basal-bolus insulin therapy results in higher rates of subsequent insulin therapy at discharge. In particular basal-bolus insulin therapy suggestion is predominant, indicating that during hospital stay an improvement in glycemic control was safely achieved and continuation of this therapy is assumed to be effective for subsequent home-therapy.

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Clinical Decision Support Systems - Advisors

ATTD19-0221

INVESTIGATING DETECTION STRATEGY FOR FALSE FOOD CONSUMPTION REPORTS BASED ON CGM SIGNALS IN GESTATIONAL DIABETES PATIENTS

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Background and Aims: False reporting of food consumption is a well-known problem that appears often in gestational diabetes mellitus (GDM) patients. An algorithm for automatic detection of false (for example, with underestimated carbohydrates consumption) reports could help in finding effective disease management strategies.

Methods: Patients with GDM were monitored with iPro2 CGMS and a specially developed app DiaCompanion, which they used to keep track on the diet. Patients were asked to choose food items and appropriate consumed grams from in-app food database, which were automatically converted into macro- and microelements by the software. CGM signals were used to verify the correctness of food reports.

Results: A total of 95 participants (78/18 GDM/healthy) were included into one-week monitoring, in which they reported food intakes. The information on 1123 food intakes was analyzed. For 60 GDM patients (77%) who sent physicians non-empty food diaries there were 7.6 ± 4.5 BG peaks specific for food intake without appropriate records in a diary, 2.8 ± 2.1 food intakes with clearly wrong time provided in a diary, 1.3 ± 0.5 food intakes with clearly underestimated carbohydrates. Corresponding values for healthy individuals did not differ significantly.

Conclusions: The results show that only 16 of 60 (27%) patients reported all food intakes with less than 5 serious mistakes that could be obviously detected. Food reports in GDM patients should be considered carefully and special rule-based algorithms should be implemented to help physicians in dealing with false food reports and missing data.

The study was funded by Russian Science Foundation (project No. 18-75-10042).

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Clinical Decision Support Systems - Advisors

ATTD19-0224

DEVELOPMENT AND IMPLEMENTATION OF A CLINICAL SUPPORT SYSTEM FOR THE MANAGEMENT OF HYPERTENSION AND DIABETES IN THE PRIMARY CARE SETTING: A SUBSTUDY OF HEALTHRISE BRAZIL

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Background: Achieving control of hypertension (HT) and diabetes mellitus (DM) is challenging. Our aim was to develop a clinical decision support system (CDSS) for DM and HT management in primary care, to implement it in a low-income region, and to evaluate its usability and user satisfaction.

Methods: This study is a substudy of HealthRise Brazil. It included: (i) CDSS development and validation; and (ii) field study in 35 primary care units in 10 small towns in Minas Gerais,

Table 1 – Main results of usability and satisfaction assessment (n=96)

Item	Score *
It is easy to be incorporated in work routine	4 (3-4)
The application fields are easy to fill	4 (4-5)
The application might improve patient care	4 (4-5)
The application assisted me to treat my patients	4 (4-5)
Overall, I am satisfied with the application	4 (3-4)
I would recomend it to other colleagues	4 (4-5)

* From 1 (strongly disagree) to 5 (strongly agree). Median (interquartile range).

Brazil. Usability and satisfaction assessment, using a Likert-scale questionnaire, was applied after six months.

Results: In total, 1,939 patients were registered in the application's database and ninety-six frontline health professionals answered the questionnaire (Table 1), 35.4% of them did not use any form of health technology before this project.

Conlcusion: The CDSS was applicable in the context of primary health care setting in a low income region, with good user's satisfaction and potential to improve adherence to evidence-based practices. The intervention is being tested to assess the impact on blood pressure and glycemic control.

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Clinical Decision Support Systems - Advisors

ATTD19-0228

DEVELOPMENT OF AN ADAPTIVE, REAL-TIME, INTELLIGENT SYSTEM TO ENHANCE SELF-CARE OF CHRONIC DISEASE (ARISES)

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Background and aims: Diabetes mobile health applications provide a front-end interface allowing interaction with data from wearable devices. Limitations in operational efficiency, usability, and functionality of health apps continue to hinder their widespread adoption and retention. To overcome these barriers, we have designed a mobile interface for a novel adaptive decision support system using deep machine learning algorithms, continuous glucose monitoring (CGM), and wearable physiological data acquisition sensors. We present here the ARISES prototype for use in type 1 diabetes (T1D) self-management.

Methods: The interface design was derived from discussions and feedback from twelve 2-hour semi-structured multidisciplinary focus meetings. The inclusion of 10 people with T1D alongside a clinician, engineer, and expert in human computer interaction allowed co-designing the system with potential future users. Documented outcomes and participant questionnaire data were anonymously shared among the design team for validation. Literature-based evidence influenced our design framework.

Results: We designed an efficient non-hierarchical interface capable of presenting graphical real-time and predicted glucose data, handling macronutrient and exercise input, and delivering adaptive insulin bolus advice all on one home screen. The dynamically interactive 30-minute predicted blood glucose profile will react in real-time to macronutrient entry, exercise, physiological data, and insulin on board. A dedicated advice domain exploiting the deep learning algorithm will present contextual temporal and behavioural trends associated with dysglycaemia.

Conclusion: Using a multidisciplinary and user-based design approach we have designed a prototype for a novel multifunctional mobile decision support system integrating multiple wearable technologies. Clinical usability and feasibility studies will commence in 2019.

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Clinical Decision Support Systems - Advisors

ATTD19-0244

INSULCLOCK®: A NOVEL INSULIN DELIVERY OPTIMIZATION AND TRACKING SYSTEM

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Achieving and maintaining controlled glycemic levels is challenging in people with insulin-treated DM, being poor treatment adherence and suboptimal insulin injections the main obstacles to treatment success.

Methods: This research article presents the main functionalities and performance tests on *Insulclock®*, an electronic device to be plugged into insulin pen devices and connected with a smartphone app to improve insulin management. *Insulclock®* tracks the date, time, dose, type of insulin, temperature, and duration of insulin injections. This information is stored and available for monitoring and analysis by patients and healthcare providers. This device also has a reminder system with visual and acoustic alerts to reduce insulin omissions and mistiming.

Results: Results of the main performance tests reveal that *Insulclock®* can detect 7 types of insulin pens with 97% correct classification rate. Among 556 injections, most of the doses were accurately detected (deviation = 0) with relative errors ranging from 3% to 7% across all the dose groups. The precision of the temperature sensor was evidenced by the high correlation of the temperatures detected by *Insulclock®* and by an external thermometer (Pearson's $r^2 = 0.90$). Moreover, the duration of injections recorded by this device strongly correlated with those detected by an external chronometer ($r^2 = 0.99$).

Conclusions: The Insulclock is a novel optimization device capable to track in dosing, timing and missing insulin administration. The promising possibilities it offers for DM self-management will likely help healthcare providers, researchers and insulin users to detect and avoid frequent errors in insulin administration.

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Clinical Decision Support Systems - Advisors

ATTD19-0245

TYPE 2 DIABETES SIMULATOR FOR TESTING BASAL INSULIN THERAPY IN INSULIN-NAIVE PATIENTS

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Background and Aim: Advanced-stage type 2 diabetes (T2D) subjects may require insulin therapy in addition to oral and other injectable antidiabetic drugs. In particular, long-acting insulin analogs are used to cover basal insulin needs.

However, finding the optimal individual insulin dose may be cumbersome and time demanding. In this regard, in silico testing is supportive. Here we develop a T2D simulator incorporating long-acting insulin Degludec (iDeg), as case study, aiming to provide a usable tool for guiding insulin therapy initiation in T2D subjects.

Methods: We first tuned our T2D simulator (T2DS, Visentin et al., ATTD 2014) to reproduce the behavior of insulin-naive T2D subjects of a clinical study (Holst et al., J Diabetes Sci Technol 2016). Then, we developed a pharmacokinetic model describing iDeg subcutaneous absorption based on average T2D clinical data, and incorporated it into the T2DS. Finally, we performed a 52-week simulation with subjects up-titrated to optimal iDeg dose, and compared final fasting plasma glucose (f-FPG) and final iDeg dose (f-iDeg) with those of a clinical study (Zinman et al., Diabetes Care 2012).

Results: After 52 weeks, in silico results were almost superimposable to clinical ones: f-FPG was 108 ± 21 mg/dL in silico vs. 106 ± 55 mg/dL in vivo; f-iDeg was 0.59 ± 0.29 U/kg in silico vs. 0.59 ± 0.35 U/kg in vivo.

Conclusions: iDeg-T2DS reproduced the main findings of a clinical trial, proving its ability to describe basal insulin therapy initiation in insulin-naive T2D subjects. Hence, T2DS represents an effective way to test in silico insulin titration to optimize safety and efficacy for T2D therapy.

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Clinical Decision Support Systems - Advisors

ATTD19-0249

LONG ACTING INSULIN DOSE RESPONSE MODELLING IN TYPE 2 DIABETES

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More than 60% of type 2 diabetes (T2D) patients in USA treated with insulin do not reach recommended HbA1c goals and a titration period can last for years. Connected devices and dose guidance tools are emerging to support this patient group in reaching better outcomes. We aim to develop a dose response model of long acting insulin to glucose dynamics to support emerging digital health and dose guidance solutions.

We perform a clinical study to collect continuous glucose monitoring (CGM) data during a long acting insulin titration period. We use the high frequency glucose data and insulin data to create a dose response model of each individual. The aim is to identify a suitable model structure of fasting glucose to long acting insulin dynamics.

The clinical study is a single centre, one arm exploratory feasibility study. We include insulin naïve adults with T2D. All patients are equipped with a smartphone, a BG meter, and a CGM during the trial period of up to 12 weeks. The primary endpoint of the study is how well a linear dose response model, given two weeks of data, can predict the dose needed to reach a target glucose level, evaluated at the end of study. We observe that a dose response model at two weeks can adequately describe the fasting glucose response at a later stage in treatment intensification.

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Clinical Decision Support Systems - Advisors

ATTD19-0282

CATEGORIZATION AND PREDICTION OF GLUCOSE PROFILES OF TYPE 1 DIABETES PATIENTS BASED ON A COMPOSITIONAL DATA ANALYSIS APPROACH

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Background and aims: This study presents an approach based on Compositional Data Analysis (CoDA) applied to glucose profiles obtained from Continuous Glucose Monitoring (CGM) of patients with type 1 diabetes (T1D). Glucose profiles limited to 24-h and 6-h duration were categorized according to the relative interpretation of time spent in different glucose ranges at different times of day. The aim is to present the prediction of the category of the next 6-h period based on the category of the previous 24-h period.

Methods: Glucose data from six T1D patients were analyzed. 24-h and 6-h glucose profiles were distributed into time spent in five glucose ranges, which determine the compositions. The log-ratio coordinates of the compositions were categorized through a clustering algorithm, which made possible the obtainment of a linear model that should be used to determine the category of the previous 24-h. A probabilistic model of transition between the category of the past 24-h of glucose to the category of the future 6-h period was obtained.

Results: Leave one out cross validation achieved an average above 90% of correct classification of the 24-h periods. The CoDA approach is suitable for the categorization of glucose profiles and is a promising tool for the prediction of different categories of glucose control.

Conclusion: This categorization of daily glucose profiles could assist physicians to tailor patient's insulin dosing profile and the prediction of the category of the next period could assist patients to take correction measures in advance to adverse situations.

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Clinical Decision Support Systems - Advisors

ATTD19-0285

PREDICTION OF NOCTURNAL HYPOGLYCEMIC EVENTS IN ADULTS WITH TYPE 1 DIABETES

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Background and aims: Nocturnal hypoglycemia is a hazard situation for subjects with type 1 diabetes (T1D), especially for those who suffer of hypoglycemia unawareness. The objective of this work is to make use of patients' retrospective data to predict the occurrence of nocturnal hypoglycemic events before the patient goes to sleep.

Methods: The OhioT1DM dataset was considered in this work, where in addition to using an insulin pump, patients wore a physical activity tracker. Information related with patients' insulin therapy, meals and physical activity were considered to create individualized prediction models. Data from the physical activity tracker was used to determine when patients started to sleep. From this instant, the previous 6-h of retrospective data was used to create input features for the models, where physiological models were also applied on the data. The following 6-h of data was used for class labeling. Multilayer perceptron networks were used to train predictive models.

Results: To evaluate the predict performance of the models, k-fold cross-validation ($k=5$) was considered and the procedure was repeated 100 times. Individualized results were obtained thought the average of these 100 runs. Mean ± SD values of sensitivity, specificity and accuracy obtained for all the patients were 43.99 ± 17.73, 85.91 ± 5.32 and 80.08 ± 8.16 respectively.

Conclusion: The information provided by this decision support system may be helpful to patients with T1D to take actions to anticipate the occurrence of nocturnal hypoglycemic events while they get ready to sleep.

Funding: MINECO-Spain DPI2016-78831-C2-2-R, CNPq-Brazil 202050/2015-7 and 207688/2014-1.

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Clinical Decision Support Systems - Advisors

ATTD19-0287

PREDICTION AND IDENTIFICATION OF INSULIN-INDEPENDENT DIABETES PROGRESSION FROM VIRTUAL PATIENT MODEL

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Background and Aim: Pathophysiological cause of Type 2 diabetes (T2D) has various complexities and uncertainties. The uncertainties includes amount of insulin being secreted, uptake of glucose among secreted insulin (insulin sensitivity), effects of Leptin and Ghrelin on insulin secretion to capture the condition of obesity and the role of Free Fatty Acids (FFA). The aim of this research is to propose a virtual patient model that incorporates all the quantities relating to blood glucose homeostasis by considering these uncertainties in order to mimic the pathophysiology of T2D patients.

Method: An integrated semi-empirical model comprising of 15 nonlinear coupled differential equations to anticipate the time profile of glucose variation for future events has been developed by assimilating the major hormonal effects. Using numerical techniques and optimization methods in Simulation Analysis and Modelling software (SAAM II, The Epsilon Group®), the model output variables have been estimated. One-at-a-time approach from local sensitivity analysis was used to find the most influential parameters in affecting the model dynamics.

Results: The model has been validated using Oral Glucose Tolerance Test (OGTT) and Meal Tolerance Test (MTT) T2D patient data from the literature. The clinically significant indices such as Insulin Resistance, Leptin Resistance, High FFA sensitivity and Ghrelin sensitivity were calculated.

Conclusion: From the simulated results, one could infer the causes of T2D with obese through the identified sensitive parameters of the proposed virtual patient. Therefore, the treatment can be primarily focused on impaired indices to attain the normal Glycemic range.

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Clinical Decision Support Systems - Advisors

ATTD19-0289

REAL WORLD COMPARISON BETWEEN APP ENGAGEMENT OF A DIGITAL THERAPEUTIC AND BLOOD GLUCOSE LEVEL MANAGEMENT AMONG PATIENTS WITH TYPE-2 DIABETES IN SOUTH ASIA

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Aim: Glycemic control among patients in South Asia is very poor. We evaluate the effectiveness of the Wellthy Care™ (WC) app in changing behaviour to improve blood glucose (BG) levels.

Methods: We used de-identified data from 102 participants enrolled in a 16-week lifestyle modification program delivered through WC. The program was developed in lines with the AADE7™ guidelines and in collaboration with the RSSDI, and included artificial intelligence powered real-time feedback and coaching from a remote health coach.

Results: A significant difference between the mean pre- and post-intervention FBS (145.38 vs 134.3 mg/dl, $p=0.0234$) and PBS (187.84 vs 166.36 mg/dl, $p=0.0287$) values was observed. The average total per-patient-week app engagement instances and duration were 12.25 and 11 minutes, respectively.

The relation between app engagement and change in FBS and PBS was studied. It was found that there was a stepwise decrease in FBS and PBS levels as app engagement level increased. The lowest tertile of app engagers reduced their FBS by 0.18 mg/dl; the middle tertile of app engagers reduced their FBS and PBS by

7.25 and 2.84 mg/dl, respectively; and those in the highest tertile of app engagers reduced their FBS by 21.4 mg/dl ($p = 0.018$, highest vs lowest), and PBS by 22.03 mg/dl ($p = 0.023$, highest vs middle; $p = 0.0022$, highest vs lowest).

Conclusion: In low cost and infrastructure economies like India, increased engagement of a digital therapeutic like Wellthy Care™ can further improve patients' BG control, without any additional burden on existing healthcare infrastructure.

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Clinical Decision Support Systems - Advisors

ATTD19-0291

GLUCOTAB@MOBILECARE: ACCEPTANCE, USABILITY, SAFETY AND EFFICACY OF THE TABLET-BASED BASAL-INSULIN ALGORITHM FOR GLYCEMIC MANAGEMENT IN PATIENTS WITH TYPE-2-DIABETES RECEIVING HOME NURSING CARE – STUDY PROTOCOL

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Introduction: Diabetes management can be complex and error-prone in elderly patients, thus international guidelines recommend simple therapy regimens with low hypoglycemia risk. To facilitate diabetes management an algorithm for basal or basal-plus insulin therapy was developed and incorporated into a tablet-based workflow and decision support system (GlucoTab@MobileCare).

Methods: In this open-label, single-centre, non-controlled study, the acceptance, usability, safety and efficacy of GlucoTab@MobileCare using a basal or basal-plus insulin algorithm in elderly patients with type-2-diabetes receiving home nursing care by the Austrian Red Cross Graz is investigated. During a three months treatment period, patients receive basal or basal-plus insulin therapy once daily suggested by the GlucoTab@MobileCare algorithm. For the primary outcome the percentage of actions GlucoTab@MobileCare supports either to capture BG values or provide insulin dose suggestions according to the algorithm will be analysed. Secondary outcomes include days with fasting blood glucose in target according to health status, mean glucose, HbA1c changes, user practicability and satisfaction with GlucoTab@MobileCare.

Results: Nine patients (5 females; age 83 years (range 63–88); initial HbA1c 62 mmol/mol (38–76); initial basal insulin dose 18 U (13–45)) were included and currently undergo the last study month. So far, no severe hypoglycemic event or diabetes-related hospitalization was observed.

Conclusion: The basal and basal-plus insulin algorithm shows good performance. It can be assumed that home diabetes management in the elderly can safely be achieved by the decision support system GlucoTab@MobileCare without requiring hospitalization or frequent contact to general practitioners in home nursing care.

Trial registration number: DRKS00015059 (German Clinical Trials Register).

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Clinical Decision Support Systems - Advisors

ATTD19-0293

WELLTHY CARE™, A DIGITAL THERAPEUTIC IMPROVES PHYSICAL ACTIVITY AND LOGGING PATIENT JOURNEY DATA IN PATIENTS WITH TYPE-2 DIABETES IN INDIA

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Aim: The amount of physical activity among patients in India is very poor. We evaluate the effectiveness of the Wellthy Care™ (WC) app in changing health behaviour to improve physical activity by coaching and nudging them with the help of an artificial intelligence (AI) powered chatbot.

Methods: We used de-identified data from 130 participants enrolled in a 16-week lifestyle modification program delivered through WC. The program was developed in lines with the AADE7™ guidelines and in collaboration with the RSSDI, and included artificial intelligence powered real-time feedback and coaching from a remote health coach (HC).

Results: The 130 participants included 84 males and 46 females (average age = 51.73 years). We examined the correlation of the HC chats and AI chats with the number of patient inputted logs (PIL) per week and weekly physical active time (WAT), and found that they had a strong positive correlation with PIL (HC: $r = 0.74$, AI: $r = 0.85$, $p < 0.001$) and WAT (HC: $r = 0.66$, AI: $r = 0.77$, $p < 0.001$).

The average WAT and PIL at the final week of the program was significantly higher than in the first week of the program (WAT: 3.42 vs 133 minutes, $p < 0.0001$; PIL: 1 vs 16 logs, $p < 0.0001$).

Conclusion: The results confirm that an AI-powered digital therapeutic like WC can be an effective prescriptive tool for physicians to help their patients improve physical activity and to gain insight into that patient's lifestyle journey between two appointments.

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Clinical Decision Support Systems - Advisors

ATTD19-0300

IMPROVING INSULIN INJECTION TECHNIQUE AND PATIENT SATISFACTION WITH INSULCLOCK®

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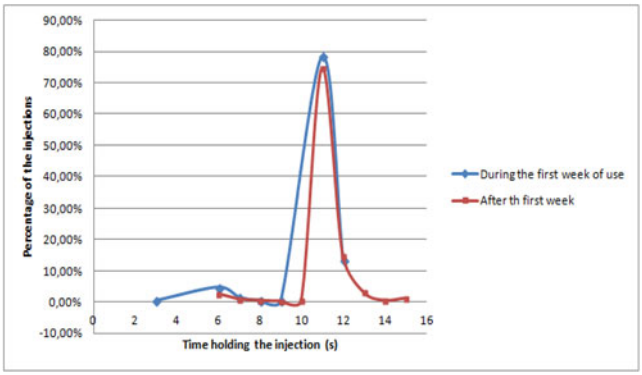
Background: Achieving and maintaining controlled glycemic levels is challenging in people with insulin-treated DM, being poor treatment adherence and suboptimal insulin injections the main obstacles to treatment success. Insulin manufacturers recommend maintaining the needle under the skin at least 6 seconds after the user primes the dose button. Insulclock®, an electronic device to be plugged into the insulin pen, records the



time of injection and makes an alert if the injection time is shorter than 6 seconds.

Methods: we measured the time of injection with Insulclock®, one week before and two weeks after setting this alarm function in 8 patients with type 1 diabetes. The Insulin Treatment Satisfaction Questionnaire (ITSQ) questionnaire was used to assess diabetic treatment-satisfaction.

Results: Performance tests revealed that Insulclock® time of injection was long after the alarm function was used (5,37% vs 2.61% of injections shorter than 7 seconds, $p < 0.05$). (Figure 1) The ITSQ showed a self-perceived benefit with the insulclock use.

Conclusions: Insulclock® insulin time duration function offers possibilities for insulin-treated diabetes self-management that would help healthcare providers and insulin users to avoid frequent errors in insulin administration.

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Clinical Decision Support Systems - Advisors

ATTD19-0303

APPLICATION OF USABILITY ENGINEERING TO THE DEVELOPMENT OF A PERSONALISED DECISION SUPPORT SYSTEM FOR TYPE 1 DIABETES SELF-MANAGEMENT

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Background and Aims: PEPPER (Patient Empowerment through Predictive PERsonalised decision support) is an EU-funded research project which aims to improve the self-management behaviour of adults with type 1 diabetes (T1D). Human factors and ergonomics play a key role in the development of this system.

Method: The usability engineering process for PEPPER adheres to the international standard IEC 62366-1:2015 - Application of usability engineering to medical devices. The iterative methodology includes multiple stages of formative evaluation and redevelopment involving both patients and clinicians. The first stage is an analytical study using heuristic evaluation and the keystroke-level model. The second stage is a laboratory study with users to measure performance with regard to the usability goals of simplicity, effectiveness, efficiency, and satisfaction. Finally, a contextual diary study is undertaken to understand the day-to-day user experience with PEPPER during a clinical feasibility study.

Results: The results of the analytical study produced a series of redesign recommendations to improve usability prior to the user study. Video analysis of the latter showed that users made few errors and most tasks were completed, indicating high simplicity and effectiveness respectively. The SUS questionnaire was used to determine satisfaction, excellent scores for the handset (74.3%) and good for the server (66.3%). The diary study is not yet completed.

Conclusion: The usability evaluation protocol used in PEPPER adheres to international standards. The iterative development methodology has potential to improve patient acceptance and safety.

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Clinical Decision Support Systems - Advisors

ATTD19-0315

A PILOT NON-INFERIORITY RANDOMIZED CONTROLLED TRIAL TO ASSESS AUTOMATIC ADJUSTMENTS OF INSULIN DOSES FOR PATIENTS WITH TYPE 1 DIABETES ON MULTIPLE DAILY INJECTIONS THERAPY

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Multiple daily injections (MDI) therapy for type 1 diabetes (T1D) involves basal insulin doses which keeps glucose levels constant under fasting conditions, and bolus insulin doses given at mealtime to cover meal-carbohydrates. Non-optimal basal and bolus injections contribute to the lack of satisfactory glycemic control in T1D patients. We have conducted a pilot non-inferiority, randomized, parallel study to compare the MDI treatment with daily physician-adjusted (PA) injections against MDI treatment with daily learning algorithm (LA)-adjusted injections in 21 children and adolescents (age 12 [10.75–15.25] years, HbA1c 7.9% [6.98%–10.05%]) who attended an 11-day diabetes camp. Participants wore a Freestyle Libre glucose sensor and their basal-bolus injections were adjusted every day by either a physician or our algorithm. The last seven days were used for outcome calculations. The time spent in target glucose sensor (3.9–10 mmol/L) was 39.80% (19.83%) in the LA group ($n = 10$) compared to 37.74% (16.73%, $P = 0.80$) in the PA group ($n = 10$). The time spent in hypoglycemia (< 3.9 mmol/L) was 3.52 (2.04%) in the LA group ($n = 10$) compared to 3.72 (4.45%, $P = 0.90$) in the PA group ($n = 10$). This is the first study assessing personalized day-to-day algorithmic adjustments in MDI patients. We conclude that a learning algorithm has the potential to facilitate MDI treatment therapy, and longer and larger studies are warranted.

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Clinical Decision Support Systems - Advisors

ATTD19-0319

OPTIMAL GLYCEMIC CONTROL IS CORRELATED TO BLOOD GLUCOSE LEVELS OF SYMPTOMATIC HYPOGLYCEMIA IN PATIENTS WITH DIABETES MELLITUS TYPE 1

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Purpose: To investigate the effect of the hypoglycemic profile on the glycemic control of patients with DM1.

Patients-Methods: 84 patients with DM1 (63.1% at multiple subcutaneous insulin injections, 21.4% at insulin pump therapy and 15.5% at insulin pump therapy with continuous glucose monitoring), 49 women/35 men with mean age = 43.4 ± 14.5 years, BMI = 24.7 ± 7.8 kg/m^2, mean DM duration = 24.5 ± 12 years and mean HbA_{1C} = 7.55 ± 1.35%. Anthropometric measurements, medical and hypoglycemia history were recorded.

Results: 66.7% of the patients sensed all hypoglycemic events, 19.4% not all, 5.6% did not sense nocturnal hypoglycemia, and 8.3% experienced hypoglycemia unawareness. HbA_{1C} was positively correlated with the blood glucose level of hypoglycemia sensing (r = 0.241, p = 0.038). 89.2% had hypoglycemic symptoms at blood glucose levels ≤70 mg/dl and 10.8% at glucose levels >70mg/dl. Patients with blood glucose levels of hypoglycemia awareness ≤70 mg/dl had significantly improved HbA_{1C} compared to patients with blood glucose levels of hypoglycemia awareness >70 mg/dl (7.4 ± 1.15 vs 8.96 ± 2.2, p = 0.002). In addition, 19.4% of the patients reported no hypoglycemic episodes, 33.3% 1–2 episodes/week, 22.2% 3–4 episodes/week, 13.9% reported at least one hypoglycemic event daily and 2.8% reported more than 2 events daily. As far as concern the mode of recovery, 14.3% used glucose tablets, 58.3% water with sugar or juice, and 27.4% consumed sweets. No significant correlation was found between HbA1C, frequency of hypoglycemic events and mode of recovery.

Conclusion: In patients with DM1, the blood glucose level of symptomatic hypoglycemia correlates with glycemic control regardless of the frequency of hypoglycemic events and the mode of recovery.

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ATTD19-0321

DIABETES NUTRITIONAL EDUCATION IMPROVES GLYCEMIC CONTROL AND QUALITY OF LIFE IN PATIENTS WITH DIABETES MELLITUS TYPE 1

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Purpose: To investigate the effectiveness of nutritional education on glycemic control and quality of life in patients with DM1.

Patients-Methods: 84 patients with DM1 (63.1% MDI, 21.4% CSII and 15.5%CSII with SAP), 49 females/35 males with age = 43.4 ± 14.5 years, BMI = 24.7 ± 7.8 kg/m^2, diabetes duration = 24.5 ± 12 years and HbA_{1C} = 7.55 ± 1.35%. Anthropometric measurements, demographic data, medical history were recorded and questionnaires of adherence to Mediterranean Diet (MDS), adherence to low fat diet (TLC) (MEDFICTS-short form Score) and quality of life (DQOL-SF) were answered.

Results: 67.9 % had medium and 32,1% high adherence to Mediterranean diet whilst 3,6% had high, 24,1% medium and 72,3% low adherence to TLC diet. No significant correlation was found between body weight, BMI, Mediterranean diet score (MDS), MEDFICTS score and HbA_{1C}. There was a significant negative correlation of MDS with HbA_{1C} (r = −0.213, p = 0.05) and patients with hypoglycemia awareness ≤70 mg/dl had higher MDS compared with patients with hypoglycemia awareness >70 mg/dl (32.7 ± 4.6 vs 29.1 ± 5, p = 0.039). Furthermore, patients that completed university had significantly higher MDS (+3 units) compared to those that completed education until high school (p = 0.013). MEDFICTS score was not correlated with HbA_{1C}, but had a positive correlation with dyslipidemia (r = 0.269, p = 0.008). Finally, patients that were counting carbohydrates were more satisfied compared to those who did not count and used standardized insulin units as meal bolus (p = 0.014).

Conclusion: The quality of diet (high adherence to Mediterranean diet) improves significantly glycemic control of patients with DM1, independently of body weight and diabetes nutritional education empowers their diabetes self-management, improving their quality of life.

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Clinical Decision Support Systems - Advisors

ATTD19-0326

IDENTIFICATION AND QUANTIFICATION OF UNMODELLED PHYSIOLOGICAL AND BEHAVIORAL DISTURBANCES IN TYPE 1 DIABETES

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Background: Many factors can affect blood glucose levels in type 1 diabetes (T1D), stress, exercise, treatment behaviors, and circadian rhythm to name a few, and most are ignored in practical insulin-glucose mathematical models. Using these models and regularized deconvolution allows to explain glycemic variations not associated with reported insulin doses or meals by generating additional inputs, or ''*net effects*''. Identifying patterns in such inputs may lead to more informed and potentially anticipatory insulin dosing strategies.

Methods: Using 1 month of continuous glucose monitoring, enhanced with meals and insulin injections records, we

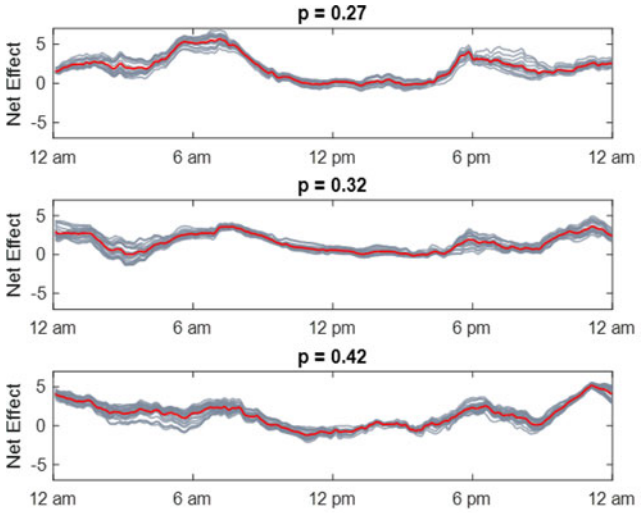

Figure 1: Clustering for a representative clinical subject. Each subplot shows an individual cluster of net effect traces that are grouped together based on their similarity. The red trace is the average value associated with each cluster. The probability of each cluster occurring is shown above each subplot.

reconstructed daily *net effect* signals for 14 T1D adult participants to NCT 03394352, using an insulin pump. 24h glucose uptake patterns (net effects) for each individual subject were then grouped using k-means clustering, cohesion and separation was assessed using silhouette coefficients (−1: no separation, 1: perfect separation, [Berkhin P. 2006])

Results: For all subjects, the analysis resolved in clearly identifiable clusters, silhouette coefficients: 0.63 ± 0.07. An example of such clustering is presented below. Each cluster is characterized by an average trace. Cluster membership frequency provides an estimate of the probability of the observed disturbance.

Conclusions: We demonstrated the feasibility of *net effect* pattern recognition in subjects with T1D, proposing a methodology capable of quantifying glycemic disturbances, their timeline, and frequency. Such method may enable care providers to detect physiological and behavioral trends, generate treatment strategies, and finally, if implemented within an appropriate closed loop scheme, enable safe and efficient anticipation of recurring disturbance patterns, e.g. meals and exercise.

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Clinical Decision Support Systems - Advisors

ATTD19-0327

FIRST ASSESSMENT OF THE PERFORMANCE OF A PERSONALIZED MACHINE LEARNING APPROACH TO PREDICTING BLOOD GLUCOSE LEVELS IN PATIENTS WITH TYPE 1 DIABETES: THE CDDIAB STUDY

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Background: Patients with type 1 diabetes (T1D) make their decisions for insulin delivery from available past and present blood glucose (BG) data and the expected effects on BG of forthcoming meals and activities according to education rules and their own experience. Enriched information on predicted BG glucose evolution could help them in better tuning insulin therapy. CDDIAB study's objective was to evaluate a new machine learning approach to predicting BG levels of each individual from a collection of personal BG measurements with contextual data.

Methods: Fourteen patients with T1D (8F/6M, age: 51+/−15, T1D duration: 26+/−17 years, HbA1c: 7.09+/−0.82%), treated by insulin pump (n = 11) or multiple daily insulin injections (n = 3) volunteered to track BG using FreeStyle Libre (n = 12), Enlite (n = 1) or Dexcom G4 (n = 1) CGM devices and log manually meal intakes and insulin doses for 30 days. Collected data were used to design patient-specific prediction models with 30- to 90-min horizons. The algorithms were initially fitted on a training dataset corresponding to an average of 9 days, using a 5-fold cross-validation method. The remaining days of available data were used to provide an unbiased evaluation of final models.

Results: The consensus Error Grid Analysis was used to evaluate accuracy of BG predictions for 30- to 90-min horizons:

Conclusion: Prediction algorithms showed promising results since 99.9, 98.6 and 96.3% of computed BG values were in EGA A + B zones at 30-, 60- and 90-min horizons, respectively. The integration into the training process of collected data by an activity tracker could further improve accuracy in future developments of the algorithm.

30-minutes Prediction

ID	MAD (mg/dl) *	MARD (%) **	Parkes A+B (%)	Parkes A (%)	Parkes B (%)	Parkes C (%)	Parkes D (%)	Parkes E (%)
Patient 01	12.19	7.78	99.68	94.10	5.59	0.32	0.00	0.00
Patient 02	11.47	5.95	99.91	97.56	2.35	0.08	0.00	0.00
Patient 03	10.70	6.76	99.99	95.90	4.09	0.01	0.00	0.00
Patient 04	12.55	9.43	99.96	91.13	8.83	0.04	0.00	0.00
Patient 05	6.55	7.29	100.00	97.10	2.90	0.00	0.00	0.00
Patient 06	7.19	4.99	100.00	97.96	2.04	0.00	0.00	0.00
Patient 07	10.90	7.93	99.89	92.08	7.81	0.11	0.00	0.00
Patient 08	10.00	6.09	100.00	96.60	3.40	0.00	0.00	0.00
Patient 09	12.87	6.55	100.00	95.29	4.72	0.00	0.00	0.00
Patient 10	12.88	9.36	99.58	90.55	9.03	0.42	0.00	0.00
Patient 11	8.60	5.56	100.00	97.33	2.67	0.00	0.00	0.00
Patient 12	11.45	7.20	99.98	93.72	6.26	0.02	0.00	0.00
Patient 13	12.36	6.30	100.00	97.20	2.80	0.00	0.00	0.00
Patient 14	9.65	6.57	100.00	96.50	3.50	0.00	0.00	0.00
MEAN ± SD	10.67 ± 2.05	6.98 ± 1.30	99.93 ± 0.13	95.22 ± 2.49	4.71 ± 2.41	0.07 ± 0.13	0.00 ± 0.00	0.00 ± 0.00

60-minutes Prediction

ID	MAD (mg/dl) *	MARD (%) **	Parkes A+B (%)	Parkes A (%)	Parkes B (%)	Parkes C (%)	Parkes D (%)	Parkes E (%)
Patient 01	27.95	17.75	97.50	71.70	25.80	2.40	0.10	0.00
Patient 02	26.31	13.93	98.40	82.30	16.10	1.40	0.20	0.00
Patient 03	23.72	14.79	98.70	77.20	21.50	1.30	0.00	0.00
Patient 04	28.45	21.55	97.40	64.40	33.00	2.50	0.00	0.00
Patient 05	14.35	9.63	100.00	87.50	12.50	0.00	0.00	0.00
Patient 06	18.43	15.58	98.50	88.30	10.20	1.50	0.00	0.00
Patient 07	28.51	14.21	99.10	77.00	22.10	0.90	0.00	0.00
Patient 08	28.20	14.22	97.20	64.50	32.70	2.80	0.00	0.00
Patient 09	17.14	19.99	99.50	86.10	13.40	0.60	0.00	0.00
Patient 10	23.34	13.40	99.50	77.20	22.30	0.50	0.00	0.00
Patient 11	13.55	10.75	97.50	83.40	14.10	2.50	0.00	0.00
Patient 12	22.68	14.49	97.50	83.00	14.50	2.40	0.10	0.00
Patient 13	27.81	14.83	99.10	81.30	17.80	0.90	0.00	0.00
Patient 14	17.73	11.42	100.00	86.10	13.90	0.00	0.00	0.00
MEAN ± SD	22.73 ± 5.49	14.78 ± 3.25	98.56 ± 1.00	79.29 ± 7.83	19.28 ± 7.27	1.41 ± 0.97	0.03 ± 0.06	0.00 ± 0.00

90-minutes Prediction

Id	MAD (mg/dl) *	MARD (%) **	Parkes A+B (%)	Parkes A (%)	Parkes B (%)	Parkes C (%)	Parkes D (%)	Parkes E (%)
Patient 01	37.87	25.27	92.60	57.60	35.00	6.90	0.50	0.00
Patient 02	41.88	21.26	96.40	65.20	31.20	3.50	0.10	0.00
Patient 03	34.30	20.96	96.90	60.80	36.10	2.90	0.20	0.00
Patient 04	38.19	30.09	94.80	51.70	43.10	4.60	0.60	0.00
Patient 05	19.93	13.21	99.90	76.30	23.60	0.10	0.00	0.00
Patient 06	25.88	20.87	98.90	62.10	36.80	1.20	0.00	0.00
Patient 07	39.01	19.74	96.60	64.60	32.00	3.00	0.30	0.00
Patient 08	34.10	19.80	92.50	55.70	36.80	7.30	0.10	0.00
Patient 09	27.44	24.63	95.50	68.70	26.80	3.60	0.90	0.00
Patient 10	30.55	17.28	98.30	67.80	30.50	1.60	0.00	0.00
Patient 11	18.20	20.41	95.70	69.90	25.80	4.30	0.00	0.00
Patient 12	31.51	17.77	96.20	72.20	24.00	3.40	0.50	0.00
Patient 13	40.33	22.22	95.50	67.70	27.80	4.50	0.00	0.00
Patient 14	25.43	17.40	98.30	71.80	26.50	1.70	0.00	0.00
MEAN ± SD	31.76 ± 7.53	20.78 ± 4.08	96.29 ± 2.15	65.15 ± 6.92	31.14 ± 5.79	3.47 ± 2.02	0.23 ± 0.29	0.00 ± 0.00

* MAD = Mean Absolute Deviation
** MARD = Mean Absolute Relative Deviation

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Clinical Decision Support Systems - Advisors

ATTD19-0335

A K-NEAREST-NEIGHBORS APPROACH TO THE DESIGN OF AN MDI DECISION SUPPORT SYSTEM IN TYPE 1 DIABETES

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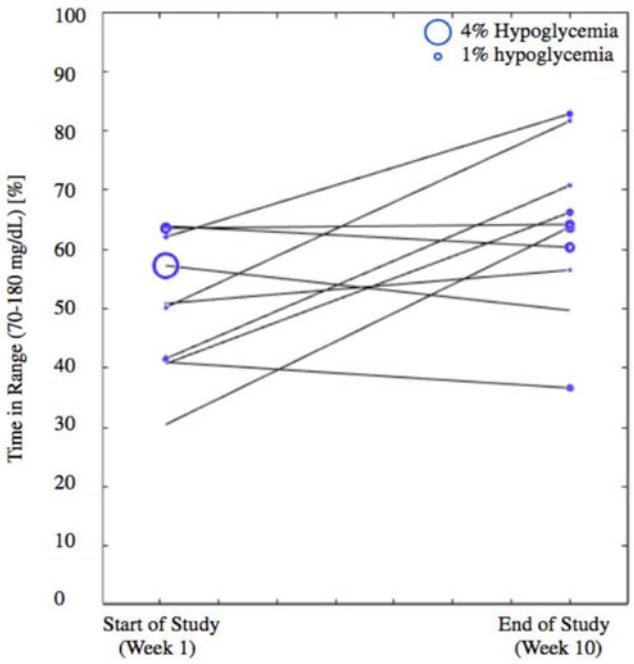
Background: We leveraged a machine learning algorithm, K-nearest-neighbors (KNN), to develop a decision support system (DSS) for people with type 1 diabetes (T1D) using multiple daily injections (MDI). Our recommendation engine utilizes CGM and insulin pen data to identify problems with glycemic control and provide dosing recommendations.

Methods: CGM, meal and insulin data are summarized into a feature vector describing problems with glucose control. A KNN is used to map these features to the best recommendation that reduces hypoglycemia (<70 mg/dL) and improves time-in-range (70–180 mg/dL). The KNN is curated from CGM data collected from 10 virtual patients exhibiting varying weight, TDIR, and circadian insulin sensitivities. The accuracy of feature-to-recommendation mapping was optimized using Greedy-Variable-Selection.

Results: Weekly recommendations from the KNN-DSS were validated during a 2-month in-silico trial of 10 new virtual patients exhibiting diverse meal scenarios and imposed insulin dosing errors. The KNN engine improved time-in-range from 47.7% at baseline, to 58.7% after two months of use of the engine (22.9% increase, $p < 0.001$). Hypoglycemia was reduced from 1.21% at baseline, to 0.93% after two months of use (23.42% decrease, $p < 0.05$). We further compared the KNN-DSS recommendations to physician recommendations on data collected from 10 subjects with T1D during a 4-week free-living study. The KNN-DSS engine recommendations were consistent with those of endocrinologists, and differed significantly 1% of the time.



Conclusion: The KNN-based recommendation engine identifies problems in glycemic control and provides insulin dose recommendations that improve time-in-range, reduce hypoglycemia, and are consistent with physician recommendations.

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Clinical Decision Support Systems - Advisors

ATTD19-0367

META-ANALYSIS OF THE EFFECTIVENESS OF THE DIGITAL INSULIN TITRATION APPS AND PLATFORMS

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Insulin intensification/titration is part of the standards of medical care in the treatment of diabetes. Despite acknowledgement that basal insulin requires titration, most people with type 2 diabetes (T2DM) are unsuccessful in achieving glycemic targets. Factors, including treatment inertia, are evident as the initial insulin dose often increases only slightly from date of initiation to six months. Consequently, there is a need for increasing healthcare providers' awareness about insulin treatment inertia, as well as more effective, patient-centered titration strategies. The pharmacologic approaches to glycemic treatment call on patients to employ a self-titration insulin algorithm, as it has been shown to improve glycemic control in those with T2DM. A recent national survey indicated that over 80 percent of diabetes educators have influence over the use of technology, including apps & devices. Moreover, the same practitioners play a critical role in insulin initiation and influence insulin titration. There are many insulin titration options that include digital therapeutics. The purpose of this meta-analysis is to examine the effectiveness and design of FDA-cleared insulin titration apps.

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Clinical Decision Support Systems - Advisors

ATTD19-0398

PREDICTING THE EARLY RISK OF CHRONIC KIDNEY DISEASE IN PEOPLE WITH DIABETES USING REAL WORLD DATA

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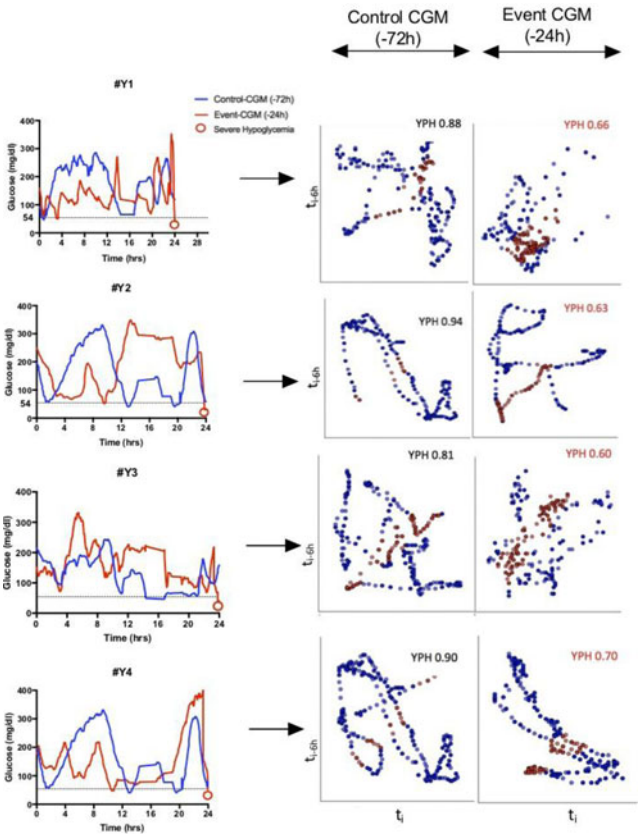
The volume of real-world medical data from clinics and medical doctors' offices greatly exceeds the information available in clinical trials. However, the increase in data volume comes at the expense of completeness, uniformity, and control when using such real-world data. We have explored Real World Data originating from more than half a million people with diabetes. A predictive algorithm was developed with the goal to identify those people with diabetes, who are at high risk for developing chronic kidney disease in the near future. In a direct comparison between the real world data-based predictive algorithm and similar, prior algorithms derived from clinical trial data, the Roche/IBM algorithm outperforms all tested methods in a one-to-one comparison as well as study cohorts selected *a posteriori*. Furthermore, the Roche/IBM algorithm was applied to independent real world data originating from almost 100.000 further people with diabetes and the prior findings were confirmed. The Roche/IBM algorithm also proved to be more tolerant to missing data. These results may fuel the fundamental debate on the future of medical evidence in that costly, long-lasting clinical trials on a limited number of patients may one day be augmented by Real World Data-driven risk assessments.



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Clinical Decision Support Systems - Advisors

ATTD19-0442

A MACHINE-LEARNING APPROACH TO EARLY RECOGNITION OF SEVERE HYPOGLYCEMIA: THE SHAPE OF GLUCOSE VARIABILITY

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Background: Adults with Type 1 Diabetes (T1D) who have previously experienced severe hypoglycemia (SH) have shown greater glycemic variability (GV) than matched T1D controls from the T1D-Exchange cohort. A real-time method to predict increased risk of SH and alert patients has not yet been developed. We assessed whether a new-approach to quantify GV based on a machine-learning-artificial-intelligence-algorithm could identify daily risk of SH based on 24-hours CGM-data.

Methods: CGM-profiles from children with T1D who had an episode of SH were analyzed during two 24-hour periods: 24-hrs prior to the SH(Event-CGM) and 72-hrs prior to the event(Control-CGM). Data were analyzed using a linear-support-vector-machine(SVM) algorithm which provided a fitting score (Yale-Padova-Harvard score,YPH;*Figure*) for both 24-hour-windows. Coefficient of variation (CV) and standard deviation(SD) were estimated from the same 24-hour windows.

Results: CGM profiles on *four*participants (11.7 ± 4.6y; 1F; T1D duration 3.4 ± 1.9y; BMI 18.0 ± 2.7) were assessed. YPH-score was lower during the 24-hrs preceding the SH event as compared to 72-h preceding the SH event (0.65 ± 0.04 vs 0.88 ± 0.05, p = 0.003) while no differences were observed in the CV(p = 0.873) or SD(p = 0.651), in both the periods.

Conclusion: Current indices of GV fail to provide a day-by-day risk for SH. Although additional studies are needed to confirm our findings, it appears that a YPH score ≤0.70 based on 24-hrs-CGM plots indicates a high risk of SH event on the following day. The ability to predict elevated risk of SH in real-time can potentially alert patients to take extra precautions managing their glucose levels during intervals where the risk of SH event is elevated.

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Closed-loop System and Algorithm

ATTD19-0089

A HYBRID CLOSED-LOOP (HCL) SYSTEM THAT ADDRESSES PERSISTENT SENSOR OVER/UNDER-READING CHALLENGES

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Table: Glycemic outcome during over- & under-reading sensor challenge		
	OVER-READING SENSOR (N=6)	UNDER-READING SENSOR (N=6)
Mean of reference glucose, mg/dL (mmol/L)	79.7 ± 11.9 (4.42 ± 0.66)	161.3 ± 25.6 (8.96 ± 1.42)
SD of reference glucose, mg/mL (mmol/L)	17.7 ± 7.4 (0.98 ± 0.41)	31.4 ± 21.9 (1.74 ± 1.22)
Minimum reference glucose, mg/mL (mmol/L)	62.1 ± 12.9 (3.45 ± 0.72)	123.3 ± 24.8 (6.85 ± 1.38)
Maximum reference glucose, mg/mL (mmol/L)	124.8 ± 17.0 (6.93 ± 0.94)	221.7 ± 66.3 (12.32 ± 3.68)
Mean of ARD of sensor, %	47.5 ± 17.9	38.5 ± 5.3
Bias of sensor, %	+47.3 ± 18.0	-38.5 ± 5.3
All values are shown as average ± SD. ARD=Absolute relative difference.		

Background: A prototype enhanced hybrid closed loop (e-HCL) system was designed to, not only, automatically adjust basal insulin delivery based on sensor glucose (SG) values, but automatically deliver correction boluses to minimize hyperglycemia. This system was evaluated by introducing intentional sensor over/under-reading challenges during a supervised overnight hotel period.

Methods: Twelve subjects (aged 48 [39–57] years) with T1D were recruited. Half underwent a sensor over-reading challenge, while the remainder underwent a sensor under-reading challenge. The morning of trial start, a new sensor was inserted that was calibrated multiple times with either a positive or negative bias of up to 35%, until dinner. The HCL control was initiated at ~10:00 PM and i-STAT reference measurements were collected at regular intervals until ~8:00 AM, next day.

Results: The reference blood glucose (BG) values are shown for each challenge during a persistent over-reading sensor and under-reading sensor bias, for the entire trial. Even with an extreme over-reading bias, no BG value <50 mg/dL (<2.8 mmol/L) occurred. For the under-reading bias scenario, no BG value >180 mg/dL (>10 mmol/L) occurred after 3:00 AM. The only instances of BG values >250 mg/dL (>13.9 mmol/L) were during three hours post-dinner for two subjects.

Conclusion: These early findings support the robustness of a prototype e-HCL system to lessen hyperglycemic and/or hypoglycemic exposure during extreme sensor inaccuracy scenarios. This is important as sensor-responsive closed-loop systems are key to improved glycemia from day to day, and throughout the day and night.

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ATTD19-0102

RESULTS OF USING HYBRID CLOSED LOOP SYSTEM ON TYPE 1 DIABETES-THE GREEK EXPERIENCE

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Objective:to investigate the differences on glycated hemoglobin (HbA1c) and hypoglycemic episodes among patients with Type 1 Diabetes (T1D), before and after the inception of hybrid closed loop (HCL) system.

Methods: The sample consisted of 11 participants (4 male and 7 female) with T1D, who initiated the HCL system composed by Dana R insulin pump, Dexcom G5 continuous glucose monitoring (CGM), two smartphone applications, xDrip and OpenAPS for android, combined with Nightscout (a web based, real-time, data management system). The mean HbA_{1c} of the sample was 7,9mg/dl. The data were recorded before and 3 months after closing the loop.

Table 1:Sample description

Participants	Male - Female	Age (years)	HbA1c (average)
11	4 - 7	39,6	7,9mg/dl

Results : *Baseline* average HbA1c of the sample was 7.9mg/dl which downgraded to 6.9mg/dl 3 months after closing the loop. A reduction on hypoglycemic episodes was also recorded. The mean hypoglycemic episodes of the sample was 5.4(n) before HCL which was reduced to 1.5(n) the first week and to 0.8(n) 3 months after using the HCL system (table 2).

Table 2: Results

HbA1c- after 3 months (average)	Hypoglycemic episodes week 0 (n)	Hypoglycemic episodes week 1 (n)	Hypoglycemic episodes after 3 months (n)
6,9mg/dl	5,4	1,5	0,8

Conclusions: Although this is only a small sample, the first results seem to be very hopeful for optimizing the management of TD1 by reducing the hypoglycemic episodes and the HbA1c levels. More studies are needed using bigger samples in order to have more clear results on the outcomes of using HCL.

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ATTD19-0105

COST EFFECITVENESS ANALYSIS OF MINIMED 670G SYSTEM VERSUS CONTINUOUS SUBCUTANEOUS INSULIN INFUSION, IN INDIVIDUALS WITH TYPE 1 DIABETES

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Objective: To assess the cost-effectiveness of the MiniMedTM670G system (HCL) versus Continuous Subcutaneous Insulin Infusion alone (CSII) in people with type 1 diabetes (T1D) in Sweden.

Methods: The IQVIA CORE Diabetes model was used to perform cost-effectiveness analyses over patient lifetimes, from a societal perspective. Clinical data were sourced from pivotal clinical study comparing HCL with CSII in patients with T1D. The use of the HCL system was associated with a reduction in HbA1c of 0.5% (5.5 mmol/mol), from 7.4% (57 mmol/mol) at baseline to 6.9% (52 mmol/mol) at the end of the study phase. Cost data, expressed in 2018 Swedish krona (SEK), were

obtained from published literature. Clinical and cost outcomes were discounted at 3% annually

Results: HCL was associated with a quality-adjusted life-year (QALY) gain of 1.90 but higher overall costs versus CSII, leading to an incremental cost-effectiveness ratio (ICER) of SEK 164,236 per QALY gained. Use of HCL resulted in a lower cumulative incidence of diabetes-related complications. Higher HCL acquisition costs were partially offset by reduced complication costs and productivity losses. In patients poorly controlled at baseline, HCL was associated with 2.25 incremental QALYs versus CSII, yielding an ICER of SEK 15,830 per QALY gained. Extensive sensitivity analysis on key drivers confirmed the robustness of results.

Conclusion: HCL was associated with clinical benefits and quality of life improvements in patients with T1D relative to CSII. At a willingness-to-pay threshold of SEK 300,000 per QALY gained, HCL likely represent a cost-effective treatment option for patients with T1D in Sweden.

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Closed-loop System and Algorithm

ATTD19-0107

THE IMPORTANCE OF MEAL MACRONUTRIENT CONTENT IN ARTIFICIAL PANCREAS USE WITH UNANNOUNCED (NO MEAL BOLUS) HIGH CARBOHYDRATE MEALS

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The effect of different macronutrients on the meal response in artificial pancreas (AP) systems is still unknown. Of special interest is the ability of future AP systems to minimize hyperglycemia when a meal bolus is not delivered. We previously reported results in an AP trial with an unannounced (no meal bolus) 65g carbohydrate lunch, with meals varying across subjects. We have subsequently analyzed the glycemic response to these meals by the meal fat and protein content, based on US dietary guidelines.

30 adult subjects with type 1 diabetes (T1D) completed the 65g carbohydrate meal twice, with no insulin bolus, each time under closed-loop control. Time in target glucose range 70-180 mg/dL for the 5-hour postprandial period for low and medium fat meals trended higher compared to the high fat meals (36.4 and 43.2 vs. 22.0%, respectively). Mean glucose and time >180 mg/dL also trended higher for high fat meals (Table 1). Higher amounts of protein did not significantly affect glycemic outcomes. There were no significant differences in insulin delivery between high vs. low/medium fat meals (Table 2).

Table 1. Glycemic metrics and total insulin delivered for the 5-hour postprandial period after the unannounced (no meal bolus) 65-gram carbohydrate lunch during the AP study. While only 8 meals were classified as high fat per US dietary guidelines, CGM glucose levels for the high fat meals trended higher compared to the medium and low fat meals.

Metric	High Fat Meal (n=8)	Medium Fat Meal (n=9)	Low Fat Meal (n=43)	High Fat vs. Med/Low Fat
Mean glucose [mg/dL]	219.0	197.3	207.5	p=0.35
Mean % time <70 [mg/dL]	0.0	0.2	1.3	p=0.06
Mean % time 70-180 [mg/dL]	22.0	43.2	36.4	p=0.10
Mean % time >180 [mg/dL]	78.0	56.8	62.6	p=0.09
Mean total insulin [Units]	7.2	7.3	8.3	p=0.57

Table 2. Mean total hourly insulin delivery by the AP for the 5-hour postprandial period after the unannounced (no meal bolus) 65-gram carbohydrate lunch. Peak mean total insulin delivery occurred at 1-2 hours after the unannounced meal for high, medium and low fat meals. There were no significant differences in mean insulin delivery between the meal types at any of the 5 hour intervals.

Mean Insulin Delivery (units)	High Fat Meal (n=8)	Medium Fat Meal (n=9)	Low Fat Meal (n=43)	High Fat vs. Med/Low Fat
0-1 Hour	1.23	1.41	1.71	p=0.12
1-2 Hours	2.44	2.52	2.76	p=0.59
2-3 Hours	1.54	1.51	1.77	p=0.61
3-4 Hours	1.31	1.29	1.34	p=0.95
4-5 Hours	1.08	0.96	1.09	p=0.97

These findings show that AP systems used without meal boluses are still challenged with high fat, high carbohydrate meals. To improve performance, AP systems may need to be informed of high fat meals, or use automated meal detection to give biphasic or multiphasic meal boluses. Our data suggest even with new AP systems coming to market there remains an important role in optimizing nutrition choices and meal bolus strategies in people with T1D.

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Closed-loop System and Algorithm

ATTD19-0109

THE PREVALENCE AND PATTERN OF PRESENTATION OF DIABETES MELLITUS IN PATIENTS ATTENDING IMSUT HOSPITAL ORLU AND IMSS HOSPITAL UMUAGUMA BETWEEN JANUARY 2018 TO SEPTEMBER 2018

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Diabetes mellitus is a clinical syndrome characterized by hyperglycemia, polyuria, polydypsia and weight loss. It is a condition, insulin is not adequately secreted or the target cells do not respond to the available insulin in the body or a combination of these factors. The general objective of this study is to determine the prevalence and pattern of presentation of diabetes mellitus among patients attending IMSUT Hospital orlu and IMSS Hospital Umuguma and the specific objective is to access the socio demographic determinants of diabetes mellitus,to access the prevalence and common symptoms at presentation and to determine the no of patients with diabetic complications at presentation. A total of 2,028 patients had diabetes and 676 were selected using systematic random sampling with an interview of 3.The six hundred and seventy six diabetic patients were selected for the study.The result shows a total of 18,912 patients attended the designated hospitals wishing the period under review. 2,028 were diabetic giving a prevalence of 107.2 per 1000 patients (107%). Out of the 676 diabetic patients studied, 75% had onset of the disease at the age above 40 years (507)while the remaining 25% had onset of the disease at the age of 40 years (169). The most affected age group was 51- 60 years with the percentage of 0.6% The most common presenting symptom is polyuria (100%). This was followed by polydypsia (96.6%) with the least

presenting symptom being prunitus vulva discharge seen in pregnant women (2.7%), the symptoms at presentation include polyuria, polydysia, weight loss, fever, cough, catarrh blurring vision.

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ATTD19-0112

MODIFIED BERGMAN MINIMAL MODEL FOR GLUCOSE-INSULIN DYNAMICS AND ESTIMATION OF MODEL PARAMETERS FOR INDIAN POPULATION

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Objective: We present a slightly *modified insulin dynamics in the Bergmann minimal model* (BMM) to accurately calculate the physiological parameters. Using this model, we also investigate the differences in Indian and Caucasian population in terms of the model parameters i.e. ***a) Insulin sensitivity b) Glucose effectiveness c) Insulin degradation and clearance rate***.

Data Collection: A total of 16 healthy Indian subjects (age: 23 ± 2yrs; BMI: 22.62 ± 1.66kg/m^2; HbA1c: $5.1 \pm 0.53\%$) were tested for glucose tolerance using OGTT. At time, 75 gm glucose solution was ingested and the blood samples were collected at -15,0,5,10,20,30,40,50,60,75,90,120,150, and 180 minutes. The samples were analysed in three different labs.

Methods: Various de-noising techniques such as Savitzky Golay, Hampel and gradient thresholding methods were used to filter intravenous glucose and insulin measurements. The filtered data was used in nonlinear *least squares and maximum likelihood estimation* algorithms to estimate the physiological parameters of modified *BMM*.

$$\dot{G} = -p_1(G(t) - G_b) - X(t)G(t) + \frac{U_G(t)}{V_G}$$

$$\dot{X}(t) = -p_2X(t) + p_3(I(t) - I_b)$$

Modified insulin dynamics	Original insulin dynamics
$\dot{I}(t) = -n(I(t) - I_b) + \left(\frac{Y + K\tanh[\beta(G(t) - G_b)]}{V_I}\right)$	$\dot{I}(t) = -n(I(t) - I_b) + \gamma(G(t) - h)^+ t$

Results: The mean percentage fit error using modified BMM is 11.4% as compared to mean percentage fit error of 31.3% using original BMM. Comparative analysis on the two population, it is found that, in comparison with the Caucasian population, the mean insulin sensitivity of Indian population is lower by 11.38%, and the mean glucose effectiveness, insulin degradation rate and insulin clearance rate in the Indian population are higher by 44.89%, 24.57% and 37.78% respectively.

Conclusion: Our study presents a modified BMM which is superior as compared to original BMM. Comparative analysis suggests that physiological parameters of the Indian population are different from the Caucasian population.

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Closed-loop System and Algorithm

ATTD19-0122

A DEEP NEURAL NETWORK PLATFORM FOR PREDICTING BLOOD GLUCOSE LEVELS

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Background and Aims: Deep neural networks have been proven to be a powerful tool in processing healthcare data to achieve state-of-art performance in diagnosis, classification and prediction. However, the complexity of these artificial intelligence (AI) tools limits its wide application in hospitals for clinicians and other healthcare professionals. This work aims to bridge that gap and uses glucose data prediction as a practical example.

Methods: We designed a graphical user interface (GUI) based on PyQt5 Python toolkit that enables people to generate and train the deep neural network conveniently, and implemented the model on smartphones showing the prediction curves. Users can tune the hyperparameters of the model more efficiently with less effort required to understand the codes. Specifically, healthcare professionals can master the software in short time and use machine learning techniques as an expert system. By using this framework, a dilated Recurrent Neural Network model to predict the future glucose levels in the next 30 minutes is trained.

Results: We trained a 6-layer deep neuron network using the proposed framework. It achieved an accuracy of 19.04 on the *OhioT1DM dataset* in terms of RMSE, which is one of the best in the literature. Furthermore, the trained model was implemented on smartphones, which can explicitly show predicted future blood glucose.

Conclusion: An easy-to-use deep neural network framework with GUI was developed. It was used in training glucose prediction models, and the model can be implemented on smartphones conveniently. It achieves a good prediction accuracy.

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ATTD19-0133

A MODEL-BASED ALGORITHM DESIGN (MBAD) PLATFORM: FROM VIRTUAL-PATIENTS TO FEASIBILITY IN A SINGLE STEP

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Background: A model-based algorithm design (MBAD) platform incorporating a virtual-patient simulator(Benyamin, Di et al. 2018)[1], facilitates the refinement of closed-loop (CL) algorithms *in-silico* thereby accelerating advancement into the clinical feasibility phase. The glycemic data obtained from an

	In-silico with 2087 virtual-patients	Clinical feasibility study, n=12
% time in 70 – 180 mg/dL (3.9 – 10 mmol/L)	84.4 ± 7.4 %	84.4 ± 4.9%
% < 70 mg/dL (3.9 mmol/L)	1.7 ± 2.6 %	4.3 ± 1.5 %
% > 180 mg/dL (10 mmol/L)	13.9 ± 7.4 %	11.3 ± 4.4 %
Average Glucose mg/dL (mmol/L)	136.7 ± 12.3 mg/dL (7.6 ± 0.7 mmol/L)	125.3 ± 6.9 mg/dL (7.0 ± 0.4 mmol/L)

in-silico evaluation and subsequent clinical feasibility study of an enhanced hybrid CL (e-HCL) study were compared.

Methods: Closed-loop algorithm gains were optimized using machine-learning to determine a performance function score that incorporates a tradeoff between percentage of time in target glucose range (TIR) and time in hypoglycemia for a prototype e-HCL system. The clinical evaluation occurred during a 1-week supervised hotel phase followed by 3-weeks at-home with 12 T1D subjects (age 48 [39–57] years; HbA1c 6.8% [6.2-7.2). Glycemia data from this feasibility study were compared to that determined in 2087 virtual patients.

Results: (see **Table**) The *in-silico* evaluation was conducted over 19 days and the study was conducted over five weeks. It had a bias of about 0%, 2.6%, −2.6%, −11.4 mg/dL (0.6 mmol/L) for % time in 70 to 180 mg/dL, % time <70 mg/dL (<3.9 mmol/L), % time >180 mg/dL (>10 mmol/L), and average SG, respectively. Challenges included the small study group, behavioral conditions (e.g., meal bolus timing) and simulation of real-life system performance (e.g., system adaptation over 4-weeks of continuous operation).

Conclusion: Overall the MBAD platform reduced the time to develop and test a new prototype HCL system in free-living conditions. Lessons learned are being implemented on the next iteration of the e-HCL system which will be tested in a clinical study.

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Closed-loop System and Algorithm

ATTD19-0148

A HYBRID CLOSED-LOOP (HCL) SYSTEM THAT ADDRESSES UNANNOUNCED MEALS

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Background: Hyperglycemia in type 1 diabetes (T1D) can occur due to stress, illness, dawn phenomenon, an insufficient pre-meal insulin bolus amount, or an unannounced meal (no pre-meal insulin bolus delivery). A prototype enhanced hybrid closed-loop system was designed to automatically adjust basal insulin delivery based on sensor glucose (SG) values and deliver correction boluses to address hyperglycemia. This system was assessed within a supervised setting to evaluate its effectiveness in minimizing hyperglycemia due to unannounced meals.

Methods: Twelve subjects (aged 48 [39–57]years; HbA1c 6.8 [6.2–7.2]%) with T1D skilled in carbohydrate-counting underwent a 1-week period of system use in a supervised hotel setting, followed by a 3-week unsupervised at-home period of system use. On the second day of the hotel period, subjects consumed an estimated 40-gram carbohydrate dinner without a premeal-bolus. Five hours of postprandial data were analyzed and compared to data captured after varied-carbohydrate meals consumed during the at-home period, which were always accompanied by a premeal-bolus.

Table: Five hours postprandial glycemic outcome

	Hotel Period (No Premeal Boluses)	At-home Period (Meals with Premeal Boluses)					
Number of meals	12	85		33		11	
*Meal size, grams	40	40	P**	60	P**	80	P**
Mean postprandial SG peak, mg/dL (mmol/L)	213 ± 46 (11.83 ± 2.55)	175 ± 42 (9.72 ± 2.33)	0.0062	189 ± 55 (10.50 ± 3.05)	0.2030	188 ± 47 (10.44 ± 2.61)	0.2254
Mean SG 5 hours post-meal, mg/dL (mmol/L)	167 ± 34 (9.27 ± 1.88)	131 ± 28 (7.27 ± 1.55)	0.0002	151 ± 38 (8.38 ± 2.11)	0.2420	159 ± 32 (8.83 ± 1.77)	0.5828
Percentage of time in sensor glucose range 5 hours post- meal							
70-180 mg/dL (3.9-10 mmol/L)	64 ± 31%	85 ± 20%	0.0034	72 ± 31%	0.4694	65 ± 30%	0.9517
>180 mg/dL (>10 mmol/L)	35 ± 32%	12 ± 20%	0.0010	26 ± 31%	0.3871	34 ± 30%	0.9500

All values are shown as average ± SD.
*Carbohydrate amount as estimated and recorded by the patient.
**Two sample t-test between no meal-bolus dinner challenge (hotel) and premeal bolus (at-home).

Results: Glycemic outcomes from the supervised and unsupervised periods of system use are listed in the table. The unannounced 40-gram meals resulted in postprandial SG values and percentages of time across SG value ranges similar to those observed for 80-gram meals accompanied by a premeal-bolus.

Conclusion: These data indicate that the prototype system performed well during an unannounced meal challenge and suggest that it can minimize hyperglycemia exposure due to a medium-sized meal of 40 grams to the same extent as a large-sized meal of 80 grams accompanied by a premeal-bolus.

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Closed-loop System and Algorithm

ATTD19-0151

MULTI-HOUR BLOOD GLUCOSE PREDICTION IN T1D: A PATIENT-SPECIFIC APPROACH USING SHALLOW NEURAL NETWORK MODELS

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Background and Aims: Considering current insulin action profiles and the nature of glycemic disturbances in type 1 diabetes (T1D) there is an acute need for longer-term, accurate, blood glucose predictions to inform insulin dosing schedules, automated or not. However, current methods only achieve acceptable accuracy about one-hour ahead while prandial excursions and insulin action profiles last for 4 to 6 hours. In this work,

horizon	RMSE	MARD	Clark Error Grid Analysis				
			Zone A	Zone B	Zone C	Zone D	Zone E
60min	24 ± 5mg/dL	15 ± 3%	74%	23%	0%	3%	0%
90min	28 ± 6mg/dL	18 ± 3%	65%	29%	0%	6%	0%
120min	34 ± 6mg/dL	21 ± 4%	58%	36%	0%	6%	0%
240min	44 ± 9mg/dL	28 ± 6%	49%	44%	1%	6%	0%

Table 1: Accuracy metrics and percentages of predictions within Clarke error zones of clinical correctness. Both Zone A and B are clinically acceptable errors with Zone A corresponding to deviations of <20%, or predictions in the hypoglycemic range and Zone B corresponding to benign errors. Zones C-E are potentially dangerous, with increasing degree of inaccuracy.

we presents models leveraging shallow neural networks applied to prediction horizons of 60–240min.

Methods: Individualized predictive models are constructed using a neural-network based approach using CGM and insulin pump data. Models are developed and tested on previously collected data from a cohort of twenty-four subjects with T1D. Aggregate data is leveraged in a transfer learning approach for improved accuracy for patients where data is limited.

Results: Prediction accuracy as computed by root mean square error was 24 ± 5 mgdL, 28 ± 6 mgdL, 34 ± 6 mgdL, and 44 ± 9mg/dL for 60, 90, 120, and 240 minutes respectively. For all prediction horizons, at least 93% of predictions are clinically acceptable by the Clarke error grid. Variance of historic CGM values was a strong predictor for the need of transfer learning approaches.

Conclusions: A shallow neural network, using features extracted from past CGM data and insulin logs and a novel, physiologically-motivated network structure, is able to achieve night time and day time multi-hour glucose predictions with high accuracy. These models pave the way for new advisory and closed loop algorithms able to encompass most of the insulin action time-frame.

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Closed-loop System and Algorithm

ATTD19-0180

REDUCING HYPOGLYCEMIA IN TYPE 1 PATIENTS WITH AUTOMATED INSULIN SUSPENSION IN A REAL LIFE SETTING IN THE UK

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Background: The real-world effectiveness of automated insulin suspension features was evaluated from patients with type 1 diabetes (T1D) in the UK. Automated insulin suspension has been shown to reduce the burden of hypoglycemia for patients with T1D in clinical studies.

Table1:

	SAP vs SAP+LGS group (n=31)			SAP vs SAP+SmartGuard™ group (n=55)			SAP+LGS vs SAP+SmartGuard™ group (n=139)		
	SAP	SAP+LGS	P	SAP	SAP+SmartGuard™	P	SAP+LGS	SAP+SmartGuard™	P
Duration of use (days)	124.5 ± 106.9 (106.9; 45.0-152.7)	128.9 ± 94.8 (103.9;49.9-192.5)	NS	107.1 ± 123.4 (49.4; 29.7-120.8)	241.7 ± 179.7 (239.1; 79.2-362.7)	0.0002	139.8 ± 140.1 (77.2; 36.8-210.7)	239.5 ± 173.3 (213.6; 86.5-360.1)	<0.0001
Minutes per day ≤3 mmol/L	22.0 ± 38.3 (9.0;4.9-18.6)	9.0 ± 11.5 (4.7;2.2-9.3)	0.001	19.8 ± 29.0 (11.3; 5.4-23.4)	8.2 ± 10.2 (4.9; 1.9-8.3)	<0.0001	8.2 ± 9.9 (5.1; 1.8-10.3)	6.9 ± 10.9 (3.9; 1.3-7.8)	<0.0001
Minutes per day ≤3.9 mmol/L	71.6±62.1 (57.2;37.4-76.2)	52.1 ± 43.0 (37.8; 27.2-58.4)	0.0028	72.6 ± 59.8 (62.3; 29.9-90.3)	42.2 ± 33.8 (33.2; 20.2-50.3)	<0.0001	43.2 ± 37.7 (30.7; 16.9-56.7)	33.0 ± 32.6 (25.6; 12.0-42.6)	<0.0001
Number of hypoglycaemia events/month <3 mmol/L	6.2 ± 11.0 (2.5; 1.2-5.3)	3.5 ± 4.6 (1.8; 0.7-4.3)	0.0325	6.2 ± 9.0 (3.6; 1.1-8.7)	3.1 ± 4.5 (1.8; 0.5-3.8)	0.0007	2.9 ± 3.9 (1.6; 0.3-3.5)	2.5 ± 4.4 (1.3; 0.3-2.8)	0.0259
Number of hypoglycaemia events/month <3.9 mmol/L	22.9 ± 15.0 (21.8; 10.3-29.6)	18.8 ± 13.3 (14.2; 9.1-24.5)	0.0424	24.3 ± 17.4 (21.9; 10.3-29.9)	17.4 ± 15.4 (13.0; 8.1-19.3)	<0.0001	16.2 ± 13.9 (11.4; 5.9-22.5)	13.5 ± 13.4 (10.4; 4.7-18.2)	<0.0001

Data shows mean ± Standard Deviation (median; 25th quantile- 75th quantile)

Materials and methods: We retrospectively analysed anonymised data voluntarily uploaded to CareLink™ software from patients using: sensor augmented pump without insulin suspension feature enabled (SAP), SAP with Low Glucose Suspend feature enabled (SAP+LGS) or SAP with predictive insulin suspension feature enabled (SAP+SmartGuard™) from February 2016 to June 2018. Inclusion criteria were at least 15 days of sensor data per patient with ≥70% wear time from the first day of sensor wear within the 2-year observation period. Where patients changed suspend features between SAP, LGS or SmartGuard™, within patient comparisons were made for time in range and time in hypoglycaemia.

Results: In the total study population (n = 920), patients used the system for a mean of 219 day. Patients spent less time in Sensor Glucose values ≤3 mmol/l and ≤3.9 mmol/l when using SAP+SmartGuard™ than when using SAP+LGS or SAP only. During the study duration187 patients changed groups. Within the same patient, there was a reduction not only in time but also in events <3 mmol/l and <3.9 mmol/l when patients moved from SAP to LGS and when moved from LGS to SmartGuard™ (Table1).

Conclusion: This analysis shows that sensor-augmented-pumps with automated insulin suspension technology reduced the frequency and duration of hypoglycaemic events compared to sensor-augmented-pumps with no suspension.

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Closed-loop System and Algorithm

ATTD19-0209

EXPLORATORY ANALYSIS OF HYBRID CLOSED-LOOP ALGORITHM ADAPTATION DURING MINIMED™ 670G SYSTEM USE BY CHILDREN, ADOLESCENTS, AND ADULTS

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Objective: The MiniMed™ 670G system hybrid closed-loop (HCL) algorithm adjusts multiple parameters on a daily basis according to insulin utilization and sensor glucose (SG) data. In this exploratory analysis, changes in the HCL-calculated amount of insulin used for correction of SG values >150 mg/dL (ISF),

Algorithm-calculated ISF and Umax parameters, basal percentage, time in target glucose range, and sensor glucose coefficient of variation during the MiniMed™ 670G system pivotal trials.

	Children (N=105)			Adolescents (N=30)			Adults (N=94)		
	Baseline	Study	P	Baseline	Study	P	Baseline	Study	P
ISF parameter	84.4 ± 44.5	56.9 ± 22.9	<0.001	43.2 ± 13.6	34.2 ± 11.2	<0.001	50.2 ± 19.4	47.7 ± 21.4	0.110
Umax parameter	0.8 ± 0.4	1.5 ± 0.6	<0.001	1.3 ± 0.4	2.3 ± 0.7	<0.001	1.2 ± 0.6	2.0 ± 1.5	<0.001
Basal delivery, %	44.5 ± 7.4	44.0 ± 7.3	0.728	49.7 ± 12.1	46.4 ± 8.5	0.022	54.1 ± 10.9	46.8 ± 9.4	<0.001
TIR, %	56.5 ± 11.4	65.2 ± 7.7	<0.001	60.7 ± 11.0	67.4 ± 8.2	<0.001	69.2 ± 12.0	74.0 ± 8.5	<0.001
CV, %	39.6 ± 5.4	38.5 ± 3.8	0.009	38.5 ± 4.8	36.9 ± 3.0	0.053	37.3 ± 4.8	33.9 ± 3.7	<0.001

Data are shown as mean ± standard deviation.
TIR= 70-180 mg/dL (3.9-10.0 mmol/L).
CV= Coefficient of variation.

maximum basal rate (Umax), basal-bolus percentage, and glycemic control were assessed.

Method: Patients from the MiniMed™ 670G system pivotal trials aged 7–13 years (n = 105), 14–21 years (n = 30), and 22–75 years (n = 94) used the system in Manual Mode during a baseline ttwo-week run-in phase followed by a three-month study phase in which Auto Mode was enabled. Mean changes in algorithm parameters (i.e., ISF and Umax), percentage of basal insulin delivered per day, TIR (70–180 mg/dL, 3.9–10 mmol/L), and the coefficient of variation (CV) between baseline run-in and study phase were analyzed and evaluated by age group.

Result: The table shows that there were significant changes in the ISF parameter (children and adolescents) and Umax parameter (all age groups). Basal insulin delivery was <50% in all age groups and significantly decreased from baseline in adolescents and adults. Children had the lowest baseline basal percentage without a change. Both TIR and CV improved in all age groups.

Conclusion: Algorithm adaptation resulted in improved glycemia in all age groups. The improved glucose control in children and adolescents, despite a significant decrease in ISF parameter, suggests that automating insulin delivery may allow for correction of high glucose values in a more safe and effective manner than can be achieved in open loop.

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Closed-loop System and Algorithm

ATTD19-0231

COMMITTED MOVING HORIZON ESTIMATION FOR MEAL DETECTION AND ESTIMATION IN TYPE 1 DIABETES

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Background and Aims: Most artificial pancreas systems rely on manual meal announcements to calculate the correct post-meal insulin therapy. These announcements are a burden to patients; they are also inherently dangerous, as wrong or late meal announcements can compromise therapy. To rectify this situation, we develop and evaluate a meal detection and estimation (MDE) algorithm called Committed Moving Horizon Estimation (C-MHE) to automatically detect meals and estimate the carbohydrate (CHO) amount consumed based on CGM readings.

TABLE I

CHARACTERISTICS AND MDE RESULTS OF EACH MEAL: THREE LARGE MEALS: BREAKFAST, LUNCH, DINNER; AND THREE SMALL SNACKS ARE RANDOMLY GENERATED IN A SINGLE DAY.

	breakfast	snack1	lunch	snack2	dinner	snack3
Probability of Occurrence	100%	50%	100%	50%	100%	50%
CHO amount (g)	40-60	5-25	70-110	5-25	55-75	5-15
Time of day (h)	6:00-10:00	8:00-11:00	11:00-15:00	15:00-18:00	18:00-22:00	22:00-00:00
MDE performance						
Onset Deviation (min)	21.97	27.00	15.28	26.42	16.32	25.08
CHO Deviation (g)	51.44	19.45	23.30	20.27	18.93	15.10
Detection rate	100%	100%	100%	100%	100%	66.67%

Methods: We use a virtual patient based on Hovorka's model to generate CGM readings. At each time step, C-MHE invokes a Moving Horizon Estimator (MHE) that uses a linearized physiological model to estimate meal disturbances from a bounded window of CGM measurements. In C-MHE, we aggregate MHE estimations from multiple time steps to achieve a balance of estimations with different future and past awareness ratios. We design an online algorithm that, from the C-MHE estimations, detects meals and estimate their CHO amount with guaranteed time delay. We evaluate the performance using 10 random repetitions of a 3-day experiment.

Results: C-MHE can detect both large meals and snacks. We achieve an overall 95.38% daily detection rate. For the large meals, which are the most important to accurately detect, we obtain a 100% detection rate, with an average 14.9 minutes onset deviation, and a 76.6% CHO amount estimation accuracy.

Conclusions: Our C-MHE algorithm performs well in simulation. It thus has the potential to replace manual CHO announcements thereby enabling fully closed-loop T1D therapy.

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Closed-loop System and Algorithm

ATTD19-0238

ROBUST DATA-DRIVEN CONTROL OF ARTIFICIAL PANCREAS SYSTEMS USING NEURAL NETWORKS

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Background and Aims: Machine learning approaches are becoming increasingly prevalent in blood glucose (BG)

Dataset	#P	# Tr	T.H.	Avg. Hyper	Avg. Hypo	Avg. TiR
Clin. Trial	15	100	7.5h	15.3	2.7	68.9
Synthetic	6	180	8.5h	1.6	3.6	92.95

Table 1: Number of patients, trials, control horizon, average percent of time in hyper and hypoglycemia, and average percent time-in-range for our learned control scheme.

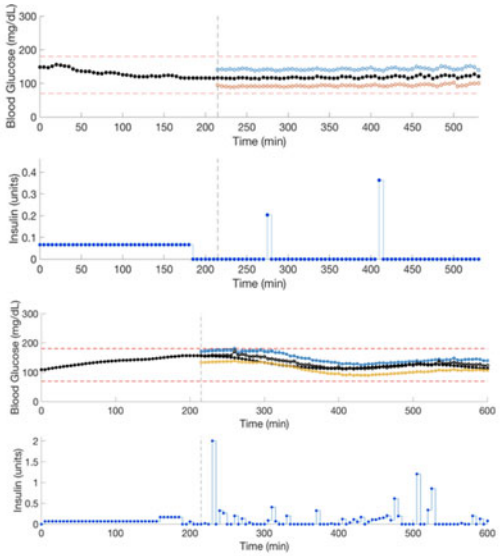

Figure 1: Example instances when the controller gave a "correction bolus" after the patient ate a meal, then reverted back to injecting only basal insulin of < 0.5U/5min until glucose began to rise again, where smaller "correction boluses" are given. Lower, upper, and mean quantile predictions are shown with actual data in black. Controller is turned on at vertical gray line. (Top) real patient data (Bottom) virtual patient data.

prediction, however, these black box models lack the verification guarantees necessary for use in safety critical systems such as the artificial pancreas. In this work we present a novel approach to patient-specific BG prediction and real-time control using quantile predictive neural networks which provide model guarantees and bounds on risk for hypoglycemia and hyperglycemia.

Methods: Patient-specific neural network models are learned from historic CGM and insulin pump data. These models predict mean as well as upper and lower 95% quantile bounds for a 30min prediction horizon. A 6hr prediction horizon is obtained by recursive unfolding of the networks, and a model predictive control scheme which adjusts both basal and bolus insulin is learned in real-time using the inferred models.

Results: The approach is evaluated on data obtained from a set of 17 patients over a course of 40 nights, as well as on 6 virtual patients through the UVA-Padova T1D simulator. Learned control schemes maintain 69% time-in-range for real-patient data, and 93% time-in-range for synthetic patients over 8hours. Disturbances from large, unannounced meals and sensor errors are handled.

Conclusion: We formulate a robust control scheme for calculating safe and optimal insulin delivery to ensure harmful risks of hypo and hyperglycemia are bound by quantile models while the mean remains close to target. The approach is evaluated over a variety of datasets, initial histories, patient models, and unannounced meal sizes, showing promising results.

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Closed-loop System and Algorithm

ATTD19-0262

A MODEL-FREE APPROACH TO INSULIN PUMP FAILURES DETECTION

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Objective: Insulin pump faults (IPF) are a critical hazard in contemporary diabetes technology for the safety of a diabetic subject. The majority of strategies for automated detection of IPF resort to the identification of a model of the patient's physiology, a task that has proven to be challenging. We propose a new approach based on unsupervised machine learning algorithms for anomaly detection (AD) that avoids the complex model identification task. Additionally, the method does not require data with tagged examples of fault occurrence to recognize them.

Method: The validation is performed *in silico*, using the Padova/UVA T1D simulator. Using N = 100 virtual patients we simulated 30 days of closed-loop therapy, with 1 IPF per patient. We extracted features that account for the dynamics of T1D physiology and is suited for detecting IPF. We tested three AD algorithms, i.e. Isolation Forest (iF), Local Outlier Factor (LOF) and Connectivity-Based Outlier Factor (COF) and compared their performance with respect to traditional Multivariate Control Chart method (MCC).

Result: Sensitivity was 81% for iF and precision 92%, i.e. only 7 false positives (FP) among all the subjects (0.002 FP per day on average). LOF exhibited similar precision (94%), but lower sensitivity (58%). MCC shows slightly worse performance (sensitivity 60% and precision 82%). COF was outperformed (50% sensitivity and 78% precision).

Conclusion: The performance obtained in the *in silico* validation shows encouraging results for further development of this innovative method for IPF automated detection.

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Closed-loop System and Algorithm

ATTD19-0270

AN ANDROIDAPS HYBRID CLOSED LOOP SYSTEM IN A HOME SETTING IS SAFE AND LEADS TO BETTER METABOLIC CONTROL

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Background: We face a massive expansion of unofficial Open Source Hybrid Closed-Loop systems among patients. Nevertheless, long term safety data on these systems are missing.

Objective: To assess the safety, effectiveness and technical pitfalls of hybrid closed-loop AndroidAPS in home use.

Methods: Twenty-two children (aged 3–14 years) with T1D participated in this retrospective study. All participants used the Open Source Hybrid Closed-Loop AndroidAPS (Smartphone with AndroidAPS app, DANA DiabecareR pump and Dexcom G5^{TM}Sensor) for at least 3 months. Parameters of glycemic control for the first three months on AndroidAPS and the three preceding months, which were on Sensor Augmented Therapy (SAP), were compared. Participants also answered a questionnaire on the number of severe adverse events (DKA or severe hypoglycaemia) and the frequency and types of technical pitfalls during AndroidAPS treatment.

Results: The median time on AndroidAPS was 8.7 months (range 3.1 to 17.8 months), representing 219 patient-months in total. No episodes of severe hypoglycaemia or DKA were reported. AndroidAPS use reduced HbA1c by 5 mmol/mol (52 → 47 mmol/mol; $p < 0.02$) compared with previous SAP therapy. This corresponded with a higher proportion of time in range (3.9 to 10 mmol/l) (67.6 → 83.6%;$p = 0.03$) and target (3.9 to 7.8 mmol/l) (59 → 69%; $p = 0.03$) and significantly lower mean blood glucose (7.9 → 7.1 mmol/l; $p = 0.03$). All these improvements were reported despite no change of time in hypoglycemia (5.2 → 4.4%; $p = 0.5$). The optimization of basal settings and necessity of upgrade of Android-smartphones were the most common reasons for temporary interruption of AndroidAPS.

Conclusion: AndroidAPS represents a safe way to improve metabolic control in children with T1D.

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Closed-loop System and Algorithm

ATTD19-0341

COORDINATING LOW-GLUCOSE INSULIN SUSPENSION AND CARBOHYDRATE RECOMMENDATIONS FOR HYPOGLYCAEMIA MINIMISATION

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Objective: Predictive low-glucose suspension systems (PLGS) have been proven to be an effective way to reduce hypoglycaemia. Similarly, carbohydrate recommenders (CDR) have shown to be a successful method to protect against hypoglycaemia. However, the simultaneous utilisations of these two methods might lead to hyperglycaemia due to overlapping actions. Hence, an effective way to combine these two methods is desired. This work presents a novel strategy to coordinate the use of PLGS and CDR with the aim of reducing the risk of hypoglycaemia without increasing hyperglycaemia.

Method: A validated model-based glucose forecasting algorithm is employed to implement PLGS and CDR methods. The CDR accounts for the suspension time of PLGS when recommending carbohydrate dose. The proposed algorithm was tuned and evaluated using the UVa-Padova T1DM simulator and compared against the PLGS, CDR algorithms, and the utilisation of these two methods without coordination. Prediction horizon, suspension thresholds, suspension time and resume time were *in silico* optimised.

Result: *In silico* results on adult population ($n = 10$) over one-month scenario showed significant ($p < 0.01$) reduction in percentage time under target (<70 mg/dL) (coordinated 0.96 ± 0.65% vs. PLGS 1.77 ± 0.70% vs. CDR 2.70 ± 1.39% vs. uncoordinated 0.86 ± 0.52%) without significant clinical increase in percentage time above target (>180mg/dL) (coordinated 16.48 ± 7.67% vs. PLGS 15.48 ± 6.44% vs. CDR 13.14 ± 7.88% vs. uncoordinated 20.05 ± 12.47%), and mean glucose levels (coordinated 140.2 ± 10.8 mg/dL vs. PLGS 137.6 ± 8.8mg/dL vs. CDR 134.0 ± 11.8 mg/dL vs. uncoordinated 147.0 ± 18.6mg/dL).

Conclusion: The proposed method for coordinating PLGS and CDR algorithms provides a significant improvement in the reduction of hypoglycaemia without a clinically significant increase in hyperglycaemia.

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Closed-loop System and Algorithm

ATTD19-0380

TIME IN TARGET GLUCOSE RANGE AND GLYCATED HEMOGLOBIN LEVELS DURING THE MINIMED 670G SYSTEM PIVOTAL TRIALS

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Background: Continuous glucose monitoring (CGM) provides sensor glucose (SG) data enabling calculation of time below, above, and within target glucose range (TIR), in addition to several metrics of glucose variability, all of which are used to make informed clinical decisions that optimize the management of diabetes. Data from patients completing the MiniMed™ 670G system with SmartGuard™ pivotal trials were analyzed to assess glycemic control and correlation between TIR and HbA1c.

Methods: For this exploratory analysis, glycemic outcomes data during the baseline two-week run-in and three-month study phases from MiniMed™ 670G system pivotal trial patients aged <14 years ($N = 105$, mean ± SD age of 10.8 ± 1.8 years) and ≥14 years ($N = 124$, 37.8 ± 16.5 years) were analyzed. The relationship between HbA1c and TIR (70-180 mg/dL, 3.9-10.0 mmol/L) and the TIR variability were evaluated.

Time in target glucose range (TIR) and TIR variability stratified across HbA1c levels during the MiniMed™ 670G system pivotal trials, by age group.

*HbA1c Range, % (mmol/mol)	Patients <14 years of age				Patients ≥14 years of age			
	Run-in		Study		Run-in		Study	
	TIR, % Mean ± SD (N)	CV, %	TIR, % Mean ± SD (N)	CV, %	TIR, % Mean ± SD (N)	CV, %	TIR, % Mean ± SD (N)	CV, %
5.0, 5.5 (31, 37)	--	--	--	--	85.5 ± 0.0 (1)	--	69.5 ± 0.0 (1)	--
5.5, 6.0 (37, 42)	73.2 ± 0.0 (1)	--	--	--	83.1 ± 6.3 (5)	7.52	83.0 ± 6.0 (10)	7.23
6.0, 6.5 (42, 48)	69.8 ± 13.9 (5)	19.97	70.9 ± 3.7 (3)	5.16	72.7 ± 7.2 (18)	9.86	75.7 ± 5.9 (27)	7.85
6.5, 7.0 (48, 53)	67.6 ± 5.8 (9)	8.56	73.9 ± 5.9 (17)	7.98	71.6 ± 8.4 (22)	11.67	73.8 ± 7.3 (39)	9.88
7.0, 7.5 (53, 58)	61.3 ± 9.2 (23)	14.99	66.2 ± 6.2 (34)	9.34	68.5 ± 10.1 (26)	14.69	69.5 ± 7.3 (30)	10.52
7.5, 8.0 (58, 64)	56.4 ± 9.2 (26)	16.25	62.9 ± 5.4 (36)	8.54	60.6 ± 9.4 (23)	15.57	63.1 ± 6.7 (13)	10.68
8.0, 8.5 (64, 69)	49.7 ± 7.1 (21)	14.31	58.4 ± 5.4 (8)	9.25	62.3 ± 16.6 (14)	26.61	52.1 ± 7.5 (3)	14.48
8.5, 9.0 (69, 75)	46.5 ± 10.2 (12)	22.05	55.1 ± 5.2 (5)	9.49	59.5 ± 11.6 (10)	19.49	--	--
9.0, 9.5 (75, 80)	45.1 ± 12.1 (5)	26.74	50.1 ± 0.7 (2)	1.32	45.3 ± 12.2 (3)	26.90	--	--
9.5, 10.0 (80, 86)	54.7 ± 4.2 (3)	7.76	--	--	57.0 ± 0.9 (2)	1.58	--	--

*= Baseline run-in HbA1c range and end of study HbA1c range were used to determine correlation for the run-in and study phase, respectively.
TIR= 70-180 mg/dL (3.9-10.0 mmol/L).
CV= Coefficient of variation.

Results: Both TIR and HbA1c improved in both groups (Table). Significant negative correlations were also observed: <14 years, Baseline slope = –0.04, intercept = 10.25, $r^2 = 0.38$ and Study slope = –0.05, intercept = 10.94, $r^2 = 0.48$; ≥14 years, Baseline slope = –0.04, intercept = 10.10, $r^2 = 0.29$ and Study slope = –0.04, intercept = 9.89, $r^2 = 0.37$. For the younger group, a significant change in TIR coefficient of variation was observed ($p = 0.016$).

Conclusions: MiniMed™ 670G system use over 3 months demonstrated a greater TIR for a lower HbA1c. Data also suggest significantly reduced TIR variability among the younger patients, but a moderate reduction in those ≥14 years. Although TIR tightly correlated with HbA1c, the combination of TIR and HbA1c may better characterize overall glycemic control than either metric alone.

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Closed-loop System and Algorithm

ATTD19-0390

GLUCOSE CONTROL USING A STANDARD VS AN ENHANCED HYBRID CLOSED LOOP SYSTEM: A PILOT STUDY

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Background: Hybrid closed loop (HCL) insulin delivery with the Medtronic MiniMed 670G system is safe and effective in improving glycemia for people with type 1 diabetes (T1D).

Aims: To compare glucose control, CL exits and alarm frequency with standard HCL vs enhanced HCL (eHCL) systems.

Methods: Pump experienced adults with T1D (n = 11; 9 women; mean[SD] age: 51[15]Y; HbA1c 7.5[1.0]%) were assigned in random order HCL and eHCL for 1 week each in a supervised live-in setting. eHCL incorporated enhanced bolus reminders and iterative changes broadening glucose and insulin delivery parameters permitting persistence in CL. For both HCL and eHCL insulin delivery was by a Medtronic pump with identical interventions (missed bolus, exercise, high GI and high fat meals), insulin action times and insulin-carbohydrate ratios implemented. The primary outcome was CGM time in target range.

Results: eHCL resulted in fewer CL alerts and exits. Time in target and mean glucose favored eHCL but did not reach significance (Table). No episodes of severe hypoglycemia or ketoacidosis occurred.

Conclusions: Iterative changes to the Medtronic HCL system resulted in trends towards improved glycemia, fewer CL exits and alerts without compromising safety, despite multiple food and exercise challenges during the study periods. Longer term studies at home are required to confirm these findings.

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Closed-loop System and Algorithm

ATTD19-0421

SYNERGY OF REINFORCEMENT LEARNING AND CLASSICAL DATA ANALYSIS APPROACHES IN ADAPTIVE, PERSONALISED INSULIN BASAL/BOLUS OPTIMISATION

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Background and Aims: The reinforcement learning (RL) based adaptive basal-bolus algorithm (ABBA) provides a holistic approach to personalised glucose control for diabetic patients with either self-monitored blood glucose or a Continuous Glucose Monitoring (CGM) device. Each day, ABBA outputs one basal rate (BR) and three bolus doses. This study aims to enhance the performance of CGM version of ABBA in the announcement of disturbances during the day.

Method: The established version of ABBA outputs the BR and bolus doses to be delivered on the following day. In an attempt to make ABBA more responsive and efficient in compensating errors in the disturbances within one day, an additional module has been integrated. This module is triggered on the basis of the latest glucose measurement and the glucose trend. The proposed approach has been evaluated *in silico* with the FDA-approved UVa/Padova T1DM Simulator v3.2 - with 33 virtual subjects for 15 simulation days. Different variabilities and uniformly distributed uncertainties were considered. The results of the ABBA with and without the insulin adjustment module were compared.

Results: The preliminary results are promising: Table 1 shows that the enhanced ABBA achieved better performance in terms of percentage of time in all glycaemic ranges, while Fig. 1 and Fig. 2 visualise the effect of the additional module in ABBA.

Table 1: Blood glucose control performance of day 9 to day 15

	BG Mean	% in range 70-180 mg/dL	% < 70 mg/dL	% > 180 mg/dL	TDI
A. Adults					
ABBA	138.8±14.5	88.9±13.0	0.5±0.8	10.6±12.7	42.13±9.46
ABBA*	137.6±9.7	**89.2±8.6**	**0.0±0.1**	**10.8±8.6**	41.76±9.20
B. Adolescents					
ABBA	153.1±12.6	73.4±13.1	0.6±1.0	26.0±13.2	30.36±7.28
ABBA*	146.0±11.1	**79.6±13.8**	**0.3±0.3**	**20.1±13.8**	31.16±7.43
C. Children					
ABBA	155.0±7.5	72.1±8.2	0.5±1.1	27.5±8.0	15.03±3.31
ABBA*	151.7±8.7	**73.6±10.4**	**0.0±0.0**	**26.4±10.4**	14.92±3.46

ABBA*: ABBA with additional module

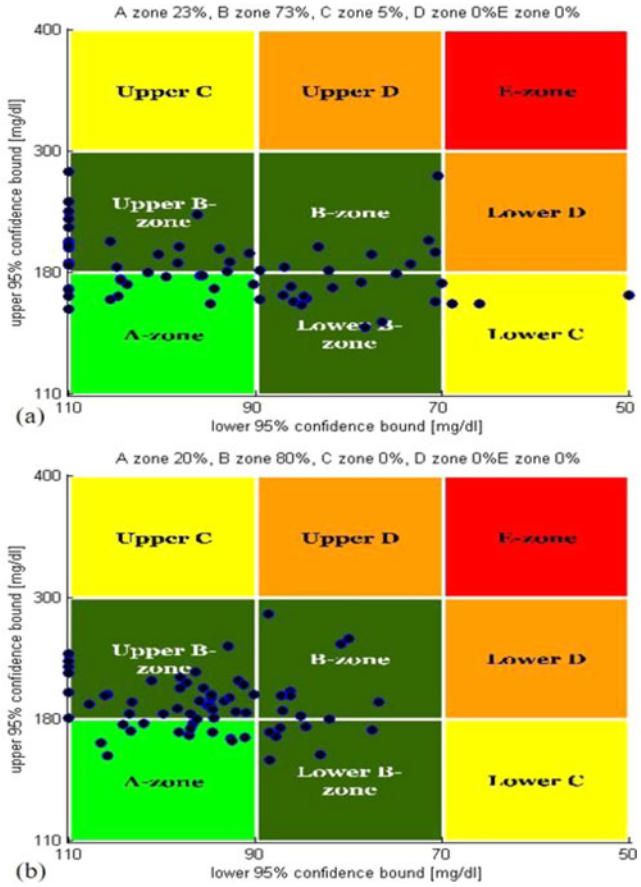

Fig. 1. The control-variability grid analysis (CVGA) plot for a) ABBA, b) ABBA*, during day 9 to day 15

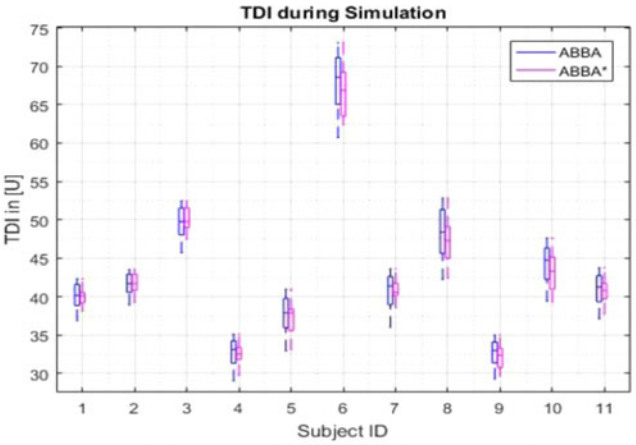

Fig. 2. Total daily insulin (TDI) of ABBA and ABBA*, during day 9 to day 15

Conclusion: The enhanced CGM version of ABBA not only learns from the user's daily patterns and habits, but is able to react to new, not necessary repeated, disturbances. The concept may be extended to other kind of disturbances, e.g. exercise.

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Closed-loop System and Algorithm

ATTD19-0430

SENSOR AUGMENTED PUMP WITH PREDICTED LOW-GLUCOSE SUSPEND FUNCTION. SHORT AND MEDIUM-TERM OUTCOMES IN YOUNG CHILDREN

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Introduction: Sensor augmented pump therapy with SmartGuard function (SAP-SmartGuard) has demonstrated a reduction in the risk of hypoglycemia. Pediatric studies are mainly short-term, do not reflect anthropometric impact.

Objective: To evaluate, in our pediatric population with diabetes mellitus type 1 (DM1), the effect of SAP-SmartGuard on glycemic control, hypoglycemia and anthropometrics.

Material And Methods: Retrospective observational study of patients with DM1 in treatment with SAP-SmartGuard. We analyzed at the beginning and every 6 months: weight, height, BMI, growth rate (GR), HbA1c, insulin dose and bolus number. We collected CGM data from the first month and then every 6 months: mean glucose (MG), mean standard deviation of glucose (SDMG), mean time in suspension on ''low'' and ''before low''. Statistical analysis with the SPSSv19.0 program.

Results: 16 patients (62.5% males). At baseline: age: 5.8 (3.8) years [mean (SD)], mean DM1 evolution: 2.2 (1.6) years. Previous treatment with ISCI: 37.5%.

We found a reduction of the MG ($p = 0.03$), of the SDMG, and of the AUC >140 mg / dl ($p = 0.043$). Bolus number increased ($p = 0.02$) and the % of the basal dose was reduced ($p = 0.05$) without changes in the total insulin dose. Regarding anthropometric parameters, the BMI decreased ($p = 0.019$) and the GR increased ($p = 0.012$). (Table1)

TABLE 1	BASAL	6 MONTHS (mean± SD)	p	12 MONTHS (mean± SD)	p	18 MONTHS (mean± SD)	p
Mean glucose (mg/dl)	170,0± 20,8	171,1±21,4	0,977	160,6±18,8	0,170	157,8± 14,4	0,030
SD of mean glucose (mg/dl)	61,5±10,0	63,9±11,1	0,069	60,7±13,4	0,646	58,3±7,3	0,080
Coeff cient of variation CV (SD/mean glucose)*100	36,4±5,9	37,3±5,2	0,215	37,5±4,8	0,093	37,0±3,3	0,345
Mean use of sensor (%)	91±5	93±3	0,986	90±9	0,865	94±5	0,916
Suspension "on low" (min/day)	3,9±4,1	3,1±5,1	0,447	5,5±8,0	0,953	11,4±22,1	0,588
Suspens on "before low" (min/day)	159,7±81,8	156,9±63,1	0,609	163,3±63,3	0,594	213,2±96,3	0,043
AUC <70 (mg/dl x day)	0,2±0,2	0,2±0,2	0,914	0,3±0,2	0,581	0,4±0,3	0,854
AUC>140 (mg/dl x day)	46,9±11	31,8±11,7	0,285	44,3±10,7	0,345	31,4±9,5	0,043
Bolus number/day	4,5±1,7	8,1±3,4	0,020	9,4±3,6	0,012	8,8±4,1	0,046
HbA1c (%) (mean± SD)	7,4±0,5	7,5±0,5	0,462	7,1%±0,4	0,341	7,1±0,6	0,581
Weight (SD)	+0,6±0,7	+0,2±0,7	0,221	+0,2±0,5	0,117	+0,1±0,3	0,176
BMI (SD)	+0,4±0,6	+0,1±0,7	0,346	-0,1±0,6	0,019	+0,1±0,3	0,043
Height (SD)	+0,1±0,9	+0,1±1,1	0,972	+0,3±0,8	0,139	0,0±0,3	0,225
Growth rate (SD)	-0,3±1,5	-0,1±1,6	0,209	+0,9±1,3	0,012	+0,8±0,4	0,080
Daily insulin total dose (UI/Kg)	0,76±0,21	0,77±0,15	0,780	0,78±0,12	0,445	0,72±0,07	0,500
Basal dose %	50±10	40±10	0,097	38±10	0,005	40±0	0,046

Conclusions: Among our patients, the SAP-SmartGuard allows to reduce the BMI and improve the growth rate. Time in hypoglycemia is minimal since the beginning of SAP-SmartGuard, and there is a progressive improvement in the measures of hyperglycemia and variability, without significant changes in HbA1c.

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Closed-loop System and Algorithm

ATTD19-0435

EXERCISE USING HYBRID CLOSED LOOP THERAPY: LESSONS FROM PEDIATRICS

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Exercise is difficult to manage in children and adolescents with Type 1 Diabetes (T1D). Hybrid closed-loop (HCL) therapy offers novel insulin delivery that is glucose responsive, and alters how clinicians and patients with T1D should approach exercise. We present two cases highlighting this challenge:

Case 1: N.W. is a 9-year-old female who exercises for two hours with a running club in the afternoons. Prior to activity, she consumes 15–30 grams of carbohydrate with no insulin bolus to prevent hypoglycemia. This practice prevented hypoglycemia when using traditional insulin pump therapy. When using HCL therapy, this approach caused an initial increase in insulin delivery via autobasal delivery, which then led to hypoglycemia during activity. N.W. now reduces or eliminates preemptive carbohydrate consumption prior to exercise and uses a temporary target to reduce autobasal delivery.

Case 2: O.H. is a 12-year-old male who participates in cross country running 3 times/week for 2–3 hours. When using HCL, O.H. experiences hypoglycemia in the first 1-2 hours of running after consuming pre-exercise carbohydrates without a bolus, presumably due to autobasal insulin delivery. O.H. now utilizes a temporary target during exercise and reduces or eliminates carbohydrate consumption prior to exercise.

Discussion: When using HCL, new ways of mitigating hypoglycemia must be considered. Pre-exercise carbohydrate consumption may result in subsequent low glucose levels due to the autobasal delivery to contend with rising glucose levels. Reducing pre-exercise carbohydrates may decrease low glucose levels during activity, and temporary target usage should be considered.

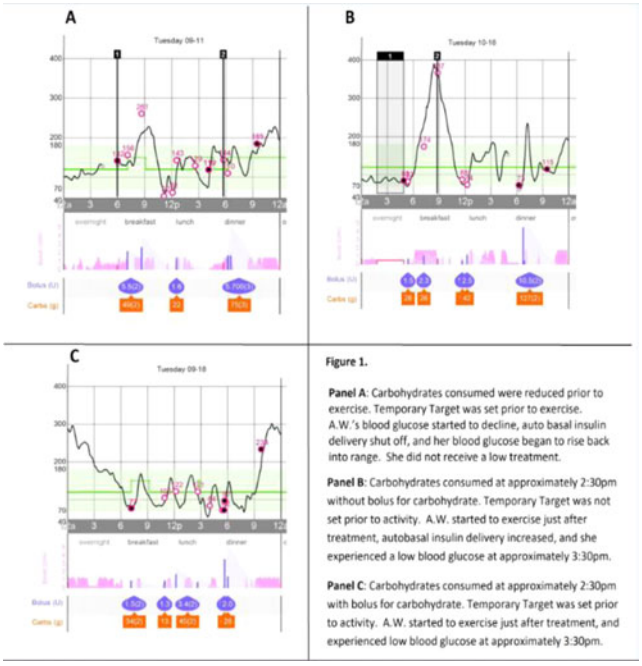

Figure 1.

Panel A: Carbohydrates consumed were reduced prior to exercise. Temporary Target was set prior to exercise. A.W.'s blood glucose started to decline, auto basal insulin delivery shut off, and her blood glucose began to rise back into range. She did not receive a low treatment.

Panel B: Carbohydrates consumed at approximately 2:30pm without bolus for carbohydrate. Temporary Target was not set prior to activity. A.W. started to exercise just after treatment, autobasal insulin delivery increased, and she experienced a low blood glucose at approximately 3:30pm.

Panel C: Carbohydrates consumed at approximately 2:30pm with bolus for carbohydrate. Temporary Target was set prior to activity. A.W. started to exercise just after treatment, and experienced low blood glucose at approximately 3:30pm.

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Closed-loop System and Algorithm

ATTD19-0458

MODELLING AND REGULATION OF THE EFFECTS OF LONG-DURATION MEDIUM-INTENSITY EXERCISE IN TYPE 1 DIABETIC PATIENTS

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Background and Aims: Physical activity is an important component in diabetes care. Although it presents many health benefits, it also presents an important challenge in glycemic control. The hormonal response to maintain homeostasis during physical activity changes the patient's glucose dynamics, thus, affecting the performance of closed-loop controllers. One of the most common interventions among patients during exercise is basal insulin reduction or suspension in order to avoid possible hypoglycemia during or after physical activity. When considering long periods of physical activity, the total suspension of insulin can lead to hypoinsulinemia.

Method: Low levels of insulin in plasma does not allow the muscle to use the glucose properly. A rebound after exercise, leading to hyperglycemia, could be product of the hypoinsulinemia and the endogenous production of glucose. Nowadays, few mathematical models were proposed for specific conditions that cannot cover the multiple glycemic responses during exercise in clinical trials. Here it is proposed to modify the DallaMan model in order to deploy the effects in endogenous glucose production, changes in insulin sensitivity and glucose utilization.

Results: Simulations with the new added dynamics during exercise showed a true potential in representing glucose excursion profiles presented in clinical data. The analysis of the effect caused by the endogenous glucose production and hypoinsulinemia, i.e. the post-exercise glucose rebound, allows determining and setting a minimum insulin constraint for closed-loop glucose controllers.

Conclusion: An exercise model representing the effects of long-term exercise of medium intensity is proposed which may be used to tune and improve glucose control algorithms.

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Devices Focused on Diabetic Preventions

ATTD19-0032

MICROALBUMINURIA IN WOMEN WITH RISK FACTORS FOR GESTATIONAL DIABETES MELLITUS IN SOME SELECTED HOSPITALS IN SOKOTO STATE, NIGERIA

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Gestational diabetes mellitus (GDM) is a common metabolic abnormality which affects approximately 2-5% of pregnancies annually. Various risk factors such as previous infants with macrosomia, a strong family history of non-insulin dependent diabetes mellitus (NIDDM) or GDM, poor glycaemic control and a high pre-pregnancy body mass index (BMI) have been implicated for the development of GDM. This study was conducted to determine the prevalence of Microalbumnuria in women with risk factors for gestational diabetes mellitus and to estimate the levels of Urinary Microalbumin in these women. In this study, 50 pregnant women with risk factors for gestational diabetes mellitus and 50 controls (pregnant women without risk factors for gestational diabetes mellitus) were evaluated for Microalbuminuria. Microalbuminuria was estimated using Turbidimetric method, Random Plasma Glucose was estimated using Glucose oxidase method, serum Urea, Creatinine and Albumin were estimated using Diacetyl Monoxime method, Jaffe Slot method and Bromo Cresol Green method respectively. The prevalence of Microalbuminuria in women with risk factors for gestational diabetes mellitus was 22%. Urinary microalbumin was significantly higher in the study subjects (56.36 ± 8.44mg/L) than in the control (17.32 ± 4.5 mg/L). The mean ± standard error of mean of random plasma glucose in the study subjects was 5.84 ± 0.16 mmol/L and that of the control was 4.33 ± 0.14 mmol/L.The mean ± standard error of mean Serum Urea, Creatinine and Albumin were 4.1 ± 0.15mmol/L, 0.70 ± 0.03mg/dL, and 3.06 ± 0.05g/dL respectively while that of the control were 3.47 ± 0.13mmol/L, 0.63 ± 0.01mg/dL and 2.78 ± 0.09g/dL respectively. Obesity was strongly correlated to microalbuminuria. Early detection of microalbuminuria will prevent the onset or the progression of renal disease in patients with Gestational Diabetes Mellitus.

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Devices Focused on Diabetic Preventions

ATTD19-0044

COMPARISON OF EFFECT OF TV VIEWING TIME AND COMPUTER USE TIME ON PHYSICAL INACTIVITY ACCORDING TO BODY MASS INDEX IN KOREAN ADOLESCENTS

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Background: Screen time is one of important components in sedentary behaviors, which are risk factors diabetes mellitus in their adult life. This study aims to compare effect of TV viewing time and computer use time on physical inactivity in Korean adolescents.

Method: We used the 3rd Korean National Health and Nutrition Examination Survey (KNHANES III) in Korea. We calculated weekly physical activity of vigorous or moderate intensity for participants between 12 and 18 years old. Screen time of weekdays and weekends were calculated separately for TV viewing time and computer use. Multiple regression was performed to elucidate association between screen time and physical activity.

Results: Among 1,033 participants, 551 were male. Mean age was 14.7 ± 1.9 years. There was significant association of weekday TV viewing time with physical activity in normal female adolescents (BMI $<23\,kg/m^2$) ($\beta = -7.70$, 95% confidence interval (CI) $-14.20 - -1.21$), while weekend computer use was negatively associated with physical activity in normal male adolescents ($\beta = -6.08$, 95% CI $-11.04 - -1.10$). However, for overweight male adolescents, both weekdays and weekends computer use were positively associated ($\beta = 7.24$ and 5.04, $P < 0.05$). Otherwise, there was no significant association of TV viewing time, or computer use time with physical activity time.

Conclusion: Weekday TV viewing was negatively associated with physical activity in normal female adolescents, while weekend computer use was associated in normal male adolescents. Unexpectedly, both weekday and weekend computer use were positively associated with physical activity in overweight male adolescents.

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Devices Focused on Diabetic Preventions

ATTD19-0084

DIABETES EDUCATIONAL AND RISK SCORING (DEAR) APP FOR PATIENTS AT APOLLO SUGAR CLINICS- A TOOL THAT GIVES AN EARLY INDICATION

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[4]*Apollo Sugar Clinic- Apollo Hospital, Diabetes and Endocrinology, Chennai, India*
[5]*Apollo Sugar Clinic- Apollo Hospital, Diabetes and Endocrinology, Madurai, India*
[6]*Apollo Sugar Clinic- Apollo Hospital, Diabetes and Endocrinology, Bangalore, India*
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Background and Aim: Diabetes education and assessment radar (DEAR) application is a patient engagement tool to educate patients visiting Apollo Sugar Clinics about the underlying diabetes risk and its complications through risk factor scoring. Hence, we aimed to screen and identify patients having the risk of complications and associated abnormalities through the DEAR app.

Methods: Prospective screening of individuals visiting Apollo Sugar Clinics for doctor consultation from June – August 2018. The screening and risk scoring was done using a mobile tab with DEAR app prior to doctor consultation. The scoring and classification of risk such as no (0–8), low (9–12), medium (13–16), high (17–20) and severe risk (21–25) were defined considering the standard ADA guidelines.

Results: Nearly 70% (2707/3867) of the patients were at medium to severe risk. The severity of score increased with increasing age (>65 years), BMI (>30 kg/m2), disease duration (>5 years), type of medication(oral and insulin) and HbA1c (>9%). 42% of the patients had at least one of the following complications-lipid, kidney, eye, or foot. Lipid abnormality was the most common with respect to age, BMI, HbA1c. Further, medium to severe risk percentages was higher in oral+insulin medication group compared to only oral medication.

Conclusion: The scoring obtained enables the healthcare professionals for thorough investigations and can also serve as an early indicator for appropriate diabetes management program to achieve glycemic, blood pressure and lipid targets to delay complications for better patient outcomes. Patients with higher risk score can be educated appropriately by a health care team.

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Devices Focused on Diabetic Preventions

ATTD19-0169

DECREASE IN GLYCEMIC VARIABILITY FOR T2D OVER SIX MONTHS IN PATIENTS MONITORING WITH A DIGITAL DIABETES MANAGEMENT SYSTEM

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High glycemic variability (GV) is a key risk factor in the presence of Diabetes. Frequent glucose fluctuations may not only contribute to increasing the average blood glucose, but also favors the development of chronic diabetes complications. Dario™ Blood Glucose Monitoring System, a digital Diabetes management system, may assist patients to reduce average glycemic levels and hyperglycemia events while simultaneously avoiding hypoglycemia.

A retrospective data evaluation study was performed on the Dario™ database. A population of T2D high-risk patients (blood glucose measurements average (GM_{avg}) >180 mg/dL) measuring more than 20 times in the first 30 days (analysis baseline) was evaluated on days 60–90 (3 months) and 150-180 days (6 months). Standard deviation (SD) and GM_{avg} were calculated and compared to the baseline.

A group of 698 T2D high-risk Dario™ users was selected. GV was reduced by 10% and 14% from baseline through 3 and 6 months, respectively (SD of 55.7, 58.4 vs.65.0). GM_{avg} was reduced by 8% and 12% from baseline through 3 and 6 months, respectively (201.1 ± 25.57, 192.8 ± 54.3 vs. 219.5 ± 38.5) while patient's hypoglycemic event (<70mg/dL) was in average, less than one (<1) during this period. Subgroup analyses (355 patients) revealed substantial GV improvement among non-Insulin T2D patients. The GV was reduced by 14% and 18% from baseline through 3 and 6 months, respectively (SD of 52.8, 50.7 vs.61.7).

To conclude: Patients using a digital Diabetes management platform have the potential to promote behavioral modification and enhance adherence to diabetes management, demonstrating better glycemic control.

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Devices Focused on Diabetic Preventions

ATTD19-0265

RANKING PHYSIOLOGICAL, LIFESTYLE AND ENVIRONMENTAL RISK FACTORS FOR PREDICTING TYPE 2 DIABETES ONSET

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Objective: Type 2 diabetes (T2D) arises from the interaction of physiological, lifestyle and environmental risk factors. Numerous models, using different variables, were proposed in the literature to identify subjects at risk of developing T2D. To assess the relative importance of different risk factors, we developed a variable ranking strategy and applied it on the Multi-Ethnic Study of Atherosclerosis (MESA) dataset, including anthropometric measures, fasting glucose values, co-morbidities, lifestyle and environmental factors.

Method: A Cox model coupled with LASSO (COX-LASSO) was trained on 4,124 subjects from the MESA dataset to predict the time until incident T2D. COX-LASSO was trained in a Monte Carlo bootstrap resampling scheme with $B = 100$ training/test splits. The Recursive Feature Elimination algorithm was used to rank variables within each bootstrap sample. Then, a global ranked list was derived ordering the variables according to their average ranking in the B resulting lists. COX-LASSO performance was assessed on the other 1,031 subjects from the MESA dataset by the Area Under the ROC curve (AU-ROC) at 10 years.

Results: COX-LASSO reaches performance comparable or superior to the other existing models (AU-ROC = 0.91). The top 12 predictive variables selected by the model are, ranked by importance: fasting glucose, HDL, waist circumference, T2D family history, alcohol use, ethnicity, noise and lack of parks in the neighbourhood, antidepressants use, occupation, blood pressure, and hypertension.

Conclusion: Our approach highlights the importance of environmental variables to predict T2D onset. Interestingly, our model also selected depression, which is related to T2D but is not included in literature models.

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Glucose Sensors

ATTD19-0011

EXPERIENCE OF CGM (CONTINUOUS GLUCOSE MONITORING) FOR CHILDREN AND ADOLESCENTS IN A PAEDRIATRIC DIABETES UNIT

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Objective: Estimate the use of CGM in a Pediatric Diabetes Unit from a Spanish region. To find out differences between the different CGM systems (included flash type or intermittent) and according to the type of treatment. To analyze the metabolic control, frequency of mild and severe hypoglycaemia among the same patients before and after using CGM and to compare patients with and without CGM.

Methods: Data are collected from September to December 2017, from patients whose diagnosis was between 2003 and 2017. Patients are grouped in age groups (<5; 6–10;> 10) and demographic, metabolic control and treatment variables are collected.

Results: 120 patients collaborated, implying a response of 80%.70% use MDI, of which 48% use CGM, being 89% in the case of patients using CSII. In older than 10 years there is a predilection for intermittent measurement systems, unlike those under 5 years prefer continuous measurement. The use of CGM significantly reduces HbA1c compared to those who do not use them and significantly reduces the number of mild hypoglycaemia, with the disappearance of severe hypoglycaemia in 6 months. 43% of patients reduce the number of glycemias/day significantly after 6 months of use. CGM decreases almost a 5% the HbAc1 value and a 19% the Coefficient of Variation.

Conclusion: There exists an improvement in the metabolic control and the glycemic variability of using CGM. Hypoglycemia is diminished by GCM, to a greater extent by the Integrated sensor-augmented pump system. Adolescents prefer to use intermittent measurement systems, reducing the number of glycemia/d.

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Glucose Sensors

ATTD19-0012

THE IMPACT OF PHYSICAL EXERCISE ON SENSOR PERFORMANCE OF THE FREESTYLE® LIBRE INTERMITTENTLY-VIEWED CONTINUOUS GLUCOSE MONITORING SYSTEM IN TYPE 1 DIABETES–A RANDOMISED CROSS-OVER TRIAL

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Background and Aims: To evaluate the sensor performance of the Abbott Freestyle® Libre intermittently-viewed continuous glucose monitoring (iCGM) system to reference blood glucose levels during moderate-intensity exercise while on either full or reduced basal insulin dose in people with type 1 diabetes (T1D).

Method: Ten participants with T1D (4 females, age 32.1 ± 9.0 years, BMI 25.5 ± 3.8 kg/m^2, HbA_{1c} 7.2 ± 0.6% (55 ± 7 mmol·mol^{-1})) exercised on a cycle ergometer for 55 min at a moderate intensity for five consecutive days at the clinical research facility, on either a usual or a 75% basal insulin dose. After a four-week washout period, participants performed the second exercise period with the remaining allocation. During exercise reference capillary blood glucose values were analysed by fully enzymatic-amperometric method and compared to the referring interstitial glucose values. iCGM accuracy was analysed by median absolute relative difference (MARD (interquartile range)), Clarke error grid and Bland-Altman analysis for overall glucose levels during exercise, stratified for glycaemic ranges and basal insulin dosing scheme ($p < 0.05$).

Results: 845 glucose values were available during exercise to evaluate iCGM sensor performance. The overall MARD across the glycaemic range was 22%(13.9–29.7%), 36.3%(24.2–45.2%) during hypoglycaemia, 22.8%(14.6–30.6%) during euglycaemia and 15.4%(9–21%) during hyperglycaemia. A usual basal insulin dose was associated with a decreased sensor performance during exercise compared to the reduced basal insulin period (MARD: 23.7%(17.2–30.7%) vs. 20.5%(12–28.1%), $p < 0.001$).

Conclusion: The iCGM sensor showed diminished accuracy during exercise. Absolute glucose readings derived from the iCGM sensor should be used cautiously and need confirmation by additional finger prick blood glucose measurements.

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Glucose Sensors

ATTD19-0027

COST EFFECTIVENESS OF REAL-TIME CONTINUOUS GLUCOSE MONITORING COMPARED WITH SELF-MONITORING OF BLOOD GLUCOSE FOR TYPE 1 DIABETES PATIENTS IN THE UNITED KINGDOM

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Background: The study was designed to estimate the economic value of a new generation rt-CGM (lasts 10 days, no calibration or SMBG, optional receiver) compared with self-monitoring of blood glucose (SMBG). Our analysis used the new Type 1 Diabetes (T1D) Consensus Guideline framework (Diabetes UK, 2018) and complication costs specific to the United Kingdom (UK).

Methods: A published and validated economic model was used to assess the long-term (50-year) cost-effectiveness of rt-CGM compared to SMBG for UK patients with T1D. All assumptions were based on published evidence with preference for randomized controlled trials when feasible, followed by other published literature on complications and costs (£2018). Key base case assumptions included: 1) starting HbA_{1c} >8.5%; 2) change in HbA_{1c}: −1.29% (rt-CGM), −0.53% (SMBG); 3) rates for non-severe hypoglycemic events (NSHEs), severe hypoglycemic events not requiring medical assistance (SHE1) and those severe hypoglycemic events requiring medical assistance (SHE2). Costs and clinical outcomes were discounted at 3.5% per year.

Results: Base case incremental cost-effectiveness ratio (ICER) for rt-CGM compared with SMBG was £3,976/QALY. Sensitivity analyses performed under shorter time horizons, increasing NSHE, SHE1 and SHE2 hypoglycemia rates for rt-CGM, and reducing all hypoglycemia disutility rates resulted in ICERs ranging from £3,584/QALY to £22,162/QALY. All ICERs in our analyses were within or very close to the £20,000/QALY threshold attributed to NICE for the UK.

Conclusions: Results demonstrate the potential economic value of rt-CGM and suggest that rt-CGM may be considered good value for money compared with SMBG for T1D patients in the UK.

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Glucose Sensors

ATTD19-0038

CHANGES İN THE GLUCOSE PROFİLES OF PREGNANT WOMEN WİTH TYPE 1 AND TYPE 2 DİABETES

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Aim: To examine and compare glycemic excursions in pregnant women with type 1 diabetes(T1DM) and type 2 diabetes (T2DM) by using continuous glucose monitoring (CGM)

Materials and Methods: 20 women with pregestational T1DM or T2DM with 5-day CGM profiles at third trimestr were included in this study. Glucose measurements were divided into periods of euglycemia (70–130 mg/dl), hyperglycemia (> 180 mg/dl) and hypoglycemia (<70 mg/dl).

Results: Of the participating women, 13 (65%) had T1DM and 7 (30%) had T2DM. The mean age of the study group was 32.8 ± 5.9 yrs (31.0 ± 6.1 yrs for T1DM v.s. 36.1 ± 6.3 yrs for T2DM; $p = 0.06$). Diabetes duration was longer (12.3 ± 0.5 yrs v.s. 4.6 ± 3.2 yrs; $p = 0.02$) and BMI was lower (mean BMI $24.4 \pm 2.7\,kg/m^2$ v.s. $28.3 \pm 3.2\,kg/m^2$; $p = 0.01$) at initial visit in women with T1DM. The pregnants with T2DM had more frequent family history of diabetes (0.05). There was significant difference in A1C (6.9 ± 0.5 and $5.9 \pm 0.5\%$, respectively; $p = 0.001$) in women with T1DM. Although the rates of hypoglycemia were similar in both groups, duration of euglycemia throughout the day was shorter 64%; the duration of hyperglycemia exposure especially during night and glycemic variability was higher in pregnants with T1DM.

Conclusions: CGM is a novel tool to assess 24-h glucose fluctuations and reveals clear differences in the glycemic status in pregnant women with T1DM and T2DM. In pregestational diabetes, CGM may have an important role for optimal glucose control and treatment adjustments.

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Glucose Sensors

ATTD19-0041

PERFORMANCE AND RESULTS FROM INTERMITTENTLY VIEWED CONTINUOUS GLUCOSE MONITORING DURING EXTREME MOUNTAIN BIKING

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Objective: Continuous glucose monitoring(CGM) can provide useful information on individual athletes in extreme conditions and for optimization of training. We aimed to provide novel data characterizing: glucose homeostasis during prolonged extreme exercise in normal healthy volunteers and the performance of intermittently viewed CGM(iCGM).

Methods: Data on glucose profile was recorded during the 2018 Edition of Titan Desert mountain bike challenge in Morocco (6 days, 650 km, day temperature 35–40°C and cumulative elevation 7500 m) from 3 healthy athlete volunteers' (40-50 years-old, 69-98 kg, 15.0-16.6 % body fat, BF) who participated. Interstitial glucose was measured with an iCGM device (FreeStyle Libre®).

Results: All three participants finished the race without major health issues. During the challenge, 100% of glucose profile was obtained from one participant and only 61–69% from the other two due to lack of permanence of the adhesion of the pad sensor/transmitter. There were not skin problems related to the device. On average MARD was $9.4 + 12.5\%$. 89% of the time, sensor glucose(SG) was within the range of 70–140mg/dl, 7%> 140mg/dl and 4% <70mg/dl. None of the <70 episodes (all asymptomatic) happened during the stages of active cycling. GS average was $107 + 15$mg/dl with a coefficient of variation of 14%. Estimated average stage expenditure was 2738 kcal. Mean carbohydrate intake ranged from 800 to 1000g/24h.

Conclusion: The performance of iCGM in healthy subjects during high intensity and prolonged exercise under extreme conditions could be considered satisfactory. This study demonstrated that glucose regulation is, generally, tightly controlled in healthy adults despite a prolonged extreme sport challenge.

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ATTD19-0054

WHY INTRAPERITONEAL GLUCOSE SENSING IS SOMETIMES SURPRISINGLY RAPID AND SOMETIMES SLOW: A HYPOTHESIS

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Intraperitoneal (IP) glucose sensing can sometimes be surprisingly rapid; reacting to intravenous glucose boluses almost as fast as intraarterial (IA) sensors (time delays of 0–26 s between IA and IP sensor locations) [1]. This study used interferometric sensors (GlucoSet AS, Trondheim, Norway).

In another study using amperometric sensors (Abbott Freestyle® Libre, Abbott Laboratories, IL, US), IP glucose sensing was nearly as slow as subcutaneous sensing, with a time delay of several minutes [2].

The large difference in time delay cannot be explained solely by the different sensing technologies. Based on the diffusion time

of glucose in water, which is approximately 7.5 s for a distance of 100 μm (using Fick's first and second law of diffusion), we hypothesize that the most rapid sensors have been measuring directly at the surface of the peritoneal lining, measuring the concentration of glucose diffusing out of the peritoneal lining, while the slower sensors measured in the peritoneal fluid.

In an artificial pancreas, time delays should be minimized. Thus, if our hypothesis is confirmed, intraperitoneal glucose sensors should aim at sensing at the peritoneal lining instead of the peritoneal fluid. Or even better, they should sense the glucose level in tissue or capillaries immediately below the peritoneal lining.

[1] Fougner, A. L. *et al.* ''Intraperitoneal Glucose Sensing is Sometimes Surprisingly Rapid'', *Modeling, Identification and Control (MIC)*, 2016. DOI: http://dx.doi.org/10.4173/mic.2016.2.4

[2] Åm, M. K. et al. ''Effect of sensor location on continuous intraperitoneal glucose sensing in an animal model'', *PLOS One*, in press.

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Glucose Sensors

ATTD19-0069

GLYCAEMIC VARIABILITY AND TIME IN RANGE IN TYPE 1 DIABETES PATIENTS ON REAL TIME CONTINUOUS GLUCOSE MONITORING AND INSULIN INJECTIONS VERSUS SENSOR-AUGMENTED INSULIN PUMP THERAPY

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Background and aims: The aim of the study was to compare glycaemic variability and time in different glycaemic ranges in patients with type 1 (T1DM) using real time continuous glucose monitoring (CGM) and multiple daily insulin injections (MDI) versus the patients using sensor-augmented pump therapy (SAP).

Material and Methods: All the T1DM patients using real time CGM in a single center were evaluated in a cross-sectional study. Fourteen days of data from CGM and/or pump downloads were analysed. Different glycaemic variability measures were obtained. Percentage of TIR (70–180 mg/dl), time <54 mg/dl, <70 mg/dl, >180 mg/dl, >250 mg/dl and >300 mg/dl were calculated. A comparison between the group on MDI (CGM-MDI) and the group on SAP was performed.

Results: 180 patients were included. No differences between the CGM-MDI group (n = 70) and the SAP group (n = 110) were found in age (42 ± 14 years *vs* 40 ± 9.2 years, p = 0.4), diabetes duration (20 ± 12 years *vs* 23 ± 11 years, p = 0.2), or baseline HbA1c before CGM (7.4 ± 1.1% *vs* 7.4 ± 0.8%, p = 0.9). In the SAP group, female sex was more prevalent (63% *vs* 36%, p = 0.001) and median duration of CGM was longer (25 [12-40] months *vs* 11 [4-28] months, p = 0.001). 87% (n = 96) of the patients in the SAP group used low-glucose or predictive low-glucose suspend functions. Differences between both groups are shown in Table 1.

Table 1. Differences between patients on CGM-MDI and patients on SAP.

	CGM-MDI n = 70	SAP n = 110	p
HbA1c (%)	7.3 ± 0.9	7.1 ± 0.7	0.2
Estimated HbA1c (%)	7.0 ± 1.0	7.1 ± 0.7	0.4
Insulin dose (U/kg/day)	0.6 ± 0.2	0.6 ± 0.6	0.3
Sensor use (days per week) median [IQR]	6.3 [4.9-6.8]	6.3 [5.6-6.6]	0.3
Mean glucose (mg/dl)	155 ± 26	158 ± 20	0.3
Standard deviation (mg/dl)	57 ± 13	56 ± 11	0.5
Coefficient of variation (%)	37 ± 6	35 ± 5	0.07
MAGE (mg/dl)	119 ± 30	117 ± 25	0.7
CONGA	135 ± 25	137 ± 20	0.6
ADDR	519 ± 43	521 ± 34	0.8
MODD	62 ± 15	59 ± 13	0.2
LI	2125 ± 910	2058 ± 796	0.7
J index	14998 ± 5007	15127 ± 3971	0.8
M value	2481 ± 390	2519 ± 387	0.5
MAG	54 ± 12	50 ± 9	0.07
Time 70-180 mg/dl (%)	65 ± 14	64 ± 14	0.7
Time > 180 mg/dl (%)	29 ± 15	33 ± 14	0.2
Time > 250 mg/dl (%)	7.9 ± 7.0	7.9 ± 6.1	0.9
Time > 300 mg/dl (%)	2.3 ± 3.0	2.3 ± 2.6	0.9
Time < 70 mg/dl (%) median [IQR]	4.4 [1.8-7.6]	2.3 [1.1-4.3]	0.02
Time < 54 mg/dl (%) median [IQR]	1.1 [0.3-2]	0.3 [0.1-0.9]	0.02

Data are expressed as mean ± standard deviation, unless specified

Conclusion: Similar outcomes regarding glycaemic variability and time in normo- and hyperglycaemic range can be achieved with real time CGM and multiple daily insulin injections and with sensor-augmented pump. Sensor-augmented pump therapy provides greater protection against hypoglycaemia.

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Glucose Sensors

ATTD19-0082

METABOLIC CONTROL OF 44 TYPE 1 DIABETIC TODDLERS FOLLOWED UP IN HELSINKI UNIVERSITY HOSPITAL IS GOOD

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Introduction: Treatment of young children with type 1 diabetes (T1D) is often challenging. In Helsinki University Hospital, department for children and adolescents, we have carefully analyzed treatment outcome of children below 3 years by using continuous glucose monitoring (CGM) or intermittent continuous glucose monitoring (iCGM) and insulin pumps with predictive low glucose suspension (Medtronic 640G) and by using patients personal pump/iCGM downloads assessed remotely when needed. Purpose of this study was to monitor the metabolic control of 44 T1D toddlers.

Table 1:

HbA1c (% / mmol/mol)	7,3 / 55,7
Mean glucose (mmol/l)	9,2
SD (mmol/l)	3,5
CV (%)	37
Time in Range (%)	60
Hypoglycaemias (%)	3

Materials and methods: The cross-sectional data was collected retrospectively in September 2018 from patient records. Inclusion criteria was T1D toddlers born in 2014-2018 and aged <3 at the time of type 1 diabetes diagnosis. Mean age at the time of analysis was 3.3 ± 0.9 years and mean duration of the disease was 18 months. HbA1c, mean glucose, standard deviation, coefficiency variation (CV), time in range (3.9-10 mmol/l) and proportion of hypoglycaemias (<3.9 mmol/l) were measured.

Results: We identified 35 patients on smart insulin pumps and CGM and 9 (20%) patients in MDI + iCGM. The mean insulin dose of these patients was 0.63/IU/kg/day. The glycemic control is shown in table 1.

Conclusion: The metabolic control in T1D toddlers, diagnosed under 3 years old, in Helsinki University Hospital area is quite good. New technology combined with frequent education, support and advising in the beginning is a key to success.

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Glucose Sensors

ATTD19-0104

PATIENT SATISFACTION AND CLINICAL EFFICACY OF FLASH GLUCOSE MONITORING IN PATIENTS WITH TYPE 1 DIABETES

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Frequent measurements of blood glucose levels, also known as self-monitoring of blood glucose (SMBG), are usually required as part of the treatment and management in patients with type 1 diabetes (T1D). Since flash glucose monitoring (FGM), a less-invasive glucose monitoring method without pricking the fingertips, was launched in Japan in September 2017, we evaluated the patient satisfaction and clinical efficacy of FGM in Japanese patients with T1D.

Patient satisfaction on FGM was assessed using Diabetes Treatment Satisfaction Questionnaire (DTSQ) and Diabetes Therapy-Related Quality of Life (DTR-QOL) before and 4 and 12 weeks after initiating the use of FGM in 20 Japanese patients with T1D. Moreover, clinical parameters related to glucose metabolism, such as glycated hemoglobin (HbA1c) and glycated albumin levels were obtained, and glucose fluctuations were evaluated using the FGM data. The correlation of glucose values between FGM and SMBG was also investigated.

DTSQ scores significantly improved 12 weeks after the use of FGM ($P < 0.001$). Furthermore, the scores related to ''treatment satisfaction'' and ''burden in social activities'' in DTR-QOL were also significantly improved ($P = 0.007$ and 0.02, respectively). HbA1c levels and percentages of glucose levels within the target range (70–140 mg/dL) also improved at 12 weeks ($P = 0.002$ and 0.016, respectively). Mean absolute relative differences in glucose values between FGM and SMBG were 12.2 ± 13.1% throughout the study period.

In conclusion, FGM contributed to improving the patient satisfaction and adjustment of blood glucose levels in patients with T1D.

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Glucose Sensors

ATTD19-0124

CORRECTING HBA1C VALUES FOR INDIVIDUAL GLYCATION FACTORS - APPLICATION OF RED BLOOD CELL GLYCATION KINETIC MODEL

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Background and Aims: Lab HbA1c can be misleading due to an individual's red blood cell (RBC) life and RBC glucose transport rates, with extreme examples related to dialysis and heart valve replacement. An RBC kinetic model can be used to calculate corrections to lab HbA1c values in these cases.

Materials and methods: With an individual's rate constants and appropriate reference values, one can adjust the lab HbA1c value use following equation:

$$\mathrm{HbA1c}_s = \mathrm{K} \bullet [\mathrm{G}_s] / (1 + \mathrm{K} \bullet [\mathrm{G}_s])$$

Where K is the ratio of RBC glycation and elimination rate constants: $K = k_{gly}/k_{age}$. RBC life is inversely proportional to k_{age}. Adjusted HbA1c can be calculated with approprate reference K.

Results: The model was applied to the experimental data. Assuming no change in individual k_{gly} values and a hypothetical reference RBC life of 63 days or k_{age} 0.011 (1/day),

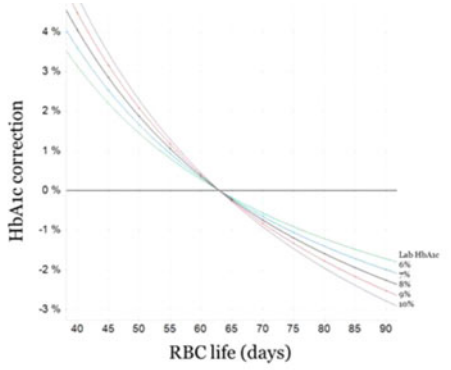

Figure 1. HbA1c correction vs. RBC life with reference RBC life of 63 days. No adjustment on k_{gly}

the correction to lab HbA1c can be calculated (Fig 1). As expected, positive corrections are seen for those with significantly shorter RBC life and negative corrections otherwise. Similarily, correction can be applied with a reference glycation rate constant.

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Glucose Sensors

ATTD19-0131

FEAR NO HYPO -FEASIBILITY EVALUATION OF THE IMPACT ON GLUCOSE CONTROL AND SAFETY OF THE EVERSENSE CONTINUOUS GLUCOSE MONITORING SYSTEM IN TYPE I DIABETIC YOUTH

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Introduction: CGM use is growing in T1D population, especially in the pediatric age group. The continuously growing number of users provides new insights on therapy data as well as a benefit in therapy outcome. But new problems such as allergic reactions to adhesives or annoying frequent sensor changes arise.

The ''Eversense®'' sensor is a subcutaneously inserted rtCGM system which only has to be changed once every 5-6 months. Actual smartphones can be used as its receiver. Its adhesive is silicone-base and therefore less aggressive to the skin than the adhesives of other CGM systems. As of today, it is only approved for use in adults.

Method: Five (5) children (6–12 years) and 10 adolescents (13–17 years) will receive the sensor. After a 30-day blinded period, the sensor will be used in an unblinded mode until the end of working period.

The primary endpoint is the time in hypoglycemia in the three weeks before the end of a 90-day period compared to the first three weeks of the blinded period.

Conclusion: As a growing number of adhesive allergic reactions are observed with CGM use, also related to the growing number of systems in use, CGM systems with an alternative approach to a transcutaneous probe which requires an aggressive, long-term adhesive patch to stay in place are needed.

It is important that studies be performed as early as possible to investigate the safety and feasibility of new technologies in the pediatric population so there are alternative solutions available for this population.

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Glucose Sensors

ATTD19-0132

PIVOTAL STUDY OF A NON-INVASIVE CONTINUOUS GLUCOSE MONITORING SYSTEM (CGM): A RETROSPECTIVE EVALUATION OF DATA FROM 75 PATIENTS WITH 525 WEAR DAYS

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Background and aims: The sugarBEAT® system is a non-invasive, Continuous Glucose Monitor (CGM) designed to provide glucose patterns and trends, by measuring interstitial glucose on the surface of the skin. sugarBEAT® consists of a daily-disposable sensor connected to a rechargeable body worn transmitter, with a mobile phone app displaying glucose readings every 5 minutes.

Methods: The study evaluated sensor performance over 7 consecutive wear days, consisting of 3 non-consecutive in-clinic visits, and 4 home wear days, recording glucose levels every 5 minutes. Venous blood samples taken at 15 minute intervals were used as a reference for an in-clinic portion of study using Architect c8000, Sensors were replaced each day, and the maximum wear period of each sensor was 14 hours per day.

Results: The sugarBEAT® agreement with reference glucose analyzer within 20 mg/dL (<80mg/dL) or 20% of glucose values (>80mg/dL) gave an overall MARD of 8.67% (for 66.7% of all paired data points, over the first 10 hours of device wear time), and an overall MARD of 16.74% for 100% of the data, using a single finger prick calibration. Similarly the MARD was 7.68% for 74.39% of the data and 14.12% for 100% of the data when 2-finger prick calibrations were applied. No device-related Serious Adverse Events (SAEs) were reported.

Conclusion: The sugarBEAT® system shows promise for diabetics wanting to trend their glucose profiles, and the first of its kind to offer the flexibility of wear of less than a day, without requiring sensor insertion into the skin.

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Glucose Sensors

ATTD19-0141

TEMPORARY USE OF GLUCOSE SENSOR IN TYPE 1 DIABETES PATIENTS

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Aim: The aim of the study is to evaluate the glycemic outcomes in temporary use of continuous glucose monitoring (CGM) in patients with type 1 diabetes (T1D) on continuous subcutaneous insulin infusion (CSII) or multiple daily injection (MDI).

Methods: A CGM for 7 days was added on T1D patients with HbA1c>7.5%. All patients did not use any CGM device in the last three months. Patients were analyzed in two groups:

CSII group, 28 patients on CSII (Minimed Veo/722, Medtronic, USA) used real-time CGM (Minilink with En-lite sensor, Medtronic, USA) for seven days, where patients could see the glucose value and respond adequately and

MDI group, 32 patients on MDI used retrospective CGM (Ipro2 with En-lite sensor, Medtronic, USA), where patients could not see the glucose value (blinded CGM).

Patients from both groups used the CGM device for 7 days. Data was downloaded using specific software (Carelink Pro and Carelink Ipro, Medtronic, Northridge, CA) and specific instructions in basal and bolus insulin, education on food, physical activity and hypoglycemia/hyperglycemia were given to the patients. HbA1c was obtained before and three months after the study.

Results: Both groups significantly improved glucose control (HbA1c) from 7.8 ± 0.6% to 7.1 ± 0.6% in CSII group and from 8.2 ± 1.1% to 7.4 ± 0.8% in MDI group. There was no significant difference between both groups at the end of the study.

Conclusions: Temporary use of CGM can improve glucose control in both T1D patients on CSII or MDI. Further investigation on larger groups should be performed to confirm our findings.

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Glucose Sensors

ATTD19-0155

A NOVEL ADAPTIVE KALMAN FILTERING ALGORITHM AND A FILTER PERFORMANCE EVALUATION METHOD

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Background and Aims: The use of Kalman filters for noise suppression of real-time continuous glucose monitoring (CGM) is well established in the prior literature[1]. However, an objective standard is needed to compare the performance of a specific filter against the prior art. The aim of this study was to develop a real-time, adaptive Kalman filtering algorithm and provide an objective evaluation method to show the performance against the family of Kalman filter implementations.

Methods: 6 *in vivo* datasets from the Eclipse® ICGM® System[2] were utilized to develop and assess the performance of the filter. Adaptive Kalman filter algorithm varied the instantaneous filter parameters utilizing a moving window noise estimation technique. The filtered signal (red) was compared against a post-processed ideal target signal (blue) to evaluate relative error and relative high frequency noise (Figure 1a).

Results: Results show that the adaptive Kalman filter improves noise suppression without negatively impacting time lag as compared to the Kalman filter with fixed parameters. Figure 1b shows an example where adaptive Kalman filter (blue circle) slightly improved noise suppression (19% vs 21%) without negatively impacting relative error, as compared to a filter with fixed parameters[1] (red circle). The black line represents the performance of a standard Kalman filter over a range of increasing noise parameters (gamma (γ) = σ^2/λ^2).

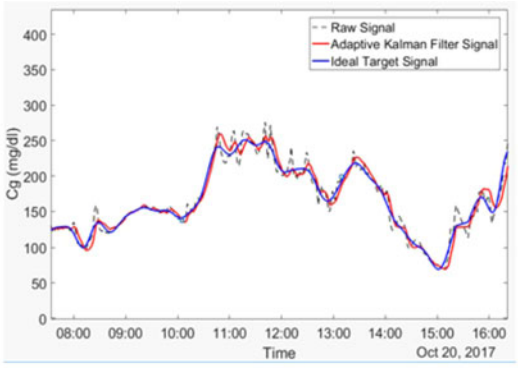

Figure 1a: The ideal target signal was obtained by applying a high-order (n=50) low-pass FIR filter (fc = 0.83 mHz) to the raw data and time-shifting the output to remove the lag.

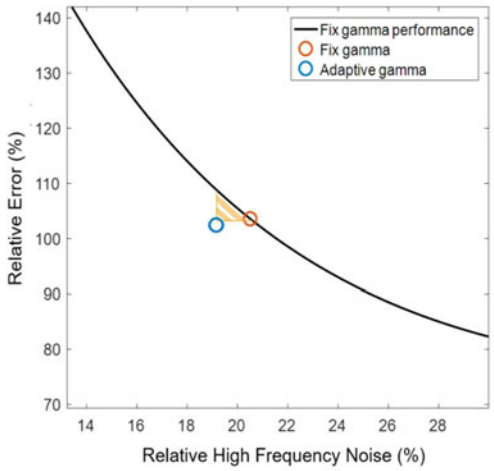

Figure 1b: Relative High Frequency Noise is evaluated as the power in high frequency band (fc = 0.83 mHz) of filtered signal divided by the power in high frequency band of the raw unfiltered signal. Relative Error is evaluated as the sum of squared errors between ideal signal and filtered signal, relative to the sum of squared errors between ideal signal and raw signal.

Conclusions: An adaptive Kalman filter, in addition to a new performance evaluation method, is presented that demonstrates improved noise suppression, which may enhance overall accuracy of the ICGM System.

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ATTD19-0173

FLASH GLUCOSE MONITORING IN TYPE 1 DIABETES MELLITUS. PATIENT EXPERIENCE AFTER THE FIRST USE

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Aim: To assess the metabolic control and patient-device interaction during the first use of flash glucose monitoring system.

Methods: Retrospective observational study. Type 1 diabetic patients without previous experience with real time and/or ''Flash'' continuous glucose monitoring system were included. They wore the sensor on the back of the upper arm for up to 14 days. They received an only educational session related to basic concepts about the use of the device was done. The metabolic control was measured and the sensor data were compared between the first and second week.

Results: 42 patients were recruited. 12 were excluded (captured data by the sensor <70%).

30 patients (7 men) were analyzed. Average age 39 ± 11. 10 subjects were on treatment with multiple dose injection and 20 on insulin pump therapy.

The monitoring results are in the following tables:

	Mean ± standard deviation
HbA1c (%)	8±1.4
Mean glucose (mg/dL)	183±40
Captured data (%)	88.5±6.8
Time in hyperglycemia (%)	48±19
Time in target range (%)	45±18
Time in hypoglycemia (%)	7±5
Duration hypoglycemias (min)	93±36

	Week 1	Week 2	sig
Mean glucose (mg/dL)	183.5±44.6	183.6±40.4	n/s
Scans/day (n)	12.1±7.3	10.3±6.9	p=0.009
Hypoglycemic events/day (n)	1.0±0.8	0.8±0.5	n/s

The events of hypoglycemia between the first and second week were reduced by 21% (n/s). It was found out that 2 patients had unawareness nocturnal hypoglycemias.

Conclusion: The information provided by the system helped patients to reduce hypoglycemia events.

A longer time of use and more education will allow the patient to gain more experience and improve the results.

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Glucose Sensors

ATTD19-0186

SHOULD WE MEASURE BY THE SAME YARDSTICK? REAL-TIME CONTINUOUS GLUCOSE MONITORING AND FLASH GLUCOSE MONITORING PROVIDE DIFFERENT ESTIMATIONS OF KEY CLINICAL PARAMETERS

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Objective: We aimed to compare glycemic control and variability parameters obtained from paired records of real-time continuous glucose monitoring (RT-CGM) and flash (intermittently-viewed) glucose monitoring (FGM, iCGM).

Research Design and Methods: Twenty one adolescents with type 1 diabetes (47.6% boys, 95% treated with continuous insulin infusion, age 15.3 ± 2.1 year, diabetes duration 7.7 ± 4.5 years, glycated hemoglobin 7.35 ± 0.7%) were equipped with RT-CGM and FGM devices for one week. Afterwards, raw measurements were obtained and processed with Glyculator 2.0 software to obtain parameters listed in the International Consensus on Use of Continuous Glucose Monitoring, with distinction into all record/night-time/day-time blocks when appropriate. Comparisons were performed in a paired design.

Results: Agreement between the two systems' measurements ranged from poor (r = 0.6215) to perfect (r = 0.9869) in individuals with satisfactory overall accordance (r = 0.8998). Consistent mismatch between FGM and RT-CGM was observed for six important metrics: coefficient of variation [median difference between RT-CGM and FGM −4.12% (25–75%: −7.50% to −2.96%), p < 0.0001], low blood glucose index [−0.88 (−1.88 to −0.18), p = 0.0004], % of time below 70mg/dl [−4.77 (−8.39 to −1.19), p = 0.0015] and 54mg/dl [−1.33 (−4.07 to 0.00), p = 0.0033], primary time in range 70–180mg/dl [8.58 (1.31 to 12.66), p = 0.0006] and secondary time in range 70-140mg/dl [5.14 (1.27 to 10.99), p = 0.0004].

Conclusions: Our data demonstrated that RT-CGM and FGM differently estimate some key parameters of glycemic control and variability when used simultaneously by the same patients. Therefore, such metrics cannot be directly compared between people using different systems without incurring bias and system-specific guidelines and targets are needed.

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Glucose Sensors

ATTD19-0189

THE IMPACT OF PREDICTIVE-SUSPEND FEATURE ON THE RELATIONSHIP BETWEEN HBA1C AND HYPOGLYCEMIA IN PATIENTS WITH TYPE 1 DIABETES TREATED WITH SAP AND LOW-GLUCOSE SUSPEND FUNCTION

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Background and Aims: Continuous glucose monitoring (CGM) changes the relationship between HbA_{1c} and hypoglycaemia in insulin pump (CSII) treated type 1 diabetes (T1D). We evaluated the impact of predictive low glucose suspend (PLGS) device on the relationship between HbA_{1c}

and hypoglycaemia in people previously treated with low glucose suspend (LGS).

Methods: Data from T1D patients using LGS (Medtronic Paradigm VEO) in 3 referral hospitals in Spain were included. Patients were switched to PLGS (Medtronic 640G) as part of usual care. Baseline and follow-up data of HbA_{1c} and 2 weeks of CGM were used to assess the relationship between HbA_{1c} and % of time <70 mg/dl and <54 mg/dl. Regression curves were compared in order to evaluate the impact of PLGS on the relationship between HbA_{1c} and hypoglycaemia.

Results: 40 patients with T1D (age 39.6 ± 11.5 years, diabetes duration 26.9 ± 11.7 years, 67.5% female) were included. The mean follow-up period was 10.4 ± 3.4 months. At baseline patients spent 7% of time ≤70 mg/dL and <2% <54 mg/dl. Treatment with PLGS was associated with lower % of time <70 mg/dl (3.8 ± 2.6 vs. 2.9 ± 2.3; $p < 0.005$) and with a significant reduction in severe hypoglycaemia frequency (52.5 vs. 0%, before vs. after PLGS). There were no significant differences in % time <54 mg/dl, >180 mg/dl and 70-180 mg/dl between baseline and end of follow-up. There was not a relationship between PLGS setting and the % of time in hypoglycaemia reduction.

Conclusions: Our data demonstrate that PLGS allows a further attenuation of hypoglycaemia in patients with T1D previously using sensor-augmented pump therapy with LGS function.

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Glucose Sensors

ATTD19-0193

SUBCUTANEOUS TISSUE RESPONSE TO IMPLANTABLE SENSORS: MULTINUCLEATED GIANT CELLS PREDOMINATION

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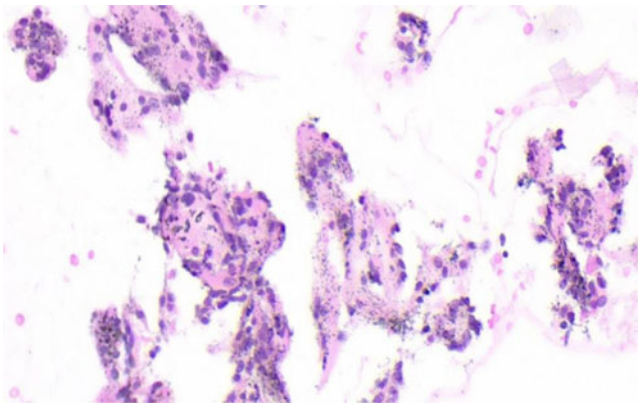
We have previously described the tissue response to enzymatic glucose sensors in humans, being macrophages the key component of the inflammatory reaction. Their accumulation is associated with sensor function impairment.

The aim of the study was to describe a method to explore the tissue response to implanted glucose sensors. Thus, we enrolled 12 type 1 diabetes patients who wore an Eversense sensor for 90 days. Sensors were removed following the manufacturer instructions. Then, an imprint smear of the probe was done for cytology study, and the probe conserved in salinum for recovering the tissue adhered to it. Additionally, the pocket where the sensor had been allocated was washed with 1 ml of saline solution, which was then recovered and processed (cell block).



A significant number of multinucleated giant cells were observed in the tissue surrounding the sensor. Unexpectedly, pigment accumulation (Figure 1) was observed free and inside the cells. This material did not show birefringence under polarized light and corresponds to some element among those used for coating the sensor surface (HEMA (hydroxethyl methacrylate), poly methyl methacrylate (PMMA) or platinum).

Multinucleated giant cells reaction to wear-particles released from the sensor surface is the commonest cell response to implantable Eversense sensors.

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Glucose Sensors

ATTD19-0200

IMPACT OF EARLY INITIATION OF CONTINUOUS GLUCOSE MONITORING ON GLYCEMIC CONTROL IN PEDIATRIC PATIENTS WITH TYPE 1 DIABETES

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Recent use of continuous glucose monitoring (CGM) has increased and initiates closer to diagnosis of type 1 diabetes (T1D)

	CGM	Control
N	42	13
Age (years)	11.2 (3.6)	10.7 (3.8)
Sex (n, % Female)	24 (57%)	4 (29%)
Race/ethnicity, N (%)		
non-Hispanic white	29 (69%)	9 (69%)
Hispanic	3 (7%)	1 (8%)
African-American	1 (2%)	0 (0%)
Other	9 (21%)	3 (23%)
Baseline HbA1c	10.5 (2.0)	10.4 (2.3)
3 month HbA1c	7.2 (1.0)	7.0 (1.0)
6 month HbA1c	7.5 (1.0) (n=41)	7.4 (1.1) (n=12)
CGM Data		
3 month		
mean glucose (mg/dl)	156 (29)	143 (31)
% time < 70 *	2.0	7.5
% time 70-180	69.5	68.9
% time > 180	28.4	23.6
% time > 250	9.5	8.6
6 month		
mean glucose (mg/dl)	164 (29)	160 (34)
% time < 70 #	1.9	4.9
% time 70-180	65.0	62.8
% time > 180	33.1	32.3
% time > 250	11.8	12.5
* p< 0.0001	# p =0.002	

among pediatric patients in the United States. However, little is known about benefits of starting CGM soon after diagnosis. We assessed glycemic control in youth initiating Dexcom G5 CGM within 40 days of diagnosis compared to no CGM use within 180 days of onset of T1D.

Methods: Data from 55 study participants (mean age 11.1 ± 3.6 years, range 2-17 years, 50% female, 69% non-Hispanic white) were obtained for 6 months. 42 participants randomized to initiate CGM within 40 days of diagnosis (CGM group) and 13 randomized to use blinded CGM one week per month for 6 months (control group). HbA1c was measured at baseline, 13, and 26 weeks. CGM data from the groups were compared using t-tests.

Results: Data in table show HbA1c decreased in both groups over 6 months with no significant difference. Time in range (70-180 mg/dl) was not significantly different at 3 and 6 months; however, time <70mg/dl was significantly less in CGM vs. control at 3 ($p < 0.0001$) and 6 months ($p = 0.002$).

Conclusions: Pediatric T1D patients initiating CGM soon after diagnosis have similar HbA1c and time in range in the initial 6 months of use compared to those not using CGM but with significantly less hypoglycemia. Almost 70% time in range may be related to the honeymoon phase. Further work is needed to determine which patients may benefit most from early initiation of CGM use.

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Glucose Sensors

ATTD19-0208

THE CONTRIBUTION OF THE FREESTYLE LIBRE® SYSTEM IN THE MANAGEMENT OF DIABETIC PATIENTS: EXPERIENCE AT LIÈGE UNIVERSITY HOSPITAL

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Diabetic patients included glycemic self-monitoring convention in Belgium can benefit from a device measuring subcutaneous glucose concentration (GC): FreeStyle Libre® (FSL)/ Abbott. The main advantage of this technology is that it is less invasive (blood sampling not required) It also allows patients to obtain, in addition to the instantaneous value of GC, retrospective kinetic data, but also prospective trend of its kinetics. In this study, we evaluated the contribution of FSL on the equilibration of diabetes, on the time spent in hypoglycaemia and on weight. We also asked patient's satisfaction with this system. Data from 838 diabetic patients (type 1 or total insulin deficiency) were collected between May 2016 and October 2017, 645 patients with FSL system and 193 preferring to continue capillary blood samples (SMBG). In the FSL group, compared to the SMBG group, there was a slight decrease in HbA1c estimated at 0.15 ± 0.073% after 15 months. This decrease appears mainly when the starting level is high (HbA1c > 7.5%). The body mass index (BMI) increases slightly in patients with the device but remains stable in subjects without FSL. Patients perform an average of 8.8 checks: the more patients perform daily scans, the greater the number of data included in the target, that is, the better the glycemic balance. A higher number of scans is also associated with a decrease in the average duration of hypoglycaemia. Finally, the satisfaction survey shows a fairly high degree of patient satisfaction with the use of FSL.

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Glucose Sensors

ATTD19-0217

ACCURACY OF FLASH GLUCOSE MONITORING SYSTEM IN HOSPITALIZED PATIENTS WITH TYPE 2 DIABETES MELLITUS - PILOT STUDY

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Background: The accuracy of the Flash Glucose Monitoring System (FGM) has been well established in outpatients with Type 2 Diabetes Mellitus (T2DM), however it has not been evaluated in hospitalized patients. Monitoring blood glucose during hospitalization is important to avoid dysglicemia episodes, that impact on clinical outcomes. Since there is no data regarding the accuracy of FGM in hospitalized patients with T2DM, we evaluated in this pilot study if FGM is reliable compared to Self-Monitoring Blood Glucose (SMBG) on those patients.

Methods: A prospective, open label, non-randomized, controlled trial was conducted in 11 T2DM hospitalized patients. FGM was compared to SMBG (preprandial and bedtime). We excluded T1DM, pregnant, hypovolemic distress, sepsis and ICU admitted patients. Patients used the sensor for a maximum period of 14 days. We accepted a Mean Absolute Relative Difference (MARD) of 20% and used the Consensus Error Grid (CEG) to evaluate the accuracy of FGM.

Results: A total of 408 glucose values were paired. FGM observation period was 10.27 ± 3.13 days (Mean ± SD). The accuracy of FGM was demonstrated by 65.44% of values in Zone A and 89.21% in zone A/B of the CEG. MARD was 18.99 ± 7.24% and the variation coefficient was 33.94 ± 10.54%. FGM detected more hypoglycemia episodes than SMBG (11 vs 1.7%).

Conclusion: This study demonstrated that FGM is accurate compared to SMBG in hospitalized patients with T2DM. It also showed that FGM is able to detect more hypoglycemia episodes than SMBG, so it might be an useful tool for patient's safety.

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Glucose Sensors

ATTD19-0234

REDUCTION OF GLYCEMIC VARIABILITY (GV) BY HAEMODIALYSIS IN TYPE 2 DIABETES

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Background: The HbA1c is a set of parameters of glycemic control in patients with type 2 diabetes (T2D), however this markers do not reflect well glycemic control in T2D patients on haemodialysis (HD). The glycemic variability (VG) could be assessed by continuous glucose monitoring (CGM). The CGM can evaluate the GV by coefficient of variation (CoV) and Mean amplitude of glucose excursion (MAGE). We aimed to evaluate the VG by CGM in T2D patients on chronic HD.

Methods: We used a 6-day CGM to monitor glucose levels in 10 HD-T2D patients including 2 days before (PRE-HD), 1 day during (INTRA-HD) and 3 days without dialysis session (POST-HD).

Results: T2D duration was 13.9 ± 2.4 (years) and HD duration was 3.7 ± 0.3(years). The mean of HbA1c was 6,41 ± 0,2 %, the CoV mean 29.6 ± 1.7 % and the mean of MAGE was 267.5 ± 16.7. We found a reduction of CoV and MAGE between PRE-HD 23.6 ± 2.6% vs INTRA-HD 13.4 ± 1.5%, $P < 0.01$; PRE-HD 142.4 ± 19.5 vs INTRA-HD 77.1 ± 12.3, $P < 0.01$; an increase of CoV and MAGE between INTRA-HD 13.4 ± 1.5% vs POST-HD 24.4 ± 2.8% $P < 0.05$; 77.1 ± 12.3 vs 145.5 ± 20.1, $P < 0.05$. The mean of CoV-PRE-HD and MAGE-PRE-HD were correlated positively ($r = 0.87$, $P < 0.01$); the mean of CoV-INTRA-HD and MAGE-INTRA-HD were correlated positively ($r = 0.67$, $P < 0.01$). No significant association with HbA1c was found.

Conclusion: The HD reduces the CoV by CGM with no associations with HbA1c. The CGM could be a validated marker of glycemic control in HD-T2D patients.

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Glucose Sensors

ATTD19-0251

MODELING PLASMA-TO-INTERSTITIAL GLUCOSE KINETICS DURING MEAL AND EXERCISE USING PLASMA AND MICRODIALYSIS TRACER DATA

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Background and Aim: Understanding plasma-to-interstitial (ISF) glucose kinetics is fundamental to determining the accuracy of subcutaneous glucose sensors. We showed that a linear two-compartment model well describes plasma-to-ISF glucose kinetics using multi-tracer plasma and microdialysis data under steady-state conditions (Schiavon et al., DTT 2015). The model also allows to estimate plasma-to-ISF equilibration time (τ). The purpose of this work was to assess the model under dynamic conditions, such as during meal and exercise, and test if τ changes.

Methods: Ten healthy and 10 type 1 diabetes (T1D) subjects (age = 48 ± 10 y; BMI = 27.0 ± 4.3 kg/m^2) were studied in two occasions undergoing either a mixed meal or an intravenous glucose challenge labeled with [1-^{13}C]glucose. Additional 7 healthy and 7 T1D subjects (age = 52 ± 9 y; BMI = 28.4 ± 4.9 kg/m^2) underwent a moderate grade exercise (50% VO_2max) two hours after a labeled meal. Microdialysis catheters were placed into the abdominal subcutaneous space and [6,6-$^2H_2$]glucose was administered i.v. as a primed-constant infusion. Tracer enrichments were measured in both plasma and ISF, together with plasma glucose and insulin concentrations. The model was fitted to ISF glucose tracer data using plasma measurements as forcing functions.

Results: The model predicted the data during meal and exercise, providing precise parameter estimates. In particular, τ was 18 ± 7 min and 21 ± 9 min (mean ± SD) in healthy and T1D subjects, respectively, almost doubled than those found in steady-state (9 ± 2 min and 12 ± 4 min, respectively).

Conclusion: A model assuming a constant τ describes plasma-to-ISF glucose kinetics in dynamic conditions. However, the slower kinetics shown in nonsteady- than steady-state conditions may call for more complex non-linear models.

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Glucose Sensors

ATTD19-0258

ASSESSMENT OF POTENTIAL ERRORS IN MANUAL CALIBRATION OF A CONTINUOUS GLUCOSE MONITORING SYSTEM

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Background: Many continuous glucose monitoring (CGM) systems require manual calibration, i.e., input of blood glucose (BG) monitoring data at specific times, in order to provide reliable CGM values. Data from a CGM performance assessment were used to investigate potential errors in manual calibration of a CGM system.

Methods: Data were obtained from 20 subjects wearing a CGM system for 14 days. The study comprised in-clinic sessions and home use phases. Subjects were educated to the calibration process and, during in-clinic sessions, they were supervised by study staff.

The following potential errors were assessed based on instructions for use: a) Calibration was not performed within the specified interval (12 hours (+0.5 hours tolerance)); b) BG values were not used within 5 minutes of the BG

	Study phase		
	Complete study	In-clinic sessions	Home use phase
No. of calibrations	1218	536	682
No. (%) of incorrect calibrations	129 (10.6%)	28 (5.2%)	101 (14.8%)
No. of errors made during calibrations	135	30	105
Calibration overdue	29	4	25
BG value used too late	41	8	33
BG value entered incorrectly	38	8	30
Glucose concentrations changed too rapidly	27	10	17

measurement; c) BG measurement was entered incorrectly; d) glucose concentration was changing too rapidly estimated from CGM data.

Results: See table.

Conclusions: Manual calibration may be associated with errors. Even well-educated diabetes patients may perform 10% of calibrations or more incorrectly. Diabetes patients should take utmost care when manually calibrating CGM systems.

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Glucose Sensors

ATTD19-0259

IMPLANTABLE CONTINUOUS GLUCOSE MONITORING AND GLUCOMETRIC PARAMETERS: PRELIMINARY DATA FROM REAL-LIFE

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Background: Eversense is a novel implantable Continuous Glucose Monitoring sensor providing accurate readings up to six months. The efficacy of Eversense on glycemic control and HbA1c has been described in the Precise studies. We have designed our research with the aim to evaluate if the system improves additional glucometric parameters in subjects with type 1 diabetes (T1D) in the real-life.

Methods: This is a multicenter observation study. Glucometric data were downloaded from the diabetes management system and collected at the time of the first implantation (baseline visit) and after 6 months as mean of 2 weeks. Variables evaluated were time in range (TIR), above (TAR) and below range (TBR), mean daily glycaemia and standard deviation. According to last guidelines indications, the range for TIR was set to 3.9-8.9 mmol/L. Anthropometric and clinical variables were also collected.

Results: A total of 21 patients with TD1 were evaluated. A statistically significant reduction of estimated HbA1c and mean glycemia were observed: eHbA1c from 56.1 ± 8.2 to 49.5 ± 6.4 mmol/mol, $\Delta = -6.6$ mmol/mol, $P = 0.004$; mean glycemia from 9.2 ± 1.4 to 7.9 ± 1.3 mmol/L, $\Delta = -1.3$mmol/l; $P = 0.002$. TIR increased from 47.4 to 58.3% ($P = 0.02$), while TAR was reduced from 49.2 to 34.8% ($P = 0.001$). TBR increased from 3.6 to 7.1% ($P = 0.01$). Reduction of glucose variability was also observed (SD from 3.3 to 2.8 mmol/l; $P = 0.02$).

Conclusions: In our preliminary data from a sample of quite well-controlled T1D patients, Eversense increases TIR and decreases TAR, while increasing TBR. Information from real life using Eversense may be advantageous to define new algorithms in the management of diabetes.

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Glucose Sensors

ATTD19-0260

REAL WORLD USE OF CGM-SYSTEMS AMONG ADOLESCENTS AND YOUNG ADULTS WITH TYPE 1 DIABETES: REDUCED BURDEN, BUT LITTLE INTEREST IN DATA-ANALYSES

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Since September 2016 CGM-systems are reimbursed by health insurance companies in Germany for patients with T1D. The rate and quality of use of CGM-systems among young people were assessed.

Participants of a German Diabetes Camp for young people with T1D (16-25 yrs.) were invited to anonymously answer a structured questionnaire on their glucose monitoring habits and satisfaction with use (11 Items), their clinical data and diabetes distress (PAID 5).

Overall 308 participants (77% response-rate) (age: 21.4 ± 3.5 yrs; diabetes-duration: 10.1 ± 5.9 yrs.; 73% female; HbA1c 7.7 ± 1.5%; CSII 60.6%) participated. Of them 29.5% used rtCGM, 45.8% iscCGM and 24.4% SMBG. HbA1c was highest with SMBG (8.0 ± 1.9%) compared to iscCGM (7.7 ± 1.4%) and rtCGM (7.7 ± 1.4%) without reaching significance. Diabetes distress was not associated with the method of glucose monitoring (PAID_5 sum-score: 6.2 ± 4.4).

Participants using either CGM-system reported of better well-being (97.6%) compared to SMBG, higher satisfaction (88.2%), better feeling of security (80.3%), important new information (62.0%); few reported of inconvenience (7.0%) or disturbances (11.0%) due to alarms of rtCGM. Regularly CGM-data analyses were reported by 19.1% of young people, their HbA1c was significantly lower compared to other CGM users (7.2 ± 1.2% vs. 7.7 ± 1.4%; $p = 0.04$).

In this huge but selected sample of Diabetes Camp participants 75% were using a CGM-system continuously. It contributes to significant improvement in several aspects of their everyday life, but was not associated with reduced diabetes distress or better glycaemic outcome as long as the young people don't analyse the CGM-data regularly. Structured education and motivation to analyse CGM-data regularly and effectively is necessary.

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Glucose Sensors

ATTD19-0264

DRIVEN TO HYPERGLYCAEMIA: ADULTS WITH TYPE 1 DIABETES HAVE HIGHER GLUCOSE LEVELS WHEN DRIVING

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Background: Hypoglycaemia impairs driving performance. Current Australian guidelines, based on this issue, require drivers using insulin therapy to be ''above 5 to drive''. This study investigated glucose levels of adults with type 1 diabetes (T1D) during driving compared with non-driving periods.

Methods: Australian drivers with T1D using intensive insulin therapy (via injections or pump) without real-time continuous glucose monitoring (CGM) were studied. All journeys were logged automatically for 3 weeks during masked CGM; data were analysed retrospectively. As most journeys (680/717; 95%) occurred between 07:00 and 22:00 hours, non-driving comparator CGM data were limited to this time. Primary outcome was CGM time-in-range of 3.9–10.0 mmol/L. CGM coefficient of variation (CGM-CV) was included to assess glucose variability while accounting for mean glucose (SD/mean).

Results: Fifteen adults participated (6 women; mean ± SD age 41 ± 12 years; BMI 25.8 ± 4.1 kg/m^2; HbA_{1c} 7.8 ± 0.9% [62 ± 11 mmol/mol]; licence duration 22 ± 12 years; journeys recorded 48 ± 12; total driving time recorded 922 ± 152 minutes). Median [IQR] time-in-range was lower during driving (33.3% [28.8,52.2]) than non-driving periods (54.8% [44.9,60.2]; $p = 0.001$; Figure 1). Conversely, glucose time >10 mmol/L was greater during driving (66.7% [42.9,71.0]) than non-driving periods (40.1% [35.4,51.7]; $p < 0.001$); no significant difference in glucose time <3.9 mmol/L was observed. CGM-CV was lower during driving (28.3% [24.2,36.2]) than non-driving periods (36.7% [34.7,41.5]; $p = 0.005$). Glucose time ≤5 mmol/L was lower during driving (2.8% [0.8,5.9]) than non-driving periods (9.4% [7.3,12.8]; $p = 0.026$).

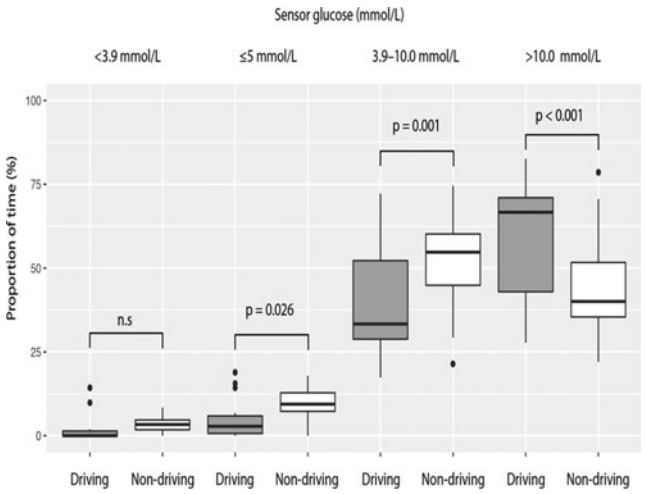

Figure 1: Each box plot represents percentage CGM time-in-range for <3.9 mmol/L, ≤ 5 mmol/L, 3.9-10.0 mmol/L and >10.0 mmol/L categories grouped by driving (gray box plots) and non-driving (white box plots, during daytime [0700–2200 h]) periods. Driving and non-driving periods were compared via Wilcoxon rank-sum test.

Conclusions: Driving is associated with sustained elevations in T1D glucose levels. This warrants further investigation and consideration for inclusion in diabetes driving guidelines.

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Glucose Sensors

ATTD19-0277

MULTI-NATIONAL PERFORMANCE ASSESSMENT OF THE WAVEFORM CASCADE CGM SYSTEM

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Background and aims: WaveForm is completing the final steps to a commercial launch of the Cascade CGM continuous glucose monitoring product intended for persons with T1D or T2D. The Cascade CGM is a transdermal filament that features trocar-free insertion and 14 days of use. The Cascade CGM demonstrated excellent performance in six previous multi-center studies (n = 87 subjects, MARD 10.4–13.5%). We are reporting on the initial results of a multinational study that will be part of our submission to obtain a CE-Mark for the Cascade CGM system.

Materials and methods: The ongoing Cascade CGM 14-day evaluation study is performed in centers in three different

countries (Slovenia, Croatia and Serbia) involving a total of 60 subjects with T1D or T2D. There are five in-clinic days (1, 4, 7, 10 and 14) that will be used to assess the accuracy of the system. Each subject wears two Cascade CGM devices in the abdominal area. YSI glucose measurements are performed on plasma from venous blood sampled every 15 minutes during each of the 12 hour in-clinic days. The overall MARD and MAD calculation is based on a comparison of paired YSI and CGM glucose values at the same time points. The CGM values were displayed and stored by the Cascade CGM using an embedded real-time algorithm. Final analysis will include more than 30 000 individual data pairs.

Results: Accuracy of the WaveForm CGM system on day 1 was a MARD of 14.5%, and a median MARD of 12.7%.

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Glucose Sensors

ATTD19-0279

DEVELOPMENT AND IN SILICO ASSESSMENT OF A CGM-BASED APPROACH TO TRIGGER ASSUMPTION OF HYPOTREATMENTS

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The standard protocol for hypoglycemia treatment recommends diabetic patients taking small amounts of carbohydrates, called hypotreatments, as soon as hypoglycemia is revealed. In this work we propose a new CGM-based approach to suggest the assumption of hypotreatments for mitigating/avoiding hypoglycemia.

The algorithm exploits the CGM datastream to forecast imminent hypoglycemic events and suggests hypotreatment ingestion. In particular, hypotreatment assumptions are triggered when the dynamic risk (DR) function (Guerra et al. Diabetes Technol. Ther., 2011) predicts a stable glucose level of 70 mg/dl. Early hypotreatment assumptions are also suggested when CGM values are below target glucose with rate-of-change<−1 mg/dl/min. The method is compared with the standard protocol by numerically evaluating the time in hypoglycemia (T_{hypo}) and the post-treatment rebound (PTR) for 100 virtual patients undergoing a single-meal experiment, with forced hypoglycemia, generated by the UVA/Padova T1D simulator.

In an ideal, noise-free, scenario the algorithm reduces, on average [5^{th}-95^{th} percentiles], T_{hypo} (from 36 [13–56] to 0 [0–25] min, $p < 0.0001$) without increasing PTR (from 136 [109–178] to 121 [108–141] mg/dl, $p < 0.0001$). Corrupting CGM traces with measurement error, brings to a lower -but still statistical relevant- improvement: T_{hypo} decreases from 41 [0–71] to 25 [0–71] min ($p < 0.0001$), PTR decreases from 176 [117–243] to 137 [109–178] mg/dl ($p < 0.0001$).

The (known) sensitivity of DR to noise suggests to improve the performance of the method in a realistic dataset with an enlarged set of merit criteria. Once the robustness of the proposed method is warranted, its applicability could be considered in both insulin pump and multiple-daily-injections therapies.

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Glucose Sensors

ATTD19-0296

PRE-PRANDIAL GLYCAEMIC LEVEL AND TREND ASSOCIATIONS WITH POST-PRANDIAL HYPERGLYCAEMIA: A WORLDWIDE OBSERVATIONAL ANALYSIS

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Background and Aims: Flash Glucose Monitoring (FreeStyle Libre™ system) is associated with significant improvement in glycaemic markers in the real-world. Due to increased availability of data, specific patterns of glycaemia around mealtime can be identified to help clinicians identify interventions to reduce postprandial hyperglycaemia.

Method: De-identified data from 421,245 meals (breakfast, lunch, dinner) from 14,864 users were analysed. Meals logged with at least 20g carbohydrate and non-zero units of insulin were included. Meals were divided into categories based on pre-prandial glucose levels (<70mg/dL, 70-180mg/dL and >180mg/dL) and glucose trends (Rising: >1mg/dL/min; Stable: ≤1mg/dL/min; Falling: >1mg/dL/min). Metrics including median post-prandial peak glucose level, time below 70mg/dL, time in range 70-180mg/dL and time above 180mg/dL were evaluated 4 hours post-meal.

Results: Meals with pre-prandial hyperglycaemia had higher levels of postprandial hyperglycaemia (153 min post-meal or 64%) compared to euglycaemic meals (63 min or 26%). Similarly, median peak glucose levels were higher in the hyperglycaemic group (239 mg/dL) compared to euglycaemic group (162 mg/dL). When pre-meal trend was rising, there was significantly more hyperglycaemia in the pre-meal hypoglycaemic (56 min or 23%) and euglycaemic groups (83 min or 35%) compared to stable pre-meal glucose (38 min/16% and 62 min/26% respectively). Median peak glucose values were also much higher when the trend was rising.

Conclusions: There are significant differences in post-prandial glucose excursions and peak times for different glucose levels and rates of glucose change at meals. Flash glucose monitoring can help identify pre-meal levels and trends which can be used to adjust interventions to address post-prandial hyperglycaemia.

Pre-meal glucose level (mg/dL)	Pre-meal glucose trend (mg/dL/min)	Number of meals (%)	Median pre-prandial glucose level (mg/dL)	Median post-prandial peak glucose level (mg/dL)	Median post-prandial change (mg/dL)	Median post-prandial peak time (min)	Minutes below 70mg/dL (of 4 hours)	Minutes within 70-180 mg/dL (of 4 hours)	Minutes above 180 mg/dL (of 4 hours)	Minutes above 250 mg/dL (of 4 hours)
<70	Falling: >1	0.3%	64	118	54	75	51	159	30	7
	Stable: ≤1	5.0%	59	128	69	75	43	159	38	9
	Rising: >1	0.1%	64	144	80	60	28	156	56	16
70-180	Falling: >1	5.0%	121	136	15	60	20	179	41	8
	Stable: ≤1	58.0%	122	162	40	75	10	167	63	13
	Rising: >1	8.8%	134	179	45	45	11	146	83	21
>180	Falling: >1	1.7%	218	212	-6	45	9	112	119	43
	Stable: ≤1	15.7%	214	237	23	60	5	81	154	66
	Rising: >1	5.4%	224	259	35	45	5	75	160	82

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Glucose Sensors

ATTD19-0298

FLASH GLUCOSE MONITORING IMPROVES HYPOGLYCAEMIA AWARENESS AND REDUCES FEAR OF HYPOGLYCAEMIA IN ADULT PATIENTS WITH TYPE 1 DIABETES

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Limited data are available on the effects of FGM use in patients with T1DM in the real world settings. We evaluated HbA1c changes, treatment satisfaction, awareness and fear of hypoglycaemia in adult patients with T1DM starting FGM.

Forty-four adult patients with T1DM naive to FGM were asked to complete validated questionnaires to assess awareness and fear of hypoglycaemia (Gold, Clarke and HFS) and satisfaction for diabetes treatment (DTSQs) before and after the first 8 weeks of FGM use. We compared interstitial glucose data from the first and last two weeks of FGM use and scores of questionnaires completed at the initial visit and after 8 weeks of FGM use.

Thirty-three of the 44 enrolled patients completed the study (25% lost to follow-up), while 5 patients scanned less than recommended and were, therefore, excluded from the analysis. Over the study period we did not observe significant changes in estimated HbA1c, mean daily glucose and glycaemic variability indices (SD, CV, HBGI, LBGI), time below range (<70 mg/dL) and time in range (70–180 mg/dL). A significant improvement of TIR was observed in patients with diabetes duration <12 years ($p = 0.037$). Analysis of questionnaires scores showed significant improvements of treatment satisfaction ($p = 0.0026$), fear of hypoglycaemia (0.0145) and hypoglycaemia awareness ($p = 0.0463$ in Clarke scoore).

In adult patients with T1DM the use of FGM was associated with an improvement of diabetes treatment satisfaction, hypolgycaemia awareness and a reduction in the fear of hypoglycaemia. Our data support tailoring educational programs of adult patients with T1DM starting FGM use.

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Glucose Sensors

ATTD19-0301

OBJECTIVELY MEASURED SLEEP VARIABILITY IS ASSOCIATED WITH GLUCOSE, DIABETES DISTRESS AND FEAR OF HYPOGLYCEMIA IN ADULTS WITH TYPE 1 DIABETES

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Sleep variability (variation in sleep duration) has been recognized as a potential contributor of glycemic control in type 1 diabetes (T1D). Diabetes management and fear of hypoglycemia may also contribute to sleep variability. The purpose of this secondary analysis was to examine associations of sleep variability with glycemic parameters using objective sleep and glucose measures. We studied 30 non-shift-working T1D adults, aged 18–39 years who wore actigraphy (BodyMedia SenseWear System®) and continuous glucose monitors (Medtronic Ipro2®) for 7 consecutive days. Sleep duration and variability (sleep duration standard deviation [SD]), mean daily glucose and glucose variability (glucose SD) were derived. Glycemic control (A1C Now®), and questionnaires measuring fear of hypoglycemia, diabetes distress and depression were obtained. Sleep duration ranged 5.1 – 10.9 hours per night; and sleep variability 0.53 – 3.18 hours. The mean daily glucose ranged 111 – 240 mg/dL; and glucose SD ranged 32 – 99 mg/dL). The bivariate analysis revealed that variability in sleep duration was significantly associated with glucose variability ($r = .458$, $p = .011$), mean daily glucose ($r = .585$, $p = .001$), diabetes regimen distress ($r = .600$, $p < .001$) and fear of hypoglycemia ($r = .460$, $p = .011$). A1C was not related to sleep duration. Multivariate linear regression, used to identify predictors of mean daily glucose, revealed that sleep duration SD was a significant predictor of mean daily glucose ($\beta = .439$, $p = .028$) Sleep variability may be a modifiable factor to consider in improving glucose indices.

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Glucose Sensors

ATTD19-0355

ESTIMATION OF NHS SAVINGS THROUGH THE INTRODUCTION OF REAL-TIME CONTINUOUS GLUCOSE MONITORING FOR PREGNANT WOMEN WITH TYPE 1 DIABETES

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Objective: To determine the budgetary impact of using real-time continuous glucose monitoring (CGM) for improved glucose control in pregnant women with Type 1 diabetes (T1D) in England.

Methods: A budget impact model was developed to calculate the expected costs over 28 weeks (10-38 weeks gestation) in T1D pregnancy with and without CGM, from the National Health Service (NHS) payer perspective. Clinical data relating to obstetric and neonatal complications (preeclampsia and neonatal intensive care unit (NICU) admissions) was sourced from a multicenter randomized controlled trial (CONCEPTT). Cost data was derived from National Tariff 2018/19, published literature and Medtronic list prices. The epidemiological data was based on National Pregnancy in Diabetes Audit 2016 and 1,519 T1D pregnant women were modeled.

Results: A potential cost saving of £10,077,958 over one year was projected if all T1D pregnant women used CGM during pregnancy, compared with no CGM use. NICU 24-hour admission cost (£3743) and average (NICU) length of stay (9.1 vs 6.6

days with vs. without CGM) were the main contributors to offsetting the cost of CGM. Sensitivity analyses on numerous parameters (percentage of complicated deliveries, 24-hour NICU admission cost, number of capillary glucose strips used, and length of hospital stay (non NICU)) confirmed the results were consistently robust with the CGM cohort showing cost savings in every scenario.

Conclusions: Implementation of CGM across T1D pregnant women in England has the potential to significantly reduce delivery complications, NICU admissions and length of stay, leading to important savings to the NHS within the first year.

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Glucose Sensors

ATTD19-0361

CONTINUOUS GLUCOSE MONITORING IN PEOPLE WITHOUT DIABETES AFTER PRE-DEFINED MEALS AND DURING DAILY LIFE

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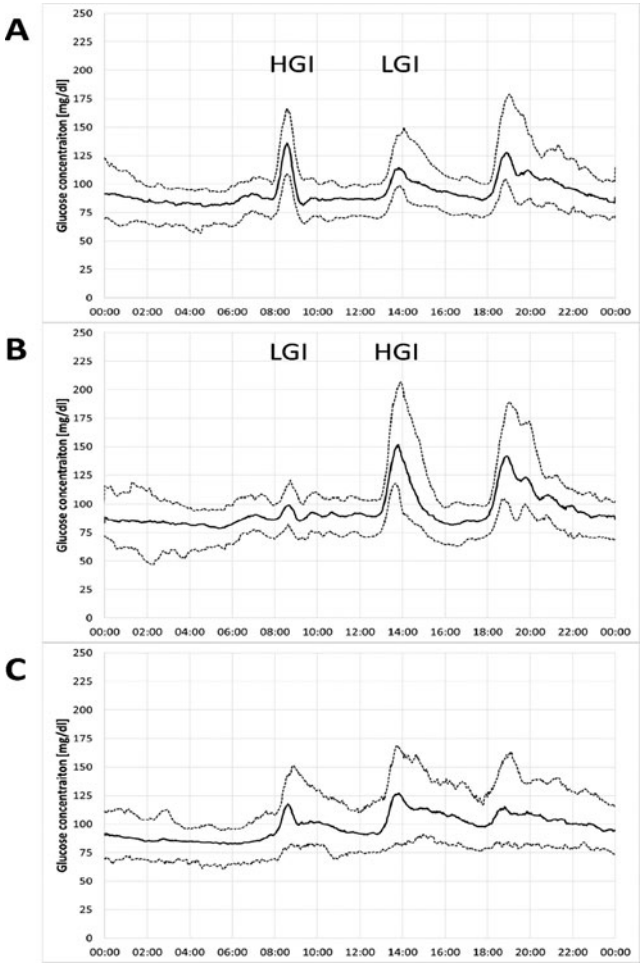
Background: Continuous glucose monitoring (CGM) is increasingly often used in diabetes management for tight glycemic control. However, diabetes therapy goals have to be realistic, i.e., they should be based on what is ''normal'' in people without diabetes.



Methods: In this study, 36 adults without diabetes (mean age 23.5 years) used two FreeStyle Libre sensors in parallel. On two days (days 4 and 5 of the 14-day sensor life), subjects were served two pre-defined meals with either low (LGI) or high glycemic index (HGI) at the study site. Subjects ate LGI meal for breakfast and HGI meal for lunch on one day, and vice versa on the other day. Dinner was selected from a buffet. On days 6 and 7, subjects only consumed three major meals at specific times and followed their daily-life activities.

Results: The figure shows median glucose (bold line) and 5%/95% quantiles (dashed lines). Median fasting glucose was approximately 80 to 100 mg/dl.

Highest glucose concentrations were observed after HGI lunch with the 95% quantiles exceeding 200 mg/dl (plot B). Postprandial peaks after LGI breakfast were nearly absent in contrast to LGI lunch.

In the daily-life setting (plot C), glucose spikes were less pronounced than after HGI meals, but in some cases considerable increases (median: 125 mg/dl, 95% quantile: 165 mg/dl) were observed.

Conclusions: Glucose concentrations in people without diabetes showed post-prandial increases depending on the specific meal composition. Considerable glucose fluctuations were also observed in people without diabetes under daily-life conditions.

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Glucose Sensors

ATTD19-0375

LITERATURE SEARCH ABOUT THE DOCUMENTATION OF SKIN-RELATED ISSUES WITH CGM USE

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Background and Aims: The average wear time of CGM systems steadily increased over the last years. Increased wear times are likely achieved by using stronger adhesives, which may have a stronger effect on the skin than less strong adhesives. Thus, an increase in skin-related issues associated with CGM use may be observed.

The objective of this project was to perform a structured literature search to assess how potential skin-related issues with CGM usage are reported in the scientific literature.

Method: The PubMed database was searched for articles about continuous or flash glucose monitoring in association with the term ''adverse'' and tagged with the MeSH term ''human'', published within the last 5 years in English language.

After exclusions, due to not suitable article type or content, 154 results were further analyzed.

Results: The number of studies (differentiated between the study objective) mentioning occurrences of skin-related issues is presented in the table.

In 8 articles it was explicitly stated that no skin-related issues were observed. The most common skin-related issues were bruising, bleeding, erythema, hypersensitivity, itching, and pain. No skin-related issue was classified as serious adverse event.

Skin-related issues mentioned	Study objective		Total n = 154, 100%
	CGM performance/ efficacy (n = 51, 33.1%)	Other* (n = 103, 66.9%)	
Yes	15 (68.2%)	7 (31.8%)	22 (14.3%)
No	36 (27.3%)	96 (72.7%)	132 (85.7%)

Conclusion: Considering all studies, approximately 15% of articles mentioned occurrences of skin-related issues at all. Of these, the percentage was substantially larger (approximately 30% (15 of 51)) for articles, in which CGM was the study's main topic.

More detailed reports about skin-related issues in scientific literature may be helpful to draw possible conclusions about the occurrence of skin-related issues during CGM use.

Table 1. Study Findings

Freestyle Libre Data	Participant									
	001	002	003	004	005	006	007	008	009	010
Age	90	80	82	80	86	87	82	92	85	81
Type of diabetes	2	2	2	1	2	2	2	2	2	2
Dementia diagnosis	No	Yes	No	No	No	No	No	No	No	Yes
AMT	5/10	n/a	8/10	8/10	8/10	7/10	7/10	7/10	8/10	n/a
Days sensor was worn	14	14	14	14	14	14	14	14	14	14
Average glucose, mmol/L	16.8	8.8	8.4	11.9	10.8	9.6	12.2	7.3	6.6	16.0
Low-glucose events (less than 4mmol/L)	0	0	1	11	none	none	none	13	21	none
Average duration of low glucose events, min	n/a	n/a	109	113	n/a	n/a	n/a	106	182	n/a
Data capture, %	70	62	65	83	38	3	34	76	92	33
Number of scans over 14 days	57	45	34	166	27	4	24	75	183	22

ISRCTN: 29516623

Research Ethics approval reference: 17/EE/0388

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Glucose Sensors

ATTD19-0376

FEASIBILITY AND ACCEPTABILITY OF CONTINUOUS GLUCOSE MONITORING IN OLDER PATIENTS LIVING WITH MEMORY PROBLEMS AND DIABETES – PRELIMINARY RESULTS

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Introduction: Older people with diabetes have increased risk of harm from hypoglycaemia, particularly where there is co-existing dementia. Continuous glucose monitoring (CGM) offers important benefits but has not been trialled in those with memory problems. We conducted a feasibility study of Freestyle Libre in the community with older patients with memory problems and diabetes.

Methods: We recruited patients aged ≥65 with diabetes and abbreviated mental test score (AMT) ≤8 or known dementia. Feasibility criteria were numbers of eligible patients, recruitment, attrition, extent of capture of glucose readings and adverse events. We conducted a qualitative interview regarding acceptability of CGM.

Results: We identified 39 eligible participants; 15 subsequently consented but five withdrew before recording of data because they, or their carers felt unable to manage study monitoring and procedures. 10 participants (median age 82 years) completed the study without any adverse events. Data capture across 14 days ranged between 3-92% (median 62%); 4 participants had <60% capture. Hypoglycaemic events (some prolonged) were recorded in 4/10 participants, principally insulin-users.

Qualitative interviews found the following themes:

1. The device does not interfere with daily activities.
2. Usability and comfort was positive.
3. Helpful for carers in monitoring participants' glucose concentration.

Conclusions: The device was acceptable to participants, and carers reported greater ease in monitoring the participant's glucose concentrations. However, completeness of data capture varied considerably with this device due to need for three daily scans. Real-Time devices with automated data transfer may be more suitable for older patients with diabetes and memory problems.

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Glucose Sensors

ATTD19-0377

ASSESSING MEASURES OF GLYCEMIC VARIABILITY TO DETERMINE THE BEST METRIC TO PREDICT THE RISK OF HYPOGLYCEMIA IN TYPE 1 DIABETES PATIENTS USING CONTINOUS GLUCOSE MONITORING

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Background: 2017 International consensus on use of CGM recommends coefficient of variation (CV) as the primary measure of glycemic variability (GV) with a cutoff threshold of 36%. Recently, we reported that CV had the highest association with hypoglycemia in T2D patients with an AUC of 0.84 (95% CI 0.77-0.91). However, there is a lack of evidence supporting the use of one particular measure of GV in T1D patients as a predictor of hypoglycemia.

Objective: To assess different measures of GV to determine the metric that best discriminate the risk of hypoglycemia and to define the optimal cutoff threshold in T1DM patients

Methods: A cohort of T1DM patients was evaluated using CGM. Rate of incidence and number of events of hypoglycemia <54 mg/dL were calculated. Univariate and multivariate analysis

of different metrics of GV was performed and optimal cutoff thresholds were determined from analysis of the ROC curves.

Results: CGM data from 73 patients were analyzed. Hypoglycemia <54 mg/dL was present in 34 (46,6%) patients with 128 events (3,76 events per patient), incidence rate of 1.75 events per patient/day. In the multivariate analysis, CV was the only parameter of GV that had statistically significant association with hypoglycemia RR 1.45 (1.1–1.87) p 0.008. The optimal cutoff threshold of CV to discriminate the risk of hypoglycemia was 34%. The AUC was 0.90 (95%CI: 0.86–0.98).

Conclusion: This analysis shows that CV with a cutoff threshold of 34% is the best metric of GV associated to risk of hypoglycemia in T1D patients.

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Glucose Sensors

ATTD19-0378

CLINICAL VARIABLES VS GLYCEMIC VARIABILITY AS A RISK FACTOR OF HYPOGLYCEMIA IN PATIENTS WITH TYPE 1 DIABETES

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Background: Different clinical variables have been associated to the risk of hypoglycemia in patients with type 1 diabetes (T1D). Glycemic Variability (GV) appears to be a stronger predictor of hypoglycemia.

Objective: To determine clinical variables and glycemic variability indexes measured by continuous glucose monitoring (CGM) associated with hypoglycemia in patients with T1D.

Methods: A cohort of T1D patients in ambulatory setting was evaluated. Demographic variables, A1c, glomerular filtration rate and physical activity were assessed. Rate of incidence and number events <54 mg/dl were estimated. Univariate and multivariate analysis of clinical variables and metrics of GV were performed to determine the association with hypoglycemia.

Results: CGM data from 73 patients were analyzed. Hypoglycemia <54 mg/dL was present in 34 patients (46.5%) with 128 events in total (3,76 events per patient), incidence rate of 1.75 events per patient/day. In the univariate analysis, time since diagnosis in years (RR 1.02 95% CI 1.02–1.04, p 0.04) and hypoglycemia unawareness (RR 1.59 IC95% 1.0 – 2.36, p 0.05) were associated with hypoglycemia. However, in the multivariate analysis, none of the clinical variables showed a significative statistically association with hypoglycemia. Only GV measured with coefficient of variation (CV) showed statistically association with hypoglycemia (RR 1.45 IC95% 1.1–1.87, p 0.008) in the multivariate analysis.

Conclusion: In this study, clinical variables were not associated to the presence of hypoglycemia <54 mg/dL. CV was the only risk factor associated with hypoglycemia. This finding reinforces the clinical importance of CGM in patients with T1D.

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Glucose Sensors

ATTD19-0402

GLUCOSE VARIABILITY BASED ON 50,000 DAYS OF CONTINUOUS GLUCOSE MONITORING: A DPV ANALYSIS IN 2,093 PEDIATRIC AND ADULT PATIENTS WITH TYPE 1 DIABETES

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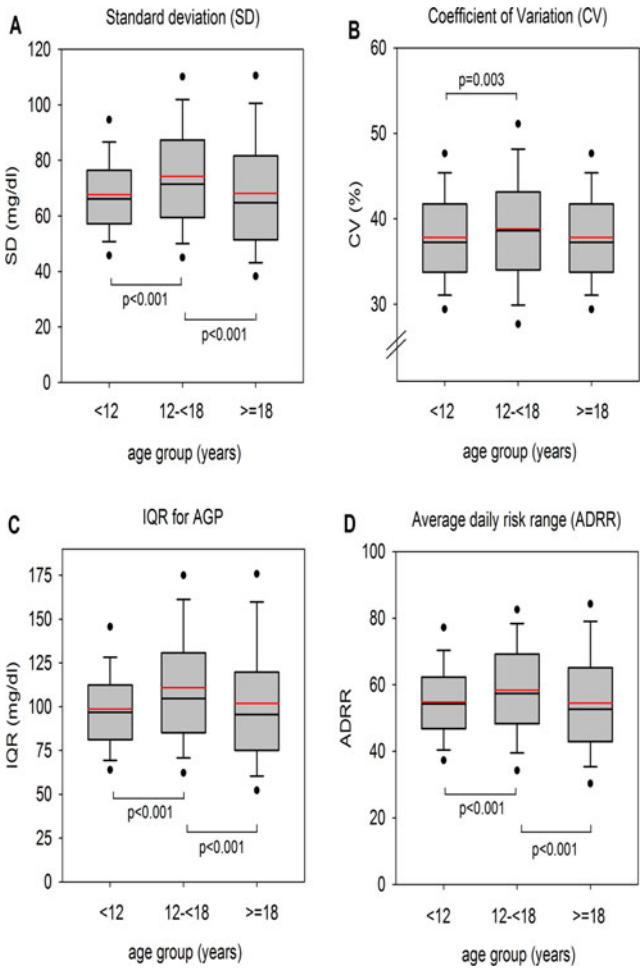
Objectives: To assess glucose variability based on continuous glucose monitoring (CGM) using different metrics in pediatric and adult patients with type 1 diabetes (T1D).



Methods: 50,200 days of CGM profiles (the most recent up to 30 days per patient) from N = 2093 patients with T1D duration ≥1 year documented in the German/Austrian/Luxembourgian DPV database were analysed. Metrics for short-term within-day glucose variablility (standard deviation (SD), coefficient of variation (CV)) and the average daily risk range (ADRR), which is a composite of within-day and between-day glucose variability, were compared between age groups (<12 years: N = 773, 12–<18 years: N = 1095, ≥18 years: N = 225) and between gender using Kruskal-Wallis tests. In addition, interquartile range for averaged glycemic profiles (IQR for AGP) and percentage of time in range (TIR, 70-180 mg/dl) were assessed.

Results: Overall, 53% of the patients were male, and 69% used insulin pumps. Mean HbA1c was 7.5 ± 1.2% (59 ± 13 mmol/mol). 31%/69% of the patients used real-time/intermittent scanning CGM.

Average TIR was lowest in adolescents aged 12-<18 years (45%) compared with children aged <12 years and adults (51% and 50%, respectively, both $p < 0.001$). Glucose variability was comparable in children and adults, but higher in adolescents (Figure). Gender comparisons revealed lower average TIR and higher glucose variability in males than in females (TIR: 47 vs. 49%, IQR: 108 vs. 103 mg/dl, ADRR: 57.8 vs. 55.3, all $p < 0.005$).

Conclusions: Glucose variability assessed using CGM data was higher during adolescence and higher in males than in females. CGM data may help to understand the potential clinical relevance of glucose variability.

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Glucose Sensors

ATTD19-0409

YOUNG CHILDREN WITH TYPE 1 DIABETES (T1D) SPEND THE MAJORITY OF TIME OUTSIDE OF TARGET GLUCOSE RANGE

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Objectives: There are limited data on sensor glucose profiles in youth under age 8 with T1D. We analyzed blinded continuous glucose monitoring (CGM) data collected at baseline from a randomized trial evaluating CGM in young children.

Methods: Data were analyzed from 143 children across 14 sites in the USA. Major eligibility criteria for the trial included age 2–<8 yrs, T1D duration ≥3 months, no CGM use in the previous 30 days and A1c between 7.0–<10.0%.(53–<86 mmol/mol) All participants wore blinded Dexcom G4 CGMs (505 algorithm) for up to 14 days and collected at least 200 hours of CGM data. Demographic and clinical characteristic associations with CGM-measured glucose values were assessed using linear regression models.

	Percent of Time Median (IQR)	Minutes/Hours per day Median (IQR)
Time in Range 70-180 mg/dL/ 3.9-10.0 mmol/mol	41% (33%, 47%)	10 (8, 11) hours/day
Time >180 mg/dL/ >10.0 mmol/mol	55% (45%, 63%)	13 (11, 15) hours/day
Time >250 mg/dL/ >13.9 mmol/mol	28% (22%, 37%)	7 (5, 9) hours/day
Time <70 mg/dL/ <3.9 mmol/mol	4.1% (2.2%, 8.1%)	59 (31, 116) minutes/ day
Time <54 mg/dL/ <3.0 mmol/mol	1.4% (0.4%, 3.6%)	20 (6, 52) minutes/ day

Results: Participants were 50% male, median age 5.9 yrs, median T1D duration 1.9 yrs, 68% non-Hispanic white, and 35% used insulin pumps. Mean A1c was 8.2% (66 mmol/mol) and mean sensor glucose 202 mg/dL (11.2 mmol/mol). Youth spent more time in hyperglycemia than in the target glucose range, and a median of 1 hr/day in a hypoglycemic range (Table). Factors associated with greater time in target range and less time in hyperglycemia included minority race and higher parent education level ($P \leq 0.03$ for all). More time spent in hypoglycemia was associated with minority race and younger age at diagnosis ($P \leq 0.02$ for both). Insulin delivery method was not associated with any of the metrics.

Conclusions: Given that both hypo and hyperglycemia may negatively impact young children's cognitive development, strategies to increase time in target glucose range are needed.

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Glucose Sensors

ATTD19-0416

AMBULATORY GLUCOSE PROFILING AND GLYCAEMIC OUTCOMES WHEN SWITCHING FLASH TO CONTINUOUS GLUCOSE MONITORING: THE I-HART CGM STUDY

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Background: The I-HART CGM Study was the first head-to-head glucose monitoring study designed to assess impact of flash and continuous glucose monitoring (CGM) in highest risk adults with type 1 diabetes. In this sub-analysis, we present ambulatory glucose profiles and glycaemic outcome measures specifically focusing on the time of switch from flash to CGM.

Methods: Randomized, parallel group study with forty participants on multiple daily injections with a Gold Score ≥4 or recent severe hypoglycaemia. Participants were randomized to CGM (DexcomG5; n = 20) or flash (Freestyle Libre; n = 20) for 8-weeks. An open extension phase enabled participants on CGM to continue for a further 8 weeks, and those on flash to switch to CGM over this period. Outcomes were analyzed for the week

	Flash glucose monitoring n=20 Median (IQR)		Difference between week 8 and week 9
% time in defined glucose range	Last week of Flash (week 8)	First week of CGM after switch (week 9)	p-value
<54mg/dL	5.43%	0.64%	p<0.001
<70mg/dL	9.58%	3.66%	P<0.001
>180mg/dL	19.59%	23.85%	p=0.15
70 – 180mg/dL	63.36%	61.37%	p= 0.16

before and after the switch (i.e. week 8 versus week 9 in the flash group).

Results: CGM was associated with reduced percentage time in hypoglycaemia (thresholds <54mg/dL and <70mg/dL, after switching from flash the week before. No difference was observed for percentage time in hyperglycaemia (CBG >180mg/dL) and percentage time in range (70–180mg/dL; Table 1). Additional ambulatory glucose profiles were analysed one week pre- and post- switching to CGM. The most marked period of reduction in percentage time in hypoglycaemia occurs nocturnally.

Conclusions: Our results indicate reduced time in hypoglycaemia occurs within a single week of CGM use, particularly addressing nocturnal hypoglycaemia. The data supports our previous findings and highlights the importance of ensuring the most appropriate glucose monitoring technique is selected for individuals at highest risk of diabetes.

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Glucose Sensors

ATTD19-0418

REAL-TIME CONTINUOUS GLUCOSE MONITORING IN PATIENTS WITH TYPE 1 DIABETES TREATED WITH MULTIPLE DAILY INJECTIONS

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Aims: The aim was to analyze the effectiveness of Real-Time Continuous Glucose Monitoring (RT-CGM) in glycemic control in patients with type 1 diabetes (T1D), children and adults, treated with multiple daily injections of insulin (MDI) in real-world use.

Methods: We retrospectively analyzed data of all patients with T1D in follow-up in the University Hospital of Badajoz who received treatment with MDI and used RT-MCG. Age, sex, time of evolution of diabetes, daily insulin dose, type of basal insulin administered, MCG device used and duration of use of RT-GCM were evaluated. HbA1c was compared before the start of the RT-CGM and at the end of the follow-up.

Results: 98 patients were evaluated, mean age was 34 ± 19 years, 29% children, with an evolution time of diabetes of 14 ± 12 years. 89% used Dexcom® system and 11% Medtronic's Guardian®. The daily insulin dose was 0.7 ± 0.3 U/kg and the basal insulins used were Glargine U100(32%), Degludec(34%), Glargine U300(14%), Levemir(6%) and NPH(1%).

Main duration of RT-CGM use was 9 months [4–24]. 8 patients started an integrated pump-sensor system after 7 months [5–14] of MCG use; only 3 patients stopped using the RT-CGM for lack of improvement.

The percentage of patients with good glycemic control (HbA1c ≤7% in adults and ≤7.5% in children) grew from 48% to 60% (p = 0.001, n = 73) at the end of follow-up.

Conclusion: The use of RT-CGM in T1D patients treated with MDI provides sustained positive results in terms of improvement of the glycemic control with a low dropout rate.

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Glucose Sensors

ATTD19-0437

FLOW-CHART TO PREVENT HYPOGLYCEMIA AND HYPERGLYCEMIA IN ADOLESCENTS WITH TYPE 1 DIABETES USING STANDALONE CONTINUOUS GLUCOSE MONITORING WITH PREDICTIVE ALARMS: 1-YEAR FOLLOW-UP DATA

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[10]Hospital Giovanni XXIII, Pediatrics, Bari, Italy
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[13]Bambin Gesù Hospital, Pediatric Diabetes, Rome, Italy

Introduction: Our aim was to determine the efficacy of a specific-designed flow-charts to limit hypo and hyper in 32 adolescents with type 1 diabetes using MDI plus Guardian Connect (Medtronic, US), under free-living conditions.

Methods: Predictive alarm (PA) system safety and efficacy were evaluated by analyzing CareLink data either during a 4-day camp, after 4 days at home, and after 1-year follow-up. Mean meter BGs,mean sensor glucose, sensor SD, %time in hypo (< 3.9 mmol/l), %time in hyper (>8.9 mmol/l),episodes of severe hypo or DKA have been analyzed. The primary outcome was the %time for hypo and hyper.

Results: We analyzed 32 patients (mean age 15.7 ± 1.5 yrs, diabetes duration 8 ± 4 yrs, HbA1c 7.8 ± 1.2%). The average BGs was 10.3 ± 1.4 mmol/l, while average sensor glucose was 10.1 ± 1.3 mmol/l, with slightly lower values during camp than at home (p = 0.000) Time spent in hypo was similar at camp and at home (0.53 ± 0.83% vs 0.40 ± 0.67, p = 0.033), as well as time spent over 10 mmol/l (27.12 ± 14.91% vs 33.42 ± 16.34, p = 0.000). After 6 months since camp, 49% of adolescents were still using glucose sensor daily, with %time in target 58%, while after 1 year 47% of teens were using glucose sensor daily with %time in target 52%.

Sensor glucose values	Current CGM trend/alert	Action	SMBG	Immediate adjustments	Follow-up
<70 mg/dl* (<3.9 mmol/l)	ALL but ↑	Check SMBG	<70 mg/dl* (<3.9 mmol/l)	Sugar 0.3 gr/kg (max 15 gr)	If still symptomatic after 15 min could be repeated
70-180 mg/dl (3.9-10 mmol/l)	Predictive hypo alert (settled 30 min before)	Check SMBG only if needed	70-180 mg/dl (3.9-10 mmol/l)	Sugar 0.1 gr/kg (max 5 gr) If exercise think of 0.2-0.3 gr/kg (max 15 gr)	
180-250 mg/dl (10-13.9 mmol/l)	No arrow or ↑	Check SMBG only if needed	180-250 mg/dl (10-13.9 mmol/l)	No action	
180-250 mg/dl (10-13.9 mmol/l)	↑↑ or ↑↑↑	See below	180-250 mg/dl (10-13.9 mmol/l)	See below	
>250 mg/dl (>13.9 mmol/l)	ALL but ↓	Check SMBG only if needed	>250 mg/dl (>13.9 mmol/l)	•If meal <2h just wait •If meal >2h correction bolus •If exercise, check ketones •If ketones <0.6 mmol/l correction bolus reduced 20% •If ketones >0.6 mmol/l NO exercise and correction bolus	Check glucose value in the next 1 h If no improvement, wait at least 2 h for another correction bolus

Conclusions: PA system in adolescents with type 1 diabetes was safe and effective, the use of the flow-charts contributed to reduce time spent in hyper. Correcting a glucose value before it reaches a hypoglycemic threshold with one third of glucose amount usually used is effective to prevent hypo and limit hyperglycemic excursion after correction.

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Glucose Sensors

ATTD19-0450

MEASURING GLUCOSE IN TEAR FLUID: A FEASIBILITY STUDY IN HUMANS WITH DIABETES

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Introduction: Current monitoring methods for glucose are invasive, painful and expensive. We report the clinical feasibility of a glucose sensor worn in the lower eye lid to continuously measure glucose levels in basal tear fluid and their correlation to blood glucose values.

Patients and Methods: In this second phase clinical trial, six patients with TD1 using CGM subcutaneously were enrolled and capability of the device to measure glucose in the tear fluid was evaluated for 5 hours. The ARD and median ARD were calculated and compared to subcutaneously and capillary glucose measurements which were performed every 15 minutes. Side effects and patient satisfaction were monitored.

Results: The NovioSense glucose sensor gives a stable signal and the results correlate well to blood- and subcutaneous glucose values obtained from finger prick measurements and CGM. No side-affects. he error grid analysis showed that 95% of data for NovioSense and 100% of data from the Abbott device was found in the A + B regions; 70% of the data for the NovioSense device was in the A region and 71% for the Abbott FreeStyle Libre. The calculated MedARD for NovioSense device is 12.5 which appears to be in line with the Abbott FreeStyle Libre. The NovioSense device could measure 70% of the data points within the 20% accuracy criteria with the Abbott device scoring only marginally better with 78% of data within 20% accuracy.

Conclusion: we present the first multi-patient clinical trial that demonstrates unequivocally that tear fluid is a valuable marker for the systemic glucose measurements.

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Glucose Sensors

ATTD19-0457

A SYDNEY DIABETES CENTRE'S EXPERIENCE OF THE AUSTRALIAN GOVERNMENT ROLL OUT OF SUBSIDISED CONTINUOUS GLUCOSE MONITORING FOR CHILDREN WITH TYPE 1 DIABETES MELLITUS

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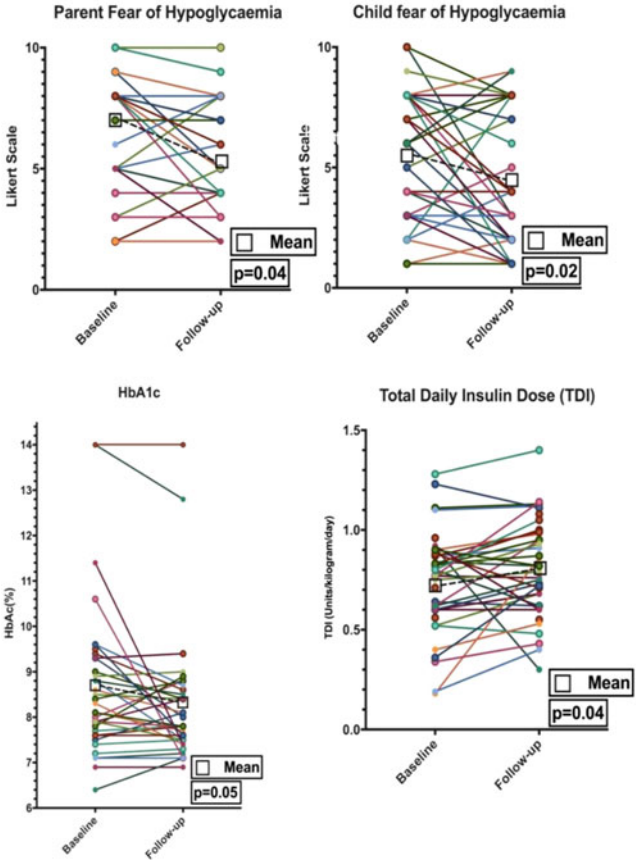
Aims:

1. Determine patient/carer expectations of continuous glucose monitoring (CGM) and short-term satisfaction after CGM government subsidy roll out.

Figure 1: Total Daily Insulin, HbA1c and Fear of Hypoglycaemia Before and After CGM Commencement



2. Assess the efficacy of CGM in improving:
   a) Fear of hypoglycaemia
   b) Glycaemic control (HbA_{1c}, ketosis, hypoglycaemia)
3. Determine time requirements of diabetes clinic staff in commencing and administering CGM.

Methods: We assessed CGM naïve patients starting on CGM at a Sydney Diabetes centre following the introduction of a nationwide government subsidy for CGM. A standardized questionnaire was administered collecting demographic and glycaemic information in addition to Likert scale assessment of expectations and satisfaction. Clinic staff reported time dedicated to CGM education, commencement, and follow-up.

Results: 55 patients or parents/carers completed baseline questionnaires, with 37 completing a 3-month follow-up questionnaire. There were high expectations of CGM prior to commencement, and high satisfaction ratings on follow-up. CGM improved fear of hypoglycaemia and total daily insulin dose increased after commencement of CGM. There was a trend towards lower HbA_{1c} that was not statistically significant. There was no statistically significant reduction in ketosis or hypoglycaemia. Comments were mostly positive, with some concern raised regarding technical issues and a lack of subsidy after 21 years of age. Staff time requirements were substantial, with an estimated average of 7.7 hours per patient per year.

Conclusions: Patients and families have high expectations of CGM and satisfaction levels are high in the short term. Total insulin delivery increased after CGM commencement and fear of hypoglycaemia decreased. Time requirements by staff are substantial, but may be worthwhile if families' overall satisfaction levels are high.

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Glucose Sensors

ATTD19-0459

FREESTYLE LIBRE FLASH GLUCOSE MONITORING SYSTEM USE IN YOUNGER PATIENTS WITH DIABETES UNDER REAL LIFE SETTINGS: REDUCTION IN HBA1C AND HYPOGLYCAEMIC EXPOSURE

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Aims: Early glycaemic control is important to reduce long-term diabetes complications. In this single centre study, we analysed the role of Freestyle Libre Flash Glucose Monitoring System in modulating glycaemic control in younger patients with type 1 diabetes (T1D)

Methods: Children and young adults with T1D aged between 4 and 19 years were started on the Freestyle Libre Flash Glucose Monitoring System due to difficulties with glycaemic management, including inadequate glucose control despite regular self-monitoring of blood glucose (SMBG), inability to perform SMBG, frequent hypoglycaemia or fear of hypoglycaemia without complete loss of awareness. HbA1c was measured at baseline, 3 and 6 monthsand data on hypoglycaemic exposure was collected.

Results: Complete glycaemic data were available in 102 patients followed up for a minimum of 6 months. Baseline HbA1c (mean ± SD) was 70.1 ± 19.6 mmol/mol dropping to 66.3 ± 19.5 mmol/mol at 3 months ($p = 0.003$) and remaining stable at 6 months at 65.7 ± 18.7 mmol/mol. Hypoglycaemic exposure reduced from 8.4 ± 7.5% at baseline to 6.3 ± 5.2% at 3 months ($p = 0.009$). The reduction in hypoglycaemia was unaffected by gender but was most pronounced in those younger than 13 years of age. The reduction in hypoglycaemia was similar in those with baseline HbA1c <60 mmol/mol and those with baseline HbA1c between 60–90 mmol/mol.

Conclusions: Under real life settings, Freestyle Libre use in children and young adults with T1D is associated with a significant reduction in HbA1c and hypoglycaemic exposure. The reduction in hypoglycaemia in those with poor glycaemic control indicates that this glucose monitoring strategy is beneficial to decrease hypoglycaemic exposure regardless of starting HbA1c.

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Glucose Sensors

ATTD19-0487

INTERSTITIAL GLUCOSE MONITORING IN PATIENTS WITHOUT KNOWN DIABETES MELLITUS WITH HEMATOLOGIC MALIGNANCIES AND SUBMITTED TO CORTICOSTEROIDS DURING CHEMOTHERAPY (LIBREONCO STUDY)

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Glucocorticoids (GC) are widely used in the treatment of hematologic malignancies. GC are the main cause of drug-induced hyperglycemia, even in patients without known DM.

Few data in the literature has described the behavior of glycemia in cancer patients without DM and on GC during chemotherapy.

A prospective study using FreeStyle Libre Monitoring System (FSL) (Abbott®) was performed in 18 patients without DM and on GC use associated with chemotherapy for hematologic malignancies. 61% were men and mean age of the patients was 51.1 ± 16.5 years old. The mean interstitial glucose (IG) was 110 ± 26.5mg/dL, during 12 days of monitoring. The IG didn't have correlation with age ($p = 0.32$), gender ($p = 0.99$), nor over the days after initial chemotherapy ($p = 0.94$).

The mean dose of GC during chemotherapy cycle was 753 ± 533mg of prednisone or equivalent, used in 5.8 ± 1.79 days. 10 patients used dexamethasone and 8 used prednisone. In prednisone group (PG) the IG was 106 ± 23mg/dL and in dexamethasone group (DG) was 114 ± 31mg/dL, however, after adjustment by dose, there was not significant association between IG and GC type ($p = 0.58$).

Moderate correlation was observed between average IG and the total dose of GC in the chemotherapy cycle ($r = 0.52$, $p = 0.027$). The risk of development of hyperglycemia

(IG >200mg/dL) doubled if the dose was greater than 500mg of prednisone or equivalent, whose sensitivity is 91% to predict hyperglycemia.

Conclusions: Higher total doses of GCs (>500mg prednisone or equivalent) during chemotherapy increase the risk of hyperglycemia in patients without diabetes. Therefore, greater attention should be paid to glycemic control in this population.

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Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0247

USER EXPERIENCE WITH A NEW SMARTPHONE APPLICATION FOR BLOOD GLUCOSE MONITORING (BGM) IN AN INFORMATION-MOTIVATION-BEHAVIORAL SKILLS (IMB) MODEL STUDY

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The CONTOUR®NEXT ONE BGM system (BGMS) includes a wireless-enabled BG meter that links to the CONTOUR®Diabetes app installed on a mobile device. The system, based on the IMB model, detects and reports patterns of BG readings and provides guidance for self-management. The IMB model emphasizes the need for actionable information, motivation to act, and behavioral skills for acting effectively, to strengthen self-management of diabetes. This 6-week study with 46 insulin-using individuals with diabetes assessed the BGMS with the CONTOUR®Diabetes app Version 2 Prototype. Participant appraisal of the BGM/app system was positive on multiple dimensions (Table 1). Participants strongly agreed/agreed that using this BGM/app system provided them with a better understanding of their disease (98%), helped them feel more engaged with their diabetes management program (91%), they felt more motivated to adhere to their health care provider's therapy and testing recommendations (76%), that the ''My Patterns'' pattern recognition feature was helpful in managing their diabetes (73%), and that they found themselves testing more frequently throughout the day (56%).

Table 1. Study Participant Appraisal of the BGM/App System[a]

Question	Percent of participants who reported Agree/Strongly Agree
This BGM/App System will provide me with a better understanding of my disease.	98%
This BGM/App System helped me feel more engaged with my diabetes management program.	91%
Using this BGM/App System, I felt more motivated to adhere to my health care provider's therapy and testing recommendations.	76%
My Patterns was helpful to me in managing my diabetes.	73%
Using this BGM/App System, I found myself testing more frequently throughout the day.	56%
The information I learned through my blood glucose pattern messages in the App was useful/helpful for me in managing my diabetes.	74%

[a]The questions reported here represent a subset of the complete questionnaire.

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Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0269

CHANGES IN BLOOD GLUCOSE EXCURSIONS AFTER AT LEAST 180 DAYS REAL WORLD USE OF A NEW SMARTPHONE APPLICATION FOR BLOOD GLUCOSE MONITORING

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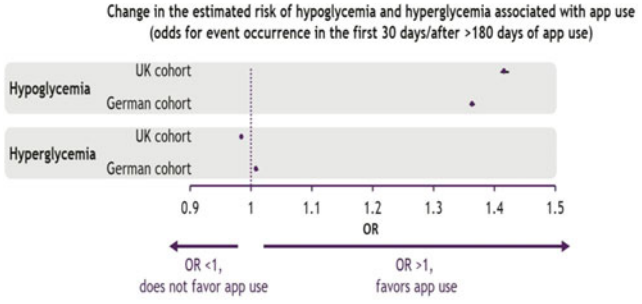
Background: Mobile apps are an emerging technology to facilitate diabetes self-management. The CONTOUR®NEXT ONE blood glucose (BG) monitor system is a wireless-enabled BG meter, linked to the CONTOUR®Diabetes mobile app (developed using the successful Information-Motivation-Behavioral Skills model, to detect and report BG patterns for self-management guidance).

Aim: To determine the effect of app use on BG excursion frequency, and identify subsets of patients with frequent excursions.

Method: Anonymized user data (N = 11,368) were collected from two cohorts that used the app for >180 days: UK (N = 3905) and Germany (N = 7463). Excursions were classified as hypoglycemia (<50 mg/dL) or hyperglycemia (>180 mg/dL); repeat excursions as ''repeat hypoglycemia'' (≥5 hypoglycemic events within the first 30 days and after 180 days) or ''repeat hyperglycemia'' (≥5 hyperglycemic events within the first 30 days and after 180 days). Odds ratios (OR) describe event-frequency in the first 30 days/after 180 days.

Results: App use for >180 days was associated with a statistically significantly lower hypoglycemia frequency in both cohorts (UK OR: 1.417 [95% CI 1.411; 1.423]; Germany OR: 1.364 [95% CI 1.360; 1.367]) and little effect on hyperglycemia frequency (minor increase in UK cohort, OR: 0.985 [95% CI 0.984; 0.986]; minor decrease in German cohort, OR: 1.009 [95% CI 1.008; 1.011]); **Figure**. The number of users with repeat hypoglycemia and hyperglycemia, respectively, were: UK, n = 169 and n = 2407; Germany: n = 229 and n = 3426.



OR are based on event frequency and describe the relative difference in the likelihood of event occurrence in first 30 days/after >180 days. An OR >1 indicates a lower event frequency was associated with app use after >180 days, compared with the event frequency during the first 30 days. Dashed vertical line = line of no effect. BG, blood glucose; CI, confidence interval; OR, odds ratio.

Conclusions: App use was associated with a lower frequency of hypoglycemia after >180 days, and few users experienced repeat hypoglycemia, supporting app use to facilitate active involvement in diabetes self-management.

Figure

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Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0290

SYSTEM FOR AUTOMATIC ESTIMATION AND DELIVERY OF QUICKLY-ABSORBABLE CARBOHYDRATES

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Background and aims: Patients with diabetes often fear hypoglycemia because of the unpleasant feeling and possible dangerous situations it may cause. This can make patients consume more carbohydrates than necessary. Ad-hoc carbohydrate estimation by the patients can be unreliable and may produce unwanted periods of high blood glucose.

Our goal was to design a solution, based on the latest hardware and software technologies, that can automatically deliver an estimated amount of juice from a reservoir to a glass, when required.

Methods: Literature review and patient-centered approach were used to define the system functionalities and requirements. Patients' needs, and feedback were used to improve the software during testing.

Results: We built a fully-functioning prototype (Figure 1.), which was tested on real patients (n = 2). After 2 months, with 2720 different CGM (Continuous Glucose Monitoring) readings, a total of 57 distributions of carbohydrates were triggered (15 or 20 grams). Based on the patients' CGM values from the Nightscout solution, users were able to request different juice dosages. Both system and personal parameters were remotely configurable using a smartphone chatbot.

Conclusion: The system automatically delivers liquid carbohydrates and reports the status through a display and chatbot. The absorption of glucose into the bloodstream was effective after one or more delivered doses, in average after 15-20 minutes. No hyperglycemia was caused by the system. Future studies will involve a larger number of patients. In future, the hardware structure made by wood could be replaced with 3D printed components, making the entire system easy reproducible and transportable.

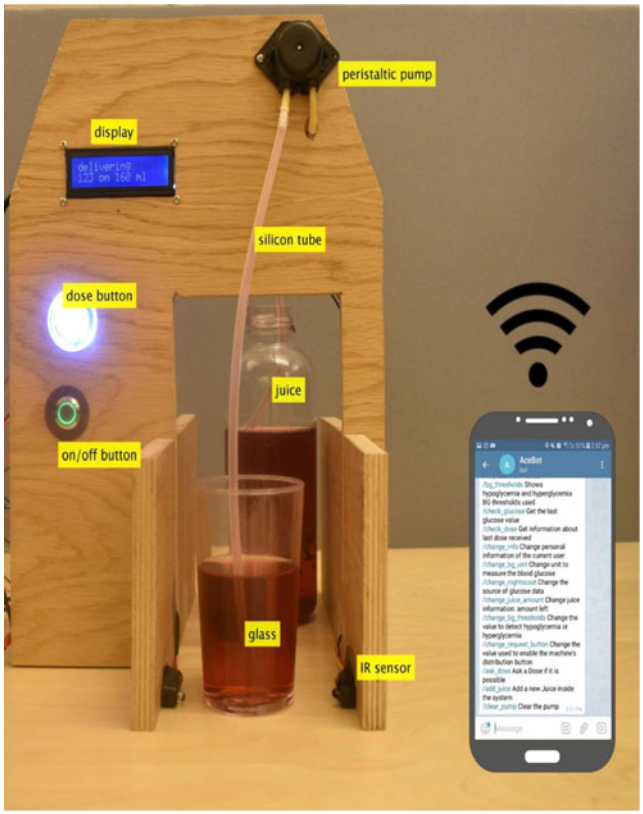

Figure 1: First Prototype, based on communication with Dexcom G4 CGM and the Nightscout solution.

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Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0306

SELF-RECRUITED T2D PATIENTS' ENGAGEMENT IN A SELF-MANAGEMENT TOOL: FEEDBACK AND SUGGESTIONS

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Introduction: Research often relies on a high level of engagement and feedback from participants. Whereas patient engagement has historically been a challenge, especially when lengthy questionnaires are involved, patients are now more willing and even motivated to participate when it comes to using mHealth tools and services.

Methods: Patients with Type 2 diabetes were ''self-recruited'' to the ''Tailoring Type 2 Diabetes Self-Management'' RCT; they responded to a Facebook post, online news article and direct messaging to current Diabetes Diary app users. Participants were randomized to two groups; the Control group used the simplified Diabetes Diary app for the first 3-months and the tailored version for 3-months. The Intervention group used the tailored app for the full 6-months. Measures were taken at 0, 3, and 6-months including demographics, HbA1c, written feedback and responses

Table 1. Users' feedback on what was perceived as most useful

Group	3 month	6 month
Control (n=16)	n=12 • A curve of your blood glucose levels for different time periods • Ability to get a full overview • Ability to keep track of how food and exercise affect my BG • Curve on measurements and ability to transfer activity • Promotes own discipline	n=6 • The curve of fasting blood sugar, and all other measurements • Integration with physical activity apps • Good overview. • The whole app. • Graph and average calculations • Overview of blood glucose over time, and ability to track weight, exercise and diet.
Intervention (n=25)	n=6 • Goal setting • Curves and BG over time • Average Measurement of Blood Sugar	n=5 • Curve of BG for the last day • Follow-up of exercise, weight control and blood sugar levels. • Graphs

Table 2. Users' suggestions for improving the app

Group	3 month	6 month
Control (n=16)	n=9 • Make it easier to enter food than just grams • Ability to connect with other activity apps • More options for physical activity • Ability to enter comments under each registration • Ability to post other drugs than insulin • More options for calculations • Ability to enter HbA1c once you have measured it	n=7 • More options for those who use insulin • More frequent feedback from the app • Ability to write down meals without weighing the food • Ability to retrieve statistics • Ability to extract data in a spreadsheet • Ability to connect with other activity apps • Make it easier to enter food than just grams* • Ability to enter HbA1c*
Intervention (n=25)	n=7 • More frequent feedback from the app • Make it easier to enter food than calories • Ability to register food by scanning [bar codes] • It is difficult to enter registrations after the fact • Reminders for SMBG • Ability to connect with other activity apps	n=4 • Ability to automatically measure BG • Reminders for SMBG • Simpler interface • Ability to adjust "ranges" for "in-range" etc. on the BG graphs • Ability to register food by scanning [bar codes]

*More frequent comments on this than at 3-months

to the following standardized questionnaires: WHO-5, Summary Of Diabetes Self-Care Activities Assessment (SDSCA), and Perceived Competence Scale (PCS). The app continuously collected patient-gathered self-management data.

Results: Participants in both groups offered written feedback regarding what was useful (Table 1) and what could be improved in the apps (Table 2).

Discussion/conclusion: Written comments are rarely answered by participants. We believe that because these participants were ''self-recruited'', they were more engaged. This is evident in their willingness to provide both constructive criticism and details for future development of mHealth technologies. This also demonstrates what we can expect from - and the value of - involving engaged users of technology aids in diabetes research today.

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Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0309

WHAT CAN BE LEARNED BY ANALYZING PATIENT-GATHERED DATA FROM A SELF-MANAGEMENT DIABETES APP

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Introduction: Self-management interventions for diabetes are still limited in the analysis of patient-gathered data and mHealth usage - focusing mainly on HbA1c. From the ''Tailoring Type 2 Diabetes Self-Management'' RCT, we analysed detailed app-data as a supplement to the traditional measures.

Methods: Participants were randomized to two groups. The Control group used the regular Diabetes Diary app for the first 3-months and the tailored version for 3-months. The Intervention group used the tailored app for the full 6-months (Figure 1). Measures were taken at 0, 3, and 6-months including HbA1c. The app continuously stored user-recorded each blood glucose, insulin dose, diet, and exercise registration.

Results: N = 16 participants were randomized to the Control group and n = 25 to the Intervention group. Total registrations made and HbA1c did not differ significantly between those who made registrations in the in the Control (n = 12) and Intervention groups (n = 8). Therefore, all participants who registered in the app were treated as one cohort in the following analysis (n = 20) (Figure 2). While not significant, participants seemed to reduce HbA1c between zero and three months.

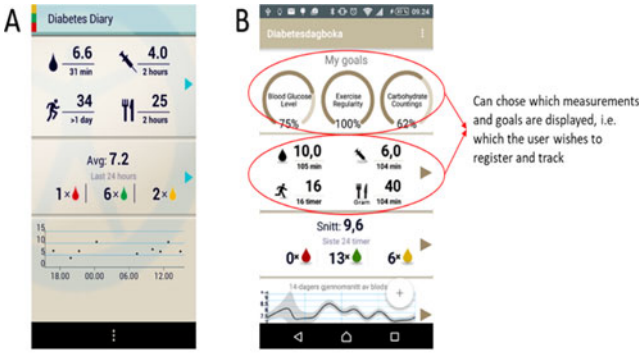

Figure 1. Illustration of the regular Diabetes Diary app (A) and Tailored Diabetes Diary app (B).

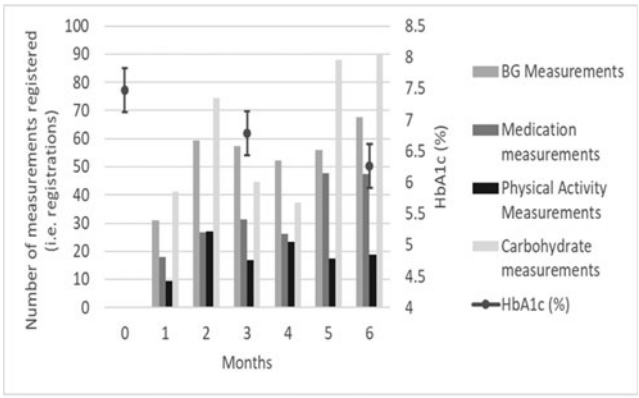

Figure 2. Distribution of types of registrations made in the app over the 6-months with HbA1c (0, 3 and 6-months) overlaid (standard error bars included).

Discussion/conclusion: By looking past assigned groups to additionally include app-usage patterns, we may be able to more effectively address how and why participants do - or do not - engage in mHealth-use over time, and which functionalities are most relevant to them. By incorporating such understanding, we may also be able to address when, and for which functionalities, users need encouragement to self-manage via apps, during both future interventions and daily clinical practice.

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Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0329

HEART RATE VARIABILITY DURING HYPOGLYCEMIA IN PATIENTS WITH TYPE 1 DIABETES AND IMPAIRED AWARENESS OF HYPOGLYCEMIA

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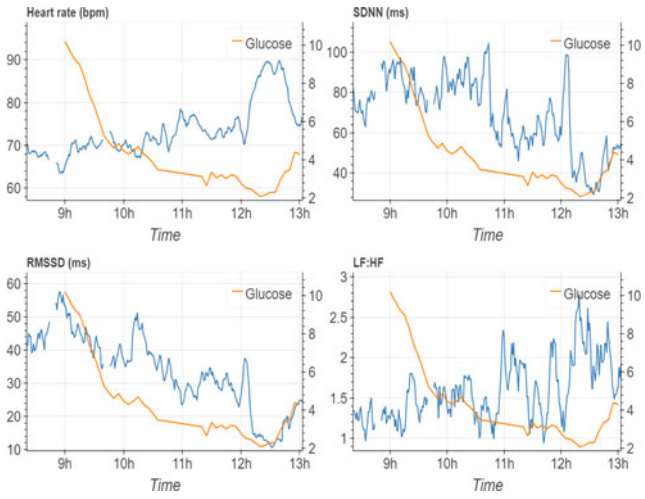
Background: Patients with type 1 diabetes (T1D) and impaired awareness of hypoglycemia (IAH) are at very high risk of severe, potentially hazardous, hypoglycemia and would benefit from an early alert device for the detection of hypoglycemia. Heart rate variability (HRV) may change at the initiation of hypoglycemia due to sympathetic nervous system activity. The aim of this study was to investigate whether these HRV-changes are retained in patients with T1D and IAH, in whom sympathetic nervous system activation during hypoglycemia is reduced.

Methods: Eligible participants underwent a modified hyperinsulinemic hypoglycemic clampwhile HRV was measured simultaneously by a Vital Connect Health Patch on their chest. Parameters of HRV included Square root of the mean standard differences of successive R-R intervals (RMSSD) representing parasympathetic nervous system activity and low and high frequency ratio (LF:HF) representing sympathetic nervous system activity.



Results: We included a total of 10 patients (4 men, age 38.5 ± 4.4 years, diabetes duration 21.7 ± 4.3 years, HbA1c 55.2 ± 1.5 mmol/L, modified Clarke score 3.7 ± 0.3). The glucose nadir during the clamp averaged 2.8 ± 0.1 mmol/L, which elicited minimal symptoms. Preliminary data analysis shows typical HRV patterns at the initiation of hypoglycemia, i.e. a decrease in RMSSD and an increase in LF:HF ratio (figure 1). Group differences also showed decreased RMMSD (36.1 ± 24.5 to 25.7 ± 9.5) and increased LF:HF ratio (1.35 ± 0.35 to 1.52 ± 0.24). Final results are pending.

Conclusion: Hypoglycemia affects HRV patterns in patients with type 1 diabetes and IAH. Considering developments in wearable devices and data analytics,real time HRV seems promising for early detection of hypoglycemia in patients with IAH.

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Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0351

DIABETES APPS USAGE AMONG INDIAN ENDOCRINOLOGISTS

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Aims: To assess the knowledge,attitudes and usage of diabetes smartphone apps among Indian Endocrinologists.

Materials and Methods: An online survey was done with REDCap and was emailed to a list of Indian Endocrinologists. The survey link was also disseminated through a WhatsApp group of Endocrinologists with 256 members. The endocrinologists were encouraged to share the link with their friends and colleagues. One hundred and ninety one(191) people completed the survey. Of these, 179 were endocrinologists. The analysis was limited to Indian Endocrinologists.

Results: 179 endocrinologists from India participated in the sur- vey. Majority of them were from the urban area. The mean experience of the respondents was 9.22 years (SD = 5.25 years). Their patient profiles included questions on litera- cy and specifically English literacy. In the survey, 74.7 % of the respondents felt their patients were literate(SD-19.47%) and 53.8% of patients were felt to be English literate (SD = 22.48%). 59.3% responded that their patients had smartphones. Only 16.5 % had ever prescribed an app. HealthifyMe, MyFitnessPal and GoogleFit were the most commonly prescribed apps.

Conclusion: The usage of diabetes apps is very low among Indian Endocrinologists. The main barriers to usage is awareness of the doctor. Availability of apps in local languages, diabetic education through the app and emergency alert/notification to the physician are the top preferred features in a prospective diabetes app. Incorporating mobile technology in diabetes management should start with improving physician awareness.

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Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0356

HARNESSING THE POWER OF SOCIAL MEDIA FOR A STRUCTURED AND INSTANT INTERVENTION, EDUCATION AND COUNSELLING IN TYPE 1 DIABETES

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T1DM is a disease where there is a challenge in every aspect of its management. Regardless of the educational status of the patients, parents or other caregivers, their questions and concerns are endless. Apart from the commonly repeated questions such as those on hypoglycemia, ketoacidosis, tiredness, adjustment of basal and bolus insulin-doses, diet, exercise, injection-site, mood swings, we also meet with queries regarding stem-cell therapy, pancreas transplantation, artificial pancreas, etc. To address these, we formed a WhatsApp® group of consenting patients to provide them with instant support and allay their fears and concerns. The social media WhatsApp® group of T1DM patients and their caregivers (KT1DP Sweet Stars) involved our multidisciplinary diabetes-care team actively responding to the queries posted. Considering the repetitive nature of the queries, questions on fake health messages from the internet, we custom created short videos. We always make it a point that those who appear in the videos are those faces that are familiar to the patients. Whereas, when there is an emergency, one of the team members will instantly communicate to resolve the concern.

A brief and confidential online survey was conducted to understand the advantages recounted by the patients/caregivers in the KT1DP Sweet Stars group, with regards to being a part of such interactive, educational groups. Details of T1DM patients: n = 166, 73% males. Majority recounted multiple advantages of being members of the group, sharing common concerns.

MERITS OF FORMING SOCIAL MEDIA GROUPS FOR T1DM MANAGEMENT

As recounted by the patients/caregivers	(% Positive responders)
• The interactions possible through the T1DM group have helped boost the confidence in managing the disease	90.36
• Appreciated the usefulness of educational/awareness videos shared through the group	93.37
• Experienced reduction in the hypoglycemic episodes, number of hospital visits etc.	69.88
• Felt that our diabetes care team, as well as other members in the group, are always available to respond to the concerns	90.36
• Felt that the T1DM group has helped gain knowledge and confidence regarding	
- Better awareness of the disease	96.38
- Management of Hypoglycemia	87.34
- Management of Lifestyle	90.36
- Insulin injection techniques	80.72
- Glucose monitoring	91.57
- Overcoming mood swings	79.87

As identified by our T1DM care team

- Highly cost-effective since the patients and caregivers can be in their own environment, need not travel and no work days are lost.
- Group educational sessions are very much effective since a question arising from one member may benefit others.
- The same educational and awareness messages though are available on the internet, most of them are mixed with fiction and fake messages, keeping the audience confused. Patients and parents are familiar with the faces and/or voices appearing in the video and audio messages, which boosts their confidence.
- Each group member can be a role model where they can extend real-time guidance and support to the lesser experienced persons in terms of managing a difficulty (e.g. a hypoglycemic episode).
- In India, until recently, type 1 patients/parents were reluctant to disclose the disease. Social media platforms have contributed to the creation of platforms promising better long-term outcomes and improved longevity.

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Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0358

CDISC PARTNERS WITH TYPE 1 DIABETES (T1D) EXPERTS AND HELMSLEY TO DEVELOP T1D RELATED DATA STANDARDS TO FOSTER DATA SHARING AND REUSE

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[1]CDISC, Data Standards, Austin, USA

Benefit Statement: The ability to access expansive collections of well-curated biological, clinical, and behavioral data will propel scientific progress and enable the discoveries needed to improve treatments for human disease. Development and adoption of data standards that facilitate data sharing and re-use can help accomplish this goal and presents a great opportunity to accelerate and increase efficiency in T1D clinical research.

Approach: CDISC's global, platform independent standards enable information system interoperability to improve medical research and related areas of healthcare. Adoption of CDISC standards by the research community encourages efficiency and enhances innovation through increased data reuse. Furthermore, in 2016, regulatory authorities in United States and Japan began to require the use of CDISC Standards for pre-clinical and clinical research for all new electronic drug submissions. The beginning to end nature of the standards provides traceability from data collection through to data analysis, improving data quality, reducing costs, streamlining processes and increasing data predictability.

CDISC began working with T1D experts to expand the current Diabetes standards, focusing on ***pediatrics, devices, exercise and prevention***. This effort is funded by the The Leona M. and Harry B. Helmsley Charitable Trust's T1D program as part of its Data Sharing Initiative.

The CDISC standards development process is consensus based. Prior to publication of the T1D standards we will invite the T1D community to participate in the public review and comment on the developed content. Information and updates on the project can be found at the CDISC T1D Website.

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Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0362

GRADE OF USE AND PRESCRIPTION OF DIGITAL TOOLS IN PEOPLE WITH DIABETES

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[2]Universidad Autónoma de Barcelona, CIBER-BBN EDUAB-HSP group, Barcelona, Spain

Introduction: Information and communications technologies have produced important changes in Health sector. In Spain, related to health, 60% of citizens use Internet, 22.3% Social Networks(SN) and 4.3% Apps. As other Health areas, their use in Diabetes Mellitus(DM) is increasing.

Objectives: The main objectives were to assess the degree of use of digital tools by people with DM in a tertiary hospital, as well as analyse the degree of prescription of these tools by healthcare team (HCT). As secondary objective, the relation between this use, therapeutic education (TE) and DM control was assessed.

Material And Methods: Descriptive and observational study in people with DM consecutively attended outpatients from a tertiary hospital during a month. Data was collected by an *ad hoc* survey.

Results: Main characteristics are shown in Table 1. 68% use additional sources for information, being Internet the main one (85%). 66% have an account in SN but only 6% use it in relation to their DM. 26% used Apps and 28% used a no face-to-face communication way with their health team. Unfamiliarity was the main reason for not using digital tools. Regarding prescription HCT recommended websites, SN and Apps in 20%, 10% and 30% respectively.

No significant relation was found between HbA1c and the use of Internet or Apps for DM. There was a relation between HbA1c and TE.

Conclusions: The use of internet for health care is high in studied sample, despite a low recommendation by professionals. Its use is not related to a better glycemic control.

TABLE 1

N	50
Mean age (years)	50 ± 16
Type of DM (%): - Type 1 / LADA - Type 2 - Others	 74 14 12
Treatment * Insulin therapy * Combined therapy (Insulin + pills) * CSII * OADs	78% 10% 6% 4%
Duration DM (years)	19 ± 13
HbA1c (%)	7.4 ± 1.07
Studies (%): - Collage - Secondary - Primary	 64 18 18
Uses Internet (%)	88
Patients with *smartphone*/Tablet (%)	88

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Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0395

GAMIFICATION FOR THE SELF-MANAGEMENT OF DIABETES

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Self-monitoring of blood glucose (SMBG) is a fundamental component of achieving optimal glycemic control among children with type 1 diabetes. Era Diabetes is a mobile application that integrates with glucometers via Bluetooth to make diabetes related data useful to patients, caregivers, and health care professionals. Gamification is used to incentivize self-management behaviour; when users meet their self-management target, a game is unlocked. This is an exploratory pilot study, published in the Canadian Journal of Diabetes. Patients of McMaster Children's Hospital Pediatric Diabetes Clinic used Era Diabetes for three months. 85% of participants self-managed their blood glucose readings at least 2 times per day using Era Diabetes. This is a significant improvement in patients' self-management regime, as none of the participants engaged in this behaviour prior to the intervention.

After this pilot study concluded, based on market and product research, the scope of research evolved to incorporate neural learning to predict diabetes related complications.

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Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0399

3D WHOLE-BODY SCAN FOR CLINICAL ANTHROPOMETRY AND DETERMINING BODY COMPOSITION IN T2DM PATIENTS

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[1]Moscow Regional Research Clinical Institute, Endocrinology, Moscow, Russia

Background: Existing anthropometric methods for assessing obesity provide very little information about features of distribution of fat and muscle mass. Virtual 3D whole-body scans of patients with obesity can provide additional information about body composition.

3D scan and DXA parameters correlaton

DXA 3D scan	Fat mass index	Appendicular lean mass index	Trunk fat mass (g)	Lean mass (g)	Fat mass (g)
Abdomen (L)	0.538 p=0.002	0.329 p=0.075	0.638 p=0.000	0.119 p=0.517	0.585 p=0.000
Abdomen (L)/ one hip (L)	0.398 p=0.027	0.103 p=0.59	0.55 p=0.001	-0.025 p=0.891	0.403 p=0.022
abdomen (L)/ two hips (L)	0.361 p=0.046	0.1 p=0.59	0.529 p=0.002	-0.007 p=0.969	0.381 p=0.031
waist circumference/ hip circumference	-0.242 p=0.198	0.693 p=0.693	0.141 p=0.45	0.29 p=0.114	-0.046 p=0.806
waist circumference	0.472 p=0.007	0.709 p=0.000	0.774 p=0.000	0.609 p=0.000	0.669 p=0.000

Material and methods: Patients with Type 2 diabetes mellitus (T2DM) over 45 years old with a body mass index (BMI) >25 kg/m2, who had ≥2 criteria for metabolic syndrome, underwent whole-body 3Dscans and dual energy X-ray absorptiometry (DXA), 3D whole-body scans were acquired on a DUBLLIK model R1000 (3DC). DXA scan was performed on a Hologic Discoveri A. Statistical analysis was performed using SPSS version 22.0 for Windows using standard methods of variation statistics.

Results: Thirty two patients with diabetes were examined: 25 women (78.13%), 7 men (21.88%), median age 63.5 [57.3; 69.0] years, weights 92.0 [82.3; 102.3] kg, BMI 33.4 [29.9; 37.2] kg/m2.

Conclusion: 3D scan allows to get indicators that indirectly characterize body composition, which correlate with DXA scan.

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Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0427

AN ENHANCED AI AND COMPUTER VISION-BASED SMARTPHONE SYSTEM FOR TRANSLATING FOOD MULTIMEDIA DATA TO NUTRIENT INFORMATION

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Background: Accurate carbohydrate (CHO) counting is vital and challenging for individuals with diabetes. GoCARB was the first end-to-end system able automatically to estimate the CHO content of plated meals using a smartphone.

Objective: goFOOD™ is an upgraded version of the GoCARB system aiming to overcome limitations of the previous system, and incorporating latest advances in artificial intelligence, computer vision and smartphone sensors.

Methods: The system requires input of two meal images. For conventional single-camera smartphones, the images must be captured from two different viewing angles; however, smartphones equipped with two rear cameras require only one press of the shutter button. A deep neural network is applied to process the two images, performing food detection, segmentation and recognition, while a 3D reconstruction-based algorithm estimates the food volume. Each meal's calorie and macro-nutrient content (CHO, protein, fat) are calculated based on each food category, volume and the USDA nutrient database.

Results: goFOOD™'s latest version supports 21 broad and 324 fine food categories, and is validated using the MADiMa2017 database, which includes 80 central-European dishes that are fully annotated, labelled, weighted and of known volume and nutrient content. Preliminary results indicate that the meals' median prediction errors (25^{th}–75^{th} percentiles) of CHO, protein, fat and calories estimation are 7.3g (2.9g–13.4g), 6.6g (3.4g–9.2g), 6.9g (3.2g–12.7g) and 94.2kcal (36.7kcal–158.5kcal), respectively.

Conclusion: goFOOD™ brings the technology developed during the GoCARB project closer to the end user.

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Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0436

DEMOCRATIZING TYPE 1 DIABETES (T1D) KNOWLEDGE IN RURAL AND UNDERSERVED COMMUNITIES: PROJECT ECHO T1D

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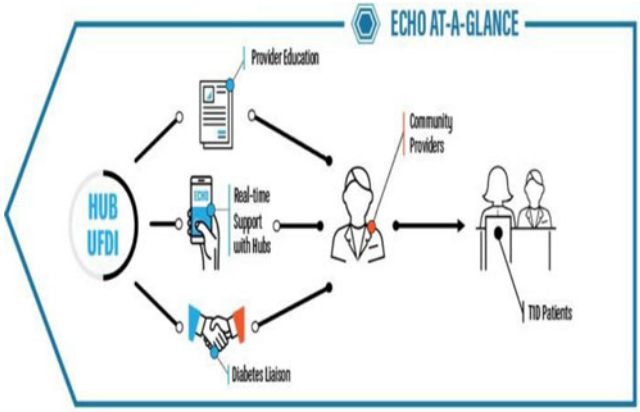
Objectives: (1) Increase the capacity of primary care providers (PCPs) to empower and safely and effectively manage underserved patients with T1D who do not receive routine specialty care (2) Demonstrate proof of concept for adaptation of Project ECHO (Extension for Community Healthcare Outcomes) model to include adult and pediatric patients with T1D.

Methods: We developed the ''Project ECHO T1D'' telehealth clinic adapted from the Project ECHO model which utilizes the hub-and-spoke model to target and partner with PCPs at non-specialty diabetes practices across the states of Florida and California.

Results: The 18-month pilot program is ongoing. Participation for the pilot program was filled beyond capacity. For California, 11 Spokes were enrolled with 47 clinics serving roughly 1,000 adult and pediatric patients with T1D who do not receive usual specialty T1D care. For Florida, 10 Spokes were enrolled with 67 clinics who serve roughly 1,300 patients with T1D who do not receive usual specialty T1D care.

Conclusions: Project ECHO T1D is an implementation of an innovative healthcare delivery model which builds capacity for diabetes self-management education in medically underserved communities through force multiplication. The current study will demonstrate whether, and to what extent, Project ECHO model is able to recruit PCPs and reach patients with T1D who



are not receiving routine specialty diabetes care. It will serve as proof-of-concept for academic medical centers wishing to replicate the model in the US and globally. Preliminary data suggests that the Project ECHO model can and should be further applied to T1D.

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Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0443

TELEMEDICINE AS A TOOL TO CONTROL BLOOD PRESSURE OF PATIENTS WITH DIABETES SUFFERING FROM HYPERTENSION

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Introduction: Patients with diabetes often suffer from hypertension, which increases the risk of development of other comorbidities. Therefore, tight blood pressure control is required among these patients. Telemedicine enables us to effectively collect and monitor patients' blood pressure and related health incidents from their homes.

Methods: A modul enabling to automatically collect data from patients with hypertension via Bluetooth-supported blood pressure monitors has been developed as a part of the Diani telemedicine system. Two ways of data collection has been implemented: 1) via connected mobile application, and 2) via mini-PC. This ensures its possible use by patients with different technical facilities. For data visualization, a web application has been created.

The usability of the system has been tested on first group of patients with hypertension.

Results: The web application visualize the data collected by connected devices in a form of graphs and tables, while the values out of range and arrhythmia detection are highlighted. Information about medication and symptoms can be registered manually. A standardized report for a doctor can be downloaded.

So far, data from 12 patients with hypertension has been successfully collected and transferred to the server. Two technical complications that occurred during the device installation at home have been solved.

Conclusion: Using this support, automatic data transfer can eliminate invalid data registered by patients manually. Moreover, timely response to unwilling blood pressure values can be ensured. Comparison of blood pressure fluctuations within a day with the time of medication and its amount can, in addition, help with an individual treatment adjustment.

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Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0448

THE RELATIONSHIP OF HEMOGLOBIN A1C TO CGM-DERIVED TIME-IN-RANGE IN PATIENTS WITH DIABETES

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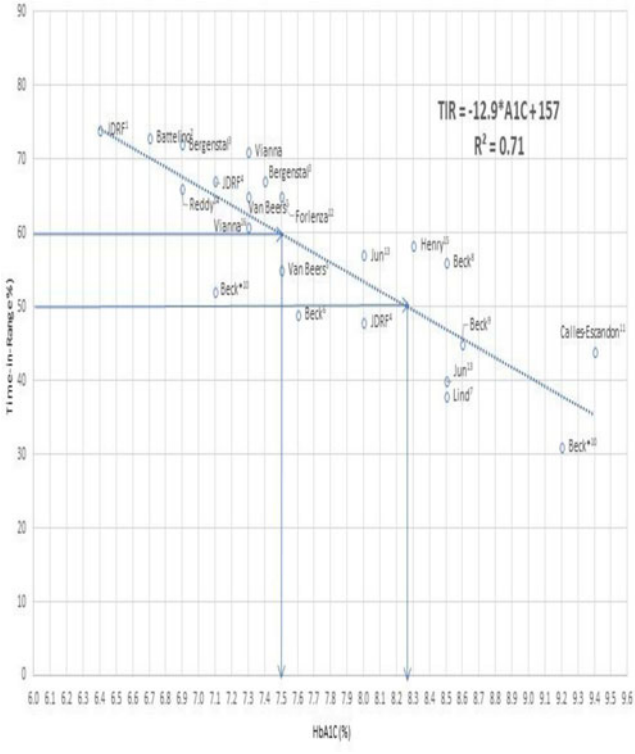
Background: CGM-derived time-in-range (TIR) is an important metric in understanding glycemia. The relationship of TIR to HbA1C has not been clearly defined.

Methods: Sixteen publications that reported paired HbA1C and TIR metrics or HbA1C and frequent self-monitoring of blood glucose (SMBG) across a wide range of HbA1C's, technologies and subject demographics were reviewed to determine the correlation of these metrics.

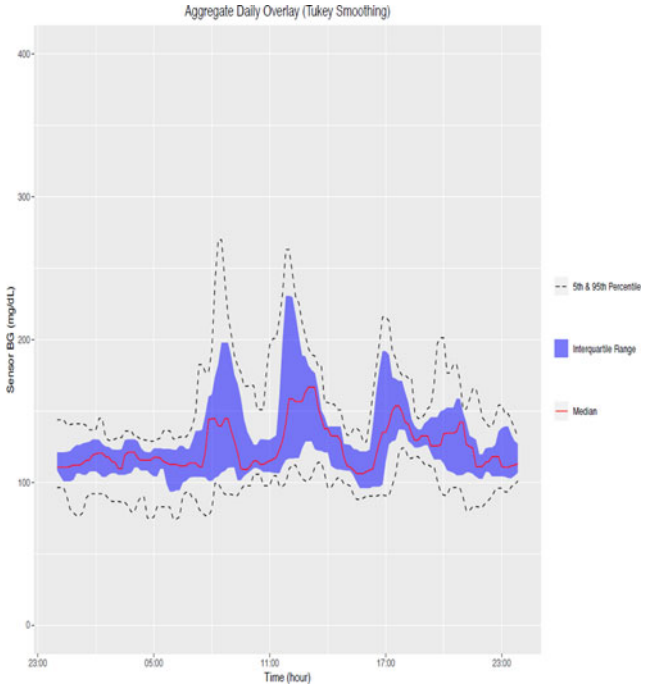
Results: There was an excellent correlation between the TIR and HbA1C ($R^2 = 0.71$) where TIR = −12.9*A1C + 157. A 10% change in TIR (e.g., between 50% and 60%) is equivalent to a 0.78% change in HbA1C (Figure).

Conclusions: There is a good correlation between HbA1C and TIR that may permit the transition to TIR as the preferred metric for determining the outcome of clinical studies, prediction of the risk of diabetes complications, and assessment of an individual patient's glycemic control.



References

1. Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group. Diab Care. 2009;32(8):1378-83.
2. Battelino T. Diab Care 2011;34:705-800.
3. Bergenstal R. J Amer Med Assoc 2016(13);316:1407-1408.
4. JDRF Continuous Glucose Monitoring Study Group. N Eng J Med 2008;359:1464-1476.
5. Van Beers CAJ. Lancet Diab Endocr 2016;4(11):893-902.
6. Beck RW. Lancet Diab Endocr 2017;5:700-708.
7. Lind M. J Amer Med Assoc 2017;317(4):379-387.
8. Beck RW. Ann Int Med 2017;67(6):365-374.
9. Beck RW. J Amer Med Assoc 2017;317(4):371-378.
10. Beck RW. Diab Care https://doi.org/10.2337/dc18-1444.
11. Calles-Escandon J. https://doi.org/10.1371/journal.pone.0194759.
12. Forlenza GP. Submitted for publication Oct. 2018.
13. Jun JE. Diab Met Res Rev 2018: Oct 21:e3092. doi: 10.1002/dmrr.3092.
14. Reddy M. Diab Tech Ther 2018; 20. DOI: 10.1089/dia.2018.0252.
15. Henry RR. Diab Tech Ther DOI: 10.1089/dia.2018.0052.
16. Vianna AGD. Diab Res Clin Pract 139, 357-365, 2018.



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Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0460

AN R PACKAGE FOR ANALYSIS OF CONTINUOUS GLUCOSE MONITOR DATA

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Objective: To develop a standardized, free, open-source method for management and analysis of continuous glucose monitor (CGM) data, including calculation of key metrics recommended in the International Consensus on Use of Continuous Glucose Monitoring (ICUCGM) and graphical tools similar to the Ambulatory Glucose Profile (AGP).

Methods: We developed a package (called cgmanalysis) written in the statistical programming language R (R Foundation for Statistical Computing, Vienna, Austria).

Results: The software can automatically recognize and read data exports from the Diasend®, Dexcom, iPro™2, Libre, and Carelink™ platforms. Other data sources can be used if formatted appropriately. The cleaning function processes raw data exported from a CGM device, and can handle multiple formats simultaneously. The analysis function calculates the key metrics in the ICUCGM, in addition to other variables, including the mean amplitude of glycemic excursion (MAGE), and creates a data set for upload into a database or statistical software. The report function creates graphical data summaries, including a figure in the style of the AGP (see Figure), using Tukey smoothing to plot the median, inter-quartile range, and 5th and 95th percentiles by time of day. Cgmanalysis is available on the Comprehensive R Archive Network, and the code and user guide are available on GitHub.

Conclusions: The cgmanalysis package provides a standardized, free, open-source approach to manage and analyze CGM data, enabling sharing of data across technology platforms, collaboration between research groups, and more effective use of the growing pool of CGM data.

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Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0478

DESIGN OF A MOBILE APP "CARNETDIA" FOR DIABETIC PATIENTS IN CAMBODIA: THE BEGINNING OF A JOURNEY

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Introduction: Diabetes, in particular type 2 diabetes, is one of the most common chronic diseases in Cambodia. Optimal management of this chronic disease requires not only medications but also patient-healthcare provider communication and proactive self-management from patients. With the increasing popularity of smartphones, the use of mobile APP, to raise the awareness of diabetes and patients' self-management, has attracted more attentions. CarnetDia is the first mobile APP developed in Khmer language in Cambodia.

Objective: The objective of this paper is to describe the development of a mobile tool in Cambodia.

Methods: We present the history, design and development of CarnetDia. A team of Cambodian clinicians who interest in patient education, created this App with the supports from software engineers. CarnetDia was designed for iOS and Android devices. Patients or their family members could download freely. In

CarnetDia, there are educational video clips, pictures and documents in PDF. More than that the patients could register to create a personal account so that they could note their glycemic datas and eaten foods. And finally patients could send those datas to their doctors.

Results: After seven weeks of launching, there are 1161 users (628 iOS devices and 533 Android devices). Among those users there are 185 registered accounts [male 71.35% and female 28.65%; the age group, most commonly, varies from 30-69 years old]. 90% of the registered patients do the self-monitoring 2 times a week.

Conclusion: Mobile APP (CarnetDia) could be an open mHealth source solution to raise the awareness of diabetes and patients' self-management in Cambodia.

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Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0480

RESULTS OF THE MULTI-CENTRIC STUDY RENACED DIABETES TIPO 1 IN MEXICO

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Background and aims: Information regarding type 1 diabetes (T1D) patients follow-up in Mexico is limited. An online-system, RENACED DT1, registers longitudinal T1D data in Mexico.

Method: Descriptive analysis of 1049 T1D patients registered on RENACED DT1, in 27 Mexican States, until 10/11/2018.

Results: Fifty percent patients were diagnosed in the last 10 years, 61% women and 39% men. Average age at diagnosis was 12.6 years old (yo), being men younger than women (12.05 vs. 12.81, $p < 0.05$). Their average HbA1c at diagnosis was 11.4%. Of those with available data, 35% are taken care of by ministry of health, 31% by social security and 34% by private insurance. At the time of analysis, 1049 patients remain active, with a ratio men:women of 1:1.6. Their average age was 24 yo. Mean BMI was 22.9 Kg/m2 and mean was HbA1c 8.7% ± 2.3. Eighteen-percent of patients uses insulin-pumps and 71% MDI. A total of 20% and 13% of patients had HbA1c<7% and 7 < 7.5%, respectively. In the last year, the presence of diabetic ketoacidosis was 5.33%, severe hypoglycemia was 1.14%, and chronic complications 18.4%.

Conclusion: The ratio of male:female T1D patients of 1:1.6, in Mexico, appears to be different to that reported in other countries. This needs to be further explored. The percentage of T1D patients in Mexico that reach the HbA1c target is low (20% <7% and 33% <7.5%), but similar to that described in the literature. Improved access to glucose monitoring technology, insulin delivery systems and adjunctive therapy are necessary to improve glycemic control in T1D patients in Mexico.

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Insulin Pumps

ATTD19-0042

THE IMPACT OF LOW-CARB HIGH-FAT DIET ON A METABOLIC CONTROL IN AN OBESE TYPE 1 DIABETIC PATIENT ON INSULIN PUMP THERAPY

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This case presentation shows the impact of low-carb high-fat (LCHF) diet on a glucose variability and metabolic control in an obese type 1 diabetic patient. 41-year old female has type 1 diabetes since the age of 13. She has been treated with an insulin pump since 2011. In addition, she is on metformin 2000 mg daily due to polycystic ovary syndrome. Her glycaemic control was poor in the last years. Her HbA1c levels were around 8.0% and there was high glucose variability. Also, the patient has been struggling with increased body weight. In July 2018 she introduced LCHF diet. Since then her glycaemic control has improved dramatically. In the next three months her HbA1c level has decreased to 6.2 % and glucose variability has reduced immensely. Total daily insulin dose has reduced from 42 to 24 units and average basal/bolus ratio has changed from 45/55 to 85/15. In addition, her body weight has decreased from 94 to 82 kg and her blood pressure has decreased from 155/85 mmHg to 127/82 mmHg. Patient also reported of improved life quality and confidence. On the other hand, her lipid profile has detoriated, with her total cholesterol level rising from 4.3 to 6.6 mmol/L and her LDL cholesterol level rising from 2.4 to 4.7 mmol/L. In conclusion, LCHF diet can improve glycaemic control as well as reduce body weight in an obese type 1 diabetic patient. However, lipid control may get worse.

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Insulin Pumps

ATTD19-0127

670G IN CHILDREN SMALLER THAN LABELLED: THE HANNOVER SMARTHOME STUDY

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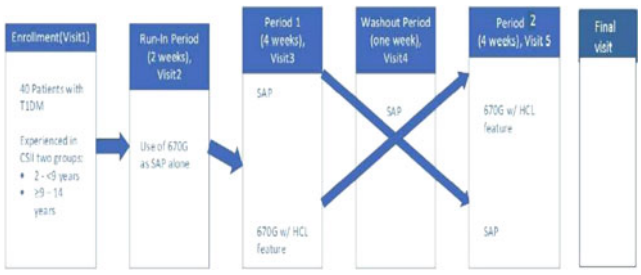
Background: Insulin pump therapy and continuous glucose monitoring users with T1D are rising more and more in pediatric age group. According to newest consensus statements (ATTD), the outcomes of CGM systems get into focus more than e.g. HbA1c.



The newest combination system is Minimed670G by Medtronic, which is the first system that allows an automated adaption of basal insulin dosage due to actual sensor glucose values. Pradnial bolus is given manually by entering the amount of carbohydrates.

As it is actually labeled only above seven years of age and 8 U of Insulin as total daily dose, one should evaluate if the system is feasible in working also in smaller children.

Method: In this monocentric, randomized cross-over study, 20 kids between 2 and <9 and 20 between 9 and 14 used the 670G system at first in the SAP mode and after randomization 4 weeks in auto mode and 4 weeks in SAP mode respectively (Fig.1). Inclusion criteria are T1D >1 year and at least 3 months of CSII experience.

Primary endpoint is the time in range [%] 70-180 mg/dl (TIR) in a period comparison. Secondary, the number of hypoglycemic events, ketosis events as well as TIR <70, TIR <54, TIR >160 mg/dl will be assessed.

Conclusion: As new technologies always take long scientific and regulatory processes until the are available to patients for daily life, it is necessary to start clinical studies as soon as possible in all age groups, to provide all patients the best available therapy options.

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Insulin Pumps

ATTD19-0140

WHAT ARE THE OPTIMAL SETTINGS IN TYPE 1 DIABETES PATIENTS USING CONVENTIONAL INSULIN PUMP?

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Aim: To describe Continuous Subcutaneous Insulin Infusion (CSII) settings in Type 1 Diabetes (T1D) patients with optimal glucose control.

Methods: The study enrolled ninety-three CSII patients with T1D (age 12–25 years) that visited our center from January to December 2016. Patient characteristics were collected through the electronic medical record system and CSII characteristics were obtained from 8 weeks reports prior to Hba1c, generated by Carelink Therapy Management Software (Medtronic, Northridge, USA).

Results: Patients were grouped according age: 12–18 years and 19–25 years. More than 70% of patients achieved HbA1c <7.5% (<58 mmol/mol). Significant difference in basal insulin was found between two age groups. Patients aged 12–18 years had five basal segments, less basal rate in early morning (03–07h) and slight decrease of afternoon basal rate (13–19h), comparing with patients aged 19–25 years with four basal segments, more basal rate in early morning (03–07h) and no decrease of afternoon basal rate (13–19h).

Conclusion: Bolus wizard settings, frequent bolusing, multiple basal segments, and close follow up can be determinants for better control in T1D patients. Simple CSII settings as a tool,

derived from our data may help clinicians to fine tune T1D patients and achieve optimal glucose control.

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Insulin Pumps

ATTD19-0161

GLYCEMIC POST-PRANDIAL CONTROL ACCORDING TO BOLUS INFUSION SPEED IN COLOMBIAN TYPE 1 DIABETICS ON SENSOR AUGMENTED PUMP THERAPY (SAP)

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Material and Methods: Eight type 1 diabetic subjects (Table 1) on continuous subcutaneous insulin infusion using the MiniMedTM 640G system with the SmartGuard feature where included. They received breakfast, with a carbohydrate content of 45g. After an initial use of standard speed bolus (1.5u/min infusion rate), the patients crossed over to a fast speed bolus (15u/min). Capillary and interstitial readings were obtained. The analysis included the comparison of capillary readings vs interstitial readings at pre-breakfast period, 1, 2, 3 and 4 hours after the bolus use, hypoglycemia events (HypoE), hyperglycemic excursions and AUC from baseline to 4h for the 2 different types of boluses.

Results: In the standard boluses, there were eight HypoE by capillary reading, with mean glucose value 60.5 ± 7.6 mg/dL, despite the use of predictive low glucose suspend feature. By interstitial measure there were 5 HypoE, with mean sensor value 59.6 ± 10.06 mg/dl. For all HypoE the mean capillary value was 60.42 ± 6.94 mg/dl. In the fast bolus period, there was only one HypoE at 4 hours. Taking into account hyperglycemia, there were seven hyperglycemic excursions in the standard bolus period. Mean glucose values for the excursions by capillary and interstitial were 202.28 ± 23.19 mg/dl and 197.14 ± 31.82 mg/dl respectively. In the quick bolus period, no hyperglycemic events were recorded. For all readings, there was no significant difference between mean glucose values with normal vs quick bolus (p = 0.86), but the coefficient of variation was 37.9% for the normal bolus period and 21.4% for the quick bolus.

Table 1. Baseline Characteristics of Insulin pump therapy of Hospital de San José, in Bogotá, (Colombia)

Characteristics	Mean (SD) / n (Percentage)
Age (years)	32.6 ± 12.28
Male	4 (37.5%)
Weight (Kg)	67.6 ± 36.56
Height (cm)	164.9 ± 8.28
BMI (Kg/m2)	26.7 ± 8.9
Renal Function CKD/EPI (ml/min/m2)	82 ± 36.96
Time from diagnosis (years)	18.9 ± 12.33
Time using insulin pump 640G (months)	10.6 ± 5.34

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Insulin Pumps

ATTD19-0216

INFUSION SET COMPLICATIONS ARE FREQUENT IN LONG-TERM CSII USERS

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Introduction: Continuous subcutaneous insulin infusion (CSII) is an effective method of type 1 diabetes (T1D) treatment, becoming essential part of closed loop systems. CSII infusion set is a limiting factor of system functionality. Several studies showed a high rate of infusion set complications in relatively short-term CSII users. The aim of our study was to assess the rate of various complications in long-term CSII users at a tertiary diabetes center.

Methods: We conducted a survey of 112 adult patients with T1D using CSII for a minimum of 1 year. Objective data were collected from electronic medical records and pump downloads. Frequency of acute and chronic, local and metabolic complications of infusion set use, preferred infusion site, type of cannula and education status, were assessed by patient survey.

Results: Patients were well educated about infusion set manipulation and site rotation. Still, 20% patients changed cannula later than recommended, 45% patients reported lipodystrophy and 47% scarring. A third of patients experienced site infection and 47% experienced DKA (diabetic ketoacidosis)/hyperglycemia due to site failure. Seven percent of patients had repeated cannula kinking and 7,5% had repeated set occlusion. Patients with a history of 1 DKA episode used more frequently alternative insertion sites (other than abdomen), whereas in patients with repeated DKA, no difference in insertion sites was observed.

Conclusion: Infusion set remains the weak point of CSII use. The rate of infusion set complications in long-term CSII users is high, regardless of education status or site choice.

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Insulin Pumps

ATTD19-0226

HOW MUCH SUCROSE IS NEEDED TO TREAT HYPOGLYCEMIA IN ADULTS WITH T1D ON CSII WITH PREDICTIVE LOW GLUCOSE SUSPEND (PLGS)? PRELIMINARY RESULTS OF A RCT

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Introduction: Recommended hypoglycemia treatment in adults considers 15 grams of carbohydrates. Suspension technology might warrant lower needs. Our aim was evaluating the response to fewer carbohydrates for treating hypoglycemia in T1D patients on CSII with PLGS.

Method: Participants were blindly randomized to receive 15 or 10 grams of sucrose per episode. Treatment was indicated when capillary glycemia (CG) was <65 mg/dL, and duplicated if it was <50 mg/dL. Fifteen minutes after treatment, if CG was <65 mg/dL re-treatment was indicated, and if it was >65 mg/dL, infusion was manually resumed. After 2 weeks, participants did crossover to the other treatment. Sensor glucose, active insulin and time in suspension were also assessed.

Results: Sixteen subjects participated. 70 episodes were recorded with 11 excluded for protocol violation. 85% episodes occurred with active insulin. Baseline CG, at 15 and 30 minutes was 57, 95 and 111 mg/dL for 26 episodes with 15 grams and 54, 77 and 112 mg/dL for 33 episodes on 10 grams ($p=0.168$, $p=0.0007$ and $p=0.899$, respectively). At baseline, 20% of episodes were <50 mg/dL and required duplicated doses, and active insulin was 1.3 units for 15 grams and 1.7 for 10 grams ($p=0.414$). None of the 15 grams episodes required re-treatment, compared with 21% of the 10 grams episodes. No severe hypoglycecmia and no rebound hyperglycemia occurred.

Conclusions: In T1D patients on CSII with PLGS, a hypoglycemia treatment protocol with 10 grams of sucrose is effective but could require repetition of treatment. Manual resuming after treatment might warrant no risk of hyperglycemia with standard doses.

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Insulin Pumps

ATTD19-0250

DIFFERENT REACTIONS ON PHYSICAL ACTIVITY IN PATIENTS RECEIVING INSULIN PUMP THERAPY

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Introduction: Insulin pump therapy is currently the most-physiological form of insulin delivery in patients with diabetes mellitus (DM). Nevertheless, exercise-induced hypoglycemia still remains a challenge in this population, as guidelines for minimizing hypoglycemia risk are general and recommendations given in the studies differ.

Aim: To evaluate the effectiveness of current recommendations in non-trained diabetic patients on insulin pump therapy.

Materials and Methods: Young patients with diabetes duration of more than a year with stable basal rate and blood glucose (BG) levels performed two sessions of a 30-minute moderate aerobic exercise. Before the first session patients installed a 50% temporary basal rate (TBR) 90 min before and during the exercise. If glucose levels remained stable, or hyperglycemia appeared during or in 2h after the exercise, the second session was performed without any BR reduction. If hypoglycemia appeared, 20% TBR was installed duting the second session.

Results: Quite opposite reactions on physical activity were observed during the study. In some patients 50% TBR caused only the elevation of BG shortly after exercise and no changes in BG in sessions without any BR reductions. In the others hypoglycemia developed. Moreover, even 20% TBR couldn't prevent hypoglycemia in some cases.

Conclusion: The proper insulin correction remains the challenge even in patients on insulin pump therapy, as a number of factors should be taken into account. Despite the increasing number of studies, there is no consensus on the schemes of BR correction. Performed results are yet more proof that further studies are needed.

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Insulin Pumps

ATTD19-0252

DISCONTINUATION RATES OF PUMP THERAPY IN MOSCOW REGION

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Introduction: Insulin pump therapy or continuous subcutaneous insulin infusion (CSII) is known to be one of the most effective methods of treatment of diabetic patients. Unfortunately, some patients decide to discontinue CSII therapy for different reasons.

Aim: To evaluate the discontinuation rates of pump therapy in Moscow Region

Materials and Methods: Patients who were switched on insulin pump therapy in Endocrinology Department of Moscow Regional Research and Clinical Institute were followed-up from 2015 to the present day. The information about the discontinuation of pump therapy was received from patients during personal visits or by phone calls.

Results: Data from 274 patients were received. About 30% of patients discontinued CSII therapy during the first 3 months. The rate of discontinuation then decreased, and after the 6 months of CSII only 7% of remained patients stopped this method of treatment. The main reason reported was the high cost of monthly consumables, such as infusion lines, syringes, batteries etc (89% of patients). The other reasons included: not feeling comfortable wearing the device (5%), lack of improvement in control (3%), dermatological problems and needle site abscesses (2%), and total pump failure (1%).

Conclusion: Despite the obvious benefits of CSII therapy,patients in Moscow Region discontinue pump therapy mainly because of the cost issues.

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Insulin Pumps

ATTD19-0255

ADHERENCE TO GUIDELINES VACCINATION IN INTENSIVE-TREATED T1DM PATIENTS

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Objective: To assess the adherence to vaccination guidelines in Type 1 Diabetes Mellitus (T1DM) patients treated with continuous subcutaneous insulin infusion (CSII) compared with multiple daily insulin injections (MDI).

Method: A descriptive study was conducted to assess the adherence to guidelines vaccination (influenza, pneumococcal and hepatitis B virus-HBV) of 111 patients on CSII or MDI treatment (1:2). Data were gathered from electronic medical record and personal interview.

Results: Complete vaccination adherence was followed only by 3.6% of study population (ISCI 2.7% vs. MDI 4.1%, $P > 0.05$). Null vaccine adherence was reported by 30.6% of the patients (CSII 27% vs. MDI 32.4%, $P > 0.05$). Only one vaccine was received by most of MDI-treated patients (43.2%), nevertheless most of CSII patients were vaccinated against two different agents (48.6%). CSII-treated patients showed greater frequency for Pneumococal vaccination compared with MDI-treated patients (51.4 vs. 17.6, $P < 0.001$). Influenzae and HBV vaccination adherence were similar between both groups (Influenzae, CSII 62.2% vs. MDI 60.8%, $P > 0.05$; HBV, CSII 13.5% vs. MDI 17.6%, $P > 0.05$).

Conclusions: Patients with T1DM on intensive regimen followed a poor adherence to vaccination recommendations. CSII-treated patients only showed a greater Pneumococal vaccine adherence. Prioritizing advice and administration of vaccinations during all points of patient contact should increase immunization coverage recommended vaccines in patients with T1DM.

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Insulin Pumps

ATTD19-0278

DISCONTINUATION OF PUMP USE IN CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES (T1D)

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The effectiveness of Continuous Subcutaneous Insulin Infusion (CSII) is debated. Several studies indicate that improvements in glycaemic control or QoL strongly depend on psychological, educational and motivational factors. We analysed decisions and reasons for discontinuation of pump use in children and youth with T1D.

In a single center retrospective cross-sectional study (Diabeter, currently 62% CSII-use), clinical data between 2007 and 2018 were extracted from EHRs of patients aged 0–25 years. Patient discontinuation reasons (practical, emotional and clinical/technical) were assessed by questionnaire.

CSII was discontinued by 198 patients (53.8% female). Age at diagnosis, pump initiation and discontinuation was 8.3 (5.2), 12.8 (6.8) and 16.2 (6.0) years (mean ± SD), respectively. Key discontinuation reasons reported (19% response rate): dissatisfaction with/by CSII (device influencing body image, 66%; increased confrontation with T1D, 58%). Clinical factors were mostly advised by diabetes team members: low daily insulin dose (skipping insulin boluses), minimal glucose measurements (leading to worse glycaemic control), and skin infections/irritations (58%). Of 85 of 198 patients with HbA1c data available before (HbA1c 9.8%) and 3–6 months post-discontinuation, 54% showed improved HbA1c (−1.7%) post-discontinuation: 34%/12% showed no change or increased HbA1c (+1.1%: here factors other than insulin delivery likely play a determining role).

Although CSII is generally associated with improved glycaemic control and QoL, our data identify a subgroup with worsening glycaemic control reporting negative experiences. Using an approach including a realistic evaluation of patients' expectations and preferences, we aim to timely identify patients at risk for unsuccessful CSII and to provide appropriate training and education before and during CSII.

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Insulin Pumps

ATTD19-0312

ANALYSIS OF INSULIN PUMP DEVICE REPLACEMENT IN A GROUP OF TYPE 1 DIABETES PATIENTS IN A STRUCTURED PROGRAM

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Aim: To change the continuous subcutaneous insulin infusion (CSII) system could be an opportunity to improve CSII management; however, security issues could appear. The aim is to report the feasibility and safety of the simultaneous transition from one CSII system to another in a specific program in a group of Type 1 Diabetes (T1D) patients.

Methods: The program consisted of 3 sessions: 1) Group system start-up training session. 2) Call from medical staff 72h after session 1. 3) Group training session regarding the use of therapy management software. Demographic data, HbA1c, pump use and settings, hypoglycaemia awareness and retrospective continuous glucose monitoring (rCGM)data were collected previously and are being collected at 4 months from the switch. During these 4 months clinical events, technical issues, and training reinforcement incidents were registered.

Results: Insulin pump device has been changed in thirty-three T1D patients during June-July 2018. Baseline characteristics and insulin pump settings/use are shown in tables 1 and 2 respectively. Baseline, the CGM mean blood glucose is 156.1 ± 60.6 mg/dL with 62.1% of time-in-range. The analysis about clinical or

Table 1: BASELINE CHARACTERISTICS	
Age	47.7 ± 13.4 years
T1D duration	27.0 ± 11.5 years
Time in CSII therapy	10.1 ± 4.8 years
BMI	27.1 ± 4.2 kg/m^2
HbA1c	7.48 ± 0.70 %
Reason to start CSII	Suboptimal metabolic control 50 % Hypoglycaemia 28.6 % Pregnancy 14.3 % Others 7 %

Table 2: INSULIN PUMP USE SETTINGS	
Blood Glucose/day (n)	5.2 ± 1.8
Bolus/day (n)	4.5 ± 1.1
% of bolus using bolus wizard (BW)	60.9 ± 35.8
Total insulin dose/day (UI)	40.0 ± 15.7
% of insulin as basal	56.4 ± 11.9
Basal rate sections (n)	11.6 ± 5.1
Insulin/CH ratios (n)	3.9 ± 1.8
BW upper limit during day (mg/dL)	134.8 ± 9.1
BW lower limit during day (mg/dL)	81.5 ± 7.0
BW upper limit during night (mg/dL)	137.9 ± 12.0
BW lower limit during night (mg/dL)	84.5 ± 9.1

technical issues during 4 months follow-up as well as clinical and pump management is currently being carried out.

Conclusions: Switching to a new insulin pump in a group of patients is a challenge and an opportunity to improve the management of the therapy. The outcomes of the process need to be evaluated.

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Insulin Pumps

ATTD19-0317

FACTORS ASSOCIATED WITH LOWER GLYCEMIC VARIABILITY IN AN COHORT OF ADULTS WITH T1D ON CSII WITH PREDICTIVE LOW GLUCOSE SUSPEND (PLGS)

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Introduction: Current paradigm of glycemic control considers lowering A1c with low glycemic variability (GV), in order to increase Time in Range. Our aim is to characterize a cohort of patients on CSII with PLGS and to identify factors associated with a lower GV.

Method: Subjects on CSII with PLGS on follow-up ≥3 months at our clinic were included. Monthly pump downloads were recorded. Coefficient of variation (CV) from sensor glucose was calculated from every download, and its association with number of daily SMBG, basal insulin percentage, daily basal segments, carbohydrate intake, hours of PLGS, days between set change and areas under the curve (AUC) <70 mg/dL and >140 mg/dL was explored.

Results: 72 subjects were included, aged 37 ± 14 years, with disease duration of 18 ± 13 years. Most recent A1c was 6.98% ± 0.56%. 49% subjects were on insulin Aspart, 39% on Lispro and 12% on Glulisin.

401 downloads were analyzed. Low GV group, defined as CV ≤36%, had mean CV of 32.5%, compared to 39.9% on the High GV group ($p < 0.0001$). Factors significantly associated with CV ≤36% were the number of daily SMBG (6.7 vs. 6.1, $p < 0.0001$), carbohydrate intake (173 vs. 187 grams, $p = 0.02$), hours of PLGS (2.3 vs. 3.1 hours, $p < 0.0001$), AUC <70 mg/dL (0.2 vs. 0.5, $p < 0.0001$) and AUC >140 mg/dL (26.2 vs. 31.9, $p < 0.0001$).

Conclusions: T1D patients on CSII with PLGS with low GV have more daily SMBG, lower intake of carbohydrates, less hours of PLGS, lower AUC <70 mg/dL and lower AUC >140 mg/dL. These factors should be evaluated and incorporated in clinical decision making.

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Insulin Pumps

ATTD19-0336

PSYCHOLOGICAL INDICATORS AND HYPOGLYCAEMIA AWARENESS STATUS AMONGST PEOPLE WITH TYPE 1 DIABETES ON INSULIN PUMP THERAPY

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Randomized clinical trials of insulin pump therapy and continuous glucose monitoring have shown that diabetes technology can prevent severe hypoglycemia, albeit without improving hypoglycemia awareness (HA). Aim of the study was to assess general psychopathology in insulin pump users in relation to HA status. Measures of psychological assessment, the T1-DDS exploring diabetes distress (DD), the **SCL-10R** assessing psychological distress, and the DSQ-40 assessing defense mechanisms, were distributed to 40 adults with Type 1 DM on insulin pump therapy. HA status was assessed using the Gold score. Sixteen people had impaired hypoglycaemia awareness (IHA) and 24 intact HA [(mean ± SD) age: 40.67 ± 9.13 vs. 42.11 ± 8.52 years, diabetes duration: 27.0 ± 10.7 vs. 27.11 ± 10.6 years, HbA1c: 7.14 ± 0.5% vs. 7.13 ± 0.8%; p = NS]. Adults with IHA reported higher levels of psychological disturbance ($t = 2.05$, $p = 0.041$). Significant differences were observed in psychoticism reflecting alienation and cognitive difficulty (feeling that something is wrong with one's mind), ($t = 2.73$, $p = 0.009$), obsessive compulsiveness reflecting difficulty in making decisions ($t = 2.21$, $p = 0.033$), phobic avoidance ($t = 2.08$, $p = 0.044$) and paranoid ideation in being talked about or watched by others ($t = 3.66$, $p = 0.001$). Participants with IHA had higher scores on the defense mechanisms of projection ($t = 3.68$, $p = 0.001$) and denial ($t = 3.84$, $p < 0.001$). They also experienced higher levels of DD in their social environment ($t = 2.05$, $p = 0.047$). Results indicate that despite the use of insulin pump therapy, IHA remains present in people with elevated levels of psychological disturbances. Psychological assessment to identify those who are less likely to benefit from modern diabetes technology should direct targeted interventions to improve hypoglycaemia awareness.

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Insulin Pumps

ATTD19-0363

AFTER SIX MONTHS,PUMP TREATMENT IN TYPE 2 DIABETIC PATIENTS LESS REDUCE PLASMA GLUCAGON VALUES THAN MULTI-DAILY INJECTIONS TREATMENT

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We showed previously with preliminary results that insulin resistance and liver fat content were correlated in type 2 diabetic patients treated with multi-daily injections (MDI) using gold-standard methods. The aim of this work was to present interesting data after randomly pump versus MDI treatment in type 2 diabetic patients (T2DP). Patients and Methods: we tested at 6 months clinical, biological, CGM registration and liver fat

content effects in T2DP with either randomly pump or MDI treatment. Results. In 13 T2DP, we found no significant modifications in term of weight and insulin doses, neither in liver fat content using spectroscopy RMN; there was a tendency to a better metabolic control in the group pump (N = 8) compared to MDI (N = 5), p = 0.09. AUC over 180 mg/dl/day was significantly lower in the pump group versus MDI, p = 0.05. In each group during CGM registration, the difference in glycaemic variability between baseline and 6 months was significantly lower in the pump group compared with the MDI group p = 0.03. Unexpected, T2DP treated with pumps less modified plasma glucagon values than patients treated with MDI, p = 0.018. Conclusions. Because of a too small number of patients in each group, more significant results could not be demonstrated. Nevertheless, AUC over 180 mg/dl/day was significantly lower in the pump group versus MDI; interesting, difference between baseline and 6 months in the two groups regarding plasma glucagon values was higher in T2DP treated with MDI. May be the meaning of this result needs to be lightening with the new biology of glucagon.

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Insulin Pumps

ATTD19-0382

FACTORS ASSOCIATED WITH LOWER GLYCEMIC VARIABILITY IN A COHORT OF CHILDREN WITH T1D ON CSII WITH PREDICTIVE LOW GLUCOSE SUSPEND (PLGS)

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Introduction: Lowering A1c with low glycemic variability (GV) could maximize the Time In Range. Our aim study is to characterize a cohort of children with T1D on CSII with PLGS and to identify factors associated with lower GV.

Method: Children on CSII with PLGS on follow-up ≥1 month at our clinic were included. Monthly pump downloads were recorded. Coefficient of variation (CV) from sensor glucose was calculated from every download, and its association with number of daily SMBG, basal insulin percentage, daily basal segments, hours of PLGS, days between set change and areas under the curve (AUC) <70 mg/dL and >140 mg/dL was explored.

Results: 55 subjects were included, aged 8.3 ± 4.6 years old, with disease duration of 3.7 ± 2.7 years, with weight 27.6 ± 12.4 kg. Most recent A1c was 7.1% ± 0.47%.

291 downloads were analyzed. Low GV group, defined as CV ≤36%, had mean CV of 33.6%, compared to 41.5% on the High GV group (p < 0.0001). Factors significantly associated with CV ≤36% AUC <70 mg/dL (0.2 vs. 0.5, p < 0.002) and AUC >140 mg/dL (29.2 vs.36.8, p < 0.0001). No other factor showed significant association.

Conclusions: Children with T1D on CSII with PLGS with low GV have lower AUC <70 mg/dL and lower AUC >140 mg/dL. Differently from our adults' cohort, other factors explored showed no significant association, which may reflect the high variability in the daily behavior of children with Diabetes. However, the fact that it was associated with lower AUC <70, reinforces the idea of the importance of aiming to reduce glycemic variability to lower the risk of hypoglycemia.

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Insulin Pumps

ATTD19-0387

USE OF CONTINUOUS SUBCUTANEOUS INSULIN INFUSION FOR MANAGEMENT OF DELAYED HYPERSENSITIVITY REACTION TO INSULIN

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A 15 year old boy with type 1 diabetes mellitus developed delayed hypersensitivity reactions to multiple different insulin formulations. In the days following injection of subcutaneous insulin, he developed localised erythema, abscess formation and ulceration at each injection site with insulins Novorapid, Humalog, Protaphane, Levemir and Lantus. A less severe reaction occurred with Actrapid and Apidra. When assessing the excipients, it was noted that unlike all the other insulin formulations, Apidra does not contain zinc compounds.

Skin biopsy detected mixed inflammatory infiltrate. Patch testing was inconclusive and intradermal testing was pursued. Unfortunately intradermal testing was also inconclusive to a specific allergen, but does not exclude T cell mediated (delayed hypersensitivity) pathology.

The decision was made to commence the patient on an insulin pump with subcutaneous infusion of Apidra via a desensitisation protocol. During inpatient admission, intravenous Actrapid infusion was commenced and all subcutaneous insulin ceased. Apidra was infused in a gradually increasing dose from 0.025 units/hour to full basal requirement over 48 hours.

This case demonstrates the use of insulin pumps for management of patients with insulin allergy and the successful use of an insulin desensitisation protocol.

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Insulin Pumps

ATTD19-0396

BASAL RATES DELIVERED ACCORDING TO TYPICAL CIRCADIAN PROFILES WITH BOLUSES: ACCURACY OF DIFFERENT INSULIN PUMPS

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Background and Aims: Insulin pumps are commonly used in the therapy of persons with type 1 diabetes. EN 60601-2-24

describes test settings and procedures for evaluating infusion pumps with constant flow rates; however, most basal rates follow a circadian pattern and boluses are given in addition. In this study, accuracy of different insulin pumps was evaluated in an experimental setting based on EN 60601-2-24.

Method: The insulin pumps Accu-Chek® Insight, Accu-Chek® Spirit Combo, MiniMed® 640G, MiniMed® 670G, OmniPod® and mylife™ YpsoPump were tested. Evaluations were based on the weight increase of a water-filled, oil-covered beaker placed on an electronic balance into which insulin was delivered. Pumps were installed outside of the balance with infusion sets or a steel pipe (for patch pump), respectively, connected to the beaker. After priming, a circadian basal rate profile (20U/24h) was run for 48h. In addition, three insulin boluses (8, 10 and 15U) were delivered during the first 24h. Each pump was tested 9 times; total deviations over 48h and percentages of individual 1h-windows inside of a target range of ±15% were calculated.

Results: Over 48h, mean total deviations from target ranged from -0.3% to +1.9% for the different systems. Percentages of 1h-windows within ±15% of target ranged from 63.9% to 94.4% during the first 24h (with included boluses) and from 68.5% to 100% during the second 24h.

Conclusion: In this study, deviations from target were small for all insulin pumps over total observation period; however, accuracy markedly differed between the pumps over shorter time windows with included boluses.

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Insulin Pumps

ATTD19-0400

DESIGN OF A NOVEL, AFFORDABLE INSULIN PUMP FOR TYPE-1 DIABETIC PATIENTS IN RESOURCE CONSTRAINED SETTINGS

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Numerous studies have extensively documented the benefits of Continuous Subcutaneous Insulin Infusion (CSII) over Multiple Daily Injections (MDI) as an insulin therapy for Type 1 Diabetes Mellitus (T1DM) patients. Despite such overwhelming evidence in support, adoption of CSII is sparse, particularly in resource constrained settings like India. Institutional factors aside, fixed and recurring costs of such a device are often found to be a withholding factor to widespread adoption. The abstract describes the development of an novel, affordable insulin pump for T1DM patients matching the specifications of a state-of-the-art pump, while bringing down the cost significantly.

Most pumps rely on a lead screw/nut coupled with a geared DC motor to achieve precise micro-motion. These motors typically make use of micro-gears as a means of speed reduction, which are inherently expensive to manufacture. Consequently, they contribute significantly to the final cost of a pump. In this work we take an approach to distribute the requisite speed reduction in multiple stages, with an acceptable compromise on the product size. The system is actuated by a nominal DC geared motor and a novel mechanism of converting continuous rotary input to intermittent output. The kinematic chain is feedback controlled which ensures volumetric accuracy of the delivered fluid. The pump can be wirelessly controlled via a remote. The same wireless channel can be used to connect to a Continuous Glucose Monitoring (CGM) device for subsequent integration with an Artificial Pancreas system. Preliminary accuracy tests show promising results comparable to commercially available devices.

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Insulin Pumps

ATTD19-0415

INTENSIVE INSULIN THERAPY WITH CONTINUOUS SUBCUTANEOUS INSULIN INFUSION

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Objective: To compare intensive insulin therapy through continuous subcutaneous insulin infusion (CSII) and multiple daily insulin injections (MIDI) regarding glycemic control,

microalbuminuria, lipid profile, body mass index and frequency of adverse events.

Material and Methods: Retrospective observational study involving 59 patients with type 1 diabetes followed at endocrinology clinic of the São João Hospital Center that performed intensive insulin therapy through CSII for more than 6 years, having previously used the MIDI for a period of more than 6 months. Data was collected from the clinical process comparing the period of MIDI and after 2, 4 and 6 years after CSII.

Results: 59 patients with a mean age of 41 ± 10 years, diagnosed with type 1 diabetes and with an average disease duration of disease of 17 ± 9 years were evaluated. The HbA1c values were significantly lower in the three CSII periods compared to the MIDI period. The parameters of the lipid profile, ISF and I:CH ratio did not show statistically significant differences in any of the periods.The median values of microalbuminuria of the MIDI period was identical to the period of CSII. Regarding body mass index, a statistically significant increase was found 6 years after start of CSII. The frequency of adverse events associated with CSII therapy was reduced.

Conclusion: The change from the MIDI to CSII strategy allowed a better glycemic control during the first 6 years, with no change in the lipid profile or high frequency of adverse events.

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Insulin Pumps

ATTD19-0433

PREGNANCY OUTCOME IN WOMEN WITH TYPE 1 DIABETES MELLITUS TREATED SENSOR AUGMENTED PUMP, PREDICTIVE LOW-GLUCOSE INSULIN SUSPEND PUMP (640G) OR MULTIPLE DAILY INSULIN INJECTION

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Background: Excellent glycemic control before and during pregnancy complicated by type 1 diabetes (T1DM) are important to limit number of poor obstetric and neonatal outcomes.

The aim of the study was to assessed pregnancy outcome of pregnant T1DM women treated three different methods: sensor augmented pump (SAP), pumps with predictive low-glucose insulin suspend (640G) or multiple daily insulin injection (MDI).

Materials and Methods: We analyzed medical records of 81 pregnant T1DM women, treated: SAP therapy (n = 56), 640G (n = 14) or MDI (n = 11). CGM were used by 13/14 (93%) women 640G group, 15/56(27%) SAP group and 0/11(0%) MDI group. We analyzed of glycemic control as assessed by the HbA1c level, pregnancy outcomes.

Results: The statistically lower level of HbA1c was observed in 640G group as compare with SAP and MDI group, before pregnancy (6.0% vs 6.5% (p = 0.31) vs 6.9% (p = 0.089), respectively, at the 1st trimester (5.7% vs 6.1% (p = 0.39) vs 6.8% (p = 0.0007); during 2nd (5.1% vs 5.6% (p = 0.042) vs 5.7% (p = 0.0025); 3rd trimester (5.2% vs 5.7% (p = 0.022) vs 6.1% (p = 0.0038). We observed higher frequency of macrosomia in MDI group (respectively 640G 14%, SAP 26% and MDI 37%; p = 0.77). In 640G group we found statistically lower frequency of composite pregnancy outcome (macrosomia, SGA, fetal malformations, end of pregnancy before 37 weeks) as compared with SAP and MDI, respectively: 21% vs 50% vs 64%; p = 0.07.

Conclusions: The observation shows the effectiveness of the predictive low-glucose suspend (640G) insulin pump during pregnancy in diabetic women in achieving the glycemic target and improvement of pregnancy outcomes.

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New Insulin Analogues

ATTD19-0017

EARLY INTENSIFICATION WITH FIXED-RATIO COMBINATION OF BASAL INSULIN AND GLP-1 RECEPTOR AGONIST IN T2DM: IMPACT OF ONLINE EDUCATION ON PRIMARY CARE PHYSICIAN KNOWLEDGE AND COMPETENCE

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Purpose: To determine if online medical education for primary care physicians (PCPs) can improve knowledge regarding clinical trial data and benefits of early intensification with basal insulin (BI)/GLP-1 receptor agonist (GLP-1 RA) fixed-ratio combinations (FRCs) and their competence in identifying appropriate patients with T2DM who would benefit most from such FRCs.

Methods: The educational activity consisted of a 30-min online, 4 faculty, video panel discussion with synchronized slides. Educational effect was assessed with a repeated pairs pre-/post-assessment study with a 3-item, multiple-choice, knowledge/competence questionnaire and one confidence assessment question. For all questions, each participant acts as his/her own control. A χi-squared test assessed statistical significance at the $P < 0.5$ level. The activity launched December 22, 2017; data were collected until January 26, 2018.

Results: Participation in this activity significantly (P < .0001) improved PCPs' (n = 501) knowledge and competence by 40% to 55%, with respect to:

- How to initiate therapy with BI/GLP-1 RA FRCs
- Their clinical benefits
- Relationship of HbA1c reduction to baseline levels
- Impact on the composite outcome of no increase in body weight, no documented hypoglycemia, and achievement of guideline-recommended glycemic control

Confidence levels for PCPs prescribing a BI/GLP-1 RA FRC in patients with T2DM improved by 26%.

Conclusions: Participation of PCPs in an online 30-minute video panel discussion with synchronized slides improved knowledge, competence and confidence regarding the clinical benefits and practical use of novel BI/GLP-1 RA FRCs in appropriate patients with T2DM. Further education is warranted on the advantages and utility of such FRCs in T2DM management.

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New Insulin Analogues

ATTD19-0194

BIOCHAPERONE COMBO, A CO-FORMULATION OF LISPRO AND GLARGINE, IMPROVES POSTPRANDIAL GLUCOSE CONTROL COMPARED TO LISPROMIX25 OR LISPRO AND GLARGINE INJECTIONS IN TYPE 2 DIABETES SUBJECTS

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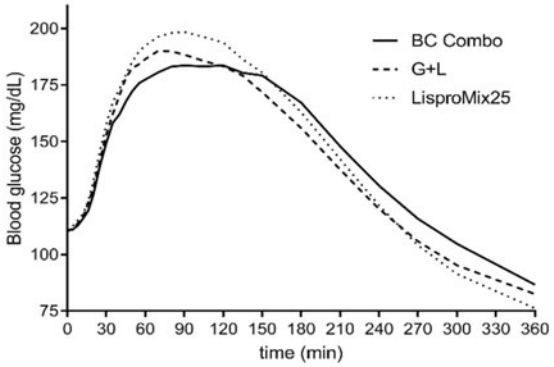
BioChaperone Combo (BC Combo) is a co-formulation of the prandial insulin lispro (25%) and the basal insulin glargine (75%) demonstrating a rapid prandial then a prolonged flat basal profile compared to the premix insulin LisproMix25 (Humalog®Mix25). In a double-blind, double dummy, cross-over trial, the effects of BC Combo on postprandial glucose control were investigated in comparison to LisproMix25 and the separate injections of glargine U-100 (Lantus®) and lispro (Humalog®) (G+L). Thirty-nine type 2 diabetes participants (mean±SD age 60.8 ± 7.5 years and HbA1c 7.97 ± 0.6 %) were randomised to receive the treatments immediately before a standardised solid meal test (610 kcal 20% protein, 30% fat, 50% carbohydrates) on three separate dosing visits. The individual insulin dose was the same with each treatment (mean 0.62 U/kg).

BC Combo demonstrated improved postprandial glucose control compared to both comparators, with reduction of incremental blood glucose excursions over two hours (ΔAUCBG,0-2h) of 18% compared to LisproMix25 ($p = 0.0009$) and 10% compared to G + L ($p = 0.0450$). Subjects spent more time in the blood glucose range 72-162 mg/dL with BC Combo than with lisproMix25 ($p = 0.0384$). The number of mealtime hypoglycaemic episodes was lower with BC Combo (22 events) than with LisproMix25 (43 episodes; $p = 0.0028$) and numerically lower than G + L (28 episode; p = NS). The PK profile of BC Combo showed a faster time to insulin peak and a lower exposure in the 2-6h period than the comparators.

In this study in type 2 diabetes subjects, BC Combo improved postprandial glucose control compared to lisproMix25 and the separate injections of glargine and lispro.

Mean blood glucose profiles after subcutaneous administration of BC Combo, LisproMix25 and Separate injections of glargine and lispro



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New Insulin Analogues

ATTD19-0424

NMR AS A METHOD TO EVALUATE THE QUALITY OF INSULIN ANALOGUES - CONCENTRATION, VARIATION AND CONTENT OF ADDING PRODUCTS

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Background: Nuclear magnetic resonance (NMR) spectroscopy is the golden standard in structure elucidation of small organic molecules. It is also used for mixture analysis and metabolomics due to the inherent quantitative aspects of the technique. The information extracted from NMR is more extensive than e.g. reverse phase HPLC methods. Even in the 1D NMR case which is swiftly recorded in the time-frame of a few minutes per sample it provides not only absolute quantification of multiple mixture components by simply integrating their corresponding peaks which are proportional to their concentrations. It is very sensitive to changes of e.g. peptide secondary and tertiary structure, peptide interactions, and pH or ionic strength variations, all seen as perturbations in the chemical shifts, i.e. slight but notable changes of peak positions along the x-axis.

Aim: To evaluate 1D 1H NMR as a method for rapid and robust characterization of insulin in terms of insulin concentration, variability and excipient content in as close to native state as possible. A comprehensive study of five of the most common commercial insulins, not directly from the manufacturer, but rather about to be delivered or already in the hands of patients, was performed.

Result: 1D 1H NMR spectroscopy, combined with minimal pre-analytical sample preparation on insulin samples can be used to rapidly detect and characterize concentration changes and general variability as well as determine the additive content. Our finding provokes the question why the established quality control method is reverse-phase HPLC where only the concentration can be assessed.

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New Insulin Analogues

ATTD19-0431

USE OF SECOND-GENERATION LONG-ACTING INSULIN ANALOGS: REAL-WORLD DATA ON INSULIN DEGLUDEC AND INSULIN GLARGIN U 300 FROM THE GERMAN DPV REGISTRY

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Insulin Degludec and insulin glargin U300 are second-generation long-acting basal insulins. In Germany, insulin degludec was available from 2013 to 2015, while insulin glargin U300 is available since 2015. This study is based on a large quality-control registry in Germany (DPV prospective follow-up). Aim: to describe patient groups who opted to use these second generation basal analogs. By September 2018, 7489 patients in the database used insulin glargin U300. 56.7% were male, mean age was 58.4 years, mean diabetes-duration was 13.5 years. 2132 patients (28.5 %) were classified as type-1 diabetes, 5023 (67.1%) as type-2, 334 (4.4%) as other types. For 1528 patients, basal insulin therapy previous to initiation of glargin300 was documented: 51.4 % switchted from glargin U100 to glargin U300, 35.4 % switched from insulin degludec, 26.8 % from insulin detemir and 18.6 % switched from NPH to glargin U300.

1536 patients used insulin degludec (51.9% male, age 41.2 years, mean duration of diabetes 12.7 years; 1019 (66.3 %) type-1-diabetes, 456 (29.7%) type-2-diabetes, 61 patients: other types (4.0 %). Most patients (41.3 %) switchend from insulin detemir to Degludec, followed by Glargin (39.2 %) and NPH (19.5 %).

In conclusion, patient characteristics differed significantly between those choosing insulin degludec or insulin glargin U300. Due to the specific situation of market availability in Germany, long acting insulins used prior to this switch again are remarkably different. Registries reflect real-world use of therapeutic options, with the respective availability / reimbursement for individual patients in different regions being an important prerequisite.

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New Insulin Delivery Systems: Inhaled, Transderma, Implanted Devices

ATTD19-0205

GLYCEMIC CONTROL AND SATISFACTION WITH ANALYSES USING AN INSULIN PEN WITH MEMORY AND DOWNLOADING FUNCTION

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Background and Aims: To evaluate glycemic control and satisfaction with the analyses at consultation using Novopen5-Plus® - an insulin pen with memory and downloading function.

Methods: 31 patients (age 9-18) followed at the pediatric clinic, Halland County Hospital, Sweden, July 2017- September 2018, were included. Each patient had a startup and a follow-up visit after 6 months. HbA1c, average glucose value, glucose variability, and percentages of time in range (70–180 mg/dl) and hypoglycemia over the last 14 days were registered. Additionally, the patients and the doctors valued their satisfaction with the analyses (of downloaded data) at both visits. Analyses with Wilcoxon signed rank tests were performed.

Results: Median HbA1c in girls exceeded HbA1c in boys at startup, but improved statistically significant between visit 1, 7,5%, (59 mmol/mol, range 45–76) and 2, 6,8%, (median 51 mmol/mol, range 45–66) ($p = 0.047$), whilst there was no statistically significant change in HbA1c amongst boys or the whole group. However, the entire group showed a statistically significant improvement in percentage of time in range between visit 1 (median 49, range 17–81) and 2 (median 51, range 28–79)($p = 0{,}033$). Patient's satisfaction with the analyses improved statistically significant between visit 1 and 2 ($p = 0.005$), and so did the doctor's ($p < 0{,}001$).

Conclusions: The use of an insulin pen with ability to download data improved both patient's and doctor's satisfaction with the analyses. For girls HbA1c was decreased, however on group level it did not improve glycemic control. All children wanted to continue with the pen at the end of the study.

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New Insulin Delivery Systems: Inhaled, Transderma, Implanted Devices

ATTD19-0305

COMPARISON OF CAPILLARY BIOMEDICAL'S INSULIN INFUSION SET WITH A SOFT/FLEXIBLE POLYMER WIRE-REINFORCED CANNULA AND MULTIPLE ORIFICES TO COMMERCIAL TEFLON SETS USING MICRO-CT & HISTOLOGY IMAGING

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Insertion of a CSII cannula through the skin into the subcutaneous tissue damages cells, connective tissue and extracellular matrix. A layer of thrombus and acute inflammatory tissue develops around the cannula due to insertion trauma, motion induced trauma, and the pro-inflammatory effects of the foreign body and insulin excipients.

We compared the performance of CapBio investigational CSII catheters with a soft/flexible polymer wire-reinforced kink-proof cannula with multiple orifices to commercial CSII catheters with a Teflon cannula with one distal orifice in large swine. An investigational and commercial CSII were inserted into the subcutaneous tissue of the abdomen every other day for 14 days. Insulin lispro (U-5) was infused through the CSII catheters using the same basal/bolus pattern. On day # 14, a 70 ul bolus of insulin/x-ray contrast agent was infused through each CSII catheter. The tissue surrounding each CSII was excised 5 minutes later, frozen, and imaged using a high-resolution micro-CT scanner. The tissue was then processed and stained to produce high-resolution histology images.

Histology images revealed a significantly thinner and smaller area of inflammatory tissue around the CapBio CSII cannulas

compared with the commercial CSII Teflon cannulas. Micro-CT images revealed a significantly larger volume and surface area of insulin/x-ray contrast agent delivered into the subcutaneous tissue when infused through the CapBio CSII compared with the commercial CSII catheters. Statistical analysis is currently being completed.

There is great clinical need for an insulin infusion set that functions reliably for more than 2–3 days with improved consistency of insulin absorption (PK).

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New Insulin Delivery Systems: Inhaled, Transderma, Implanted Devices

ATTD19-0339

CLINICAL EFFECTIVENESS OF SWITCHING FROM INSULIN PEN DEVICES TO A 24-HR WEARABLE INSULIN DELIVERY DEVICE IN PATIENTS WITH TYPE 2 DIABETES PRESCRIBED BASAL-BOLUS THERAPY

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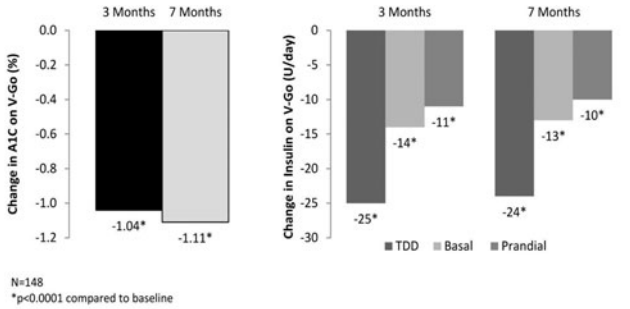
Background and Aim: Insulin pen devices address many of the concerns with vial and syringe therapy and have led to increased adherence. However, insulin pens do not address patient concerns of injection frequency, injection embarrassment or the inconvenience to carry supplies when away from home. A novel 24-hr wearable insulin delivery device (V-Go®) offers discreet basal-bolus insulin delivery, without the need for multiple daily injections or additional supplies. This analysis evaluated the clinical effectiveness of switching to V-Go for basal-bolus therapy and explored if baseline doses of basal or prandial insulin impacted the effectiveness of V-Go.

Methods: Nine diabetes centers in the United States participated in this retrospective study using electronic medical records to extract data. Patients uncontrolled (A1C ≥ 7.0%) and prescribed basal-bolus therapy administered by pen devices prior to V-Go were included in the evaluation. Change in A1C and insulin dosing compared to baseline were evaluated and based on baseline basal and prandial doses (≤ 50 or >50 U/day).

Results: Patients (N = 148) were evaluated. Mean baseline characteristics were A1C 9.1%, weight 218 lbs, insulin basal, prandial and total U/day were 47, 35 and 82, respectively. After 3 and 7 months of V-Go use, A1C and insulin doses were significantly reduced compared to baseline. Insulin needle sticks decreased from 4.2/day to 1/day with V-Go. Significant reductions



N=148
*p<0.0001 compared to baseline

Change Based on Baseline Basal and Prandial Doses	Baseline Basal U/day		Baseline Prandial U/day	
	≤ 50 U/day	> 50 U/day	≤ 50 U/day	> 50 U/day
	n=99	n=49	n= 119	n= 29
Baseline A1C, %	9.0 ± 1.4	9.1 ± 1.5	9.0 ± 1.4	9.4 ± 1.5
△ at 3 Mo of V-Go Use	-1.1*	-1.0*	-1.0*	-1.2*
△ at 7 Mo of V-Go Use	-1.1*	-1.2*	-1.0*	-1.3*
Baseline Basal Dose, U/day	31 ± 11	79 ± 30	43 ± 27	63 ± 37
△ at 3 Mo of V-Go Use	-1	-40*	-12*	-24*
△ at 7 Mo of V-Go Use	-1	-38*	-10*	-25*
Baseline Prandial Dose, U/day	30 ± 20	43 ± 32	25 ± 11	74 ± 29
△ at 3 Mo of V-Go Use	-9*	-14*	-3*	-45*
△ at 7 Mo of V-Go Use	-9*	-13*	-2	-44*
Baseline Total Dose, U/day	62 ± 25	122 ± 48	68 ± 30	137 ± 53
△ at 3 Mo of V-Go Use	-11*	-54*	-14*	-69*
△ at 7 Mo of V-Go Use	-9*	-54*	-12*	-66*

*p<0.05 compared to baseline

in A1C and total insulin were also observed when stratified based on baseline dosing.

Conclusion: Basal-bolus therapy with V-Go resulted in significant reductions in A1C and insulin compared to prior pen therapy.

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New Medications for Treatment of Diabetes

ATTD19-0045

EFFECT OF THE GLP-1 RECEPTOR AGONIST EXENATIDE ON AWARENESS OF HYPOGLYCAEMIA IN PATIENTS WITH TYPE 1 DIABETES AND IMPAIRED AWARENESS OF HYPOGLYCAEMIA

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Background: Impaired awareness of hypoglycaemia (IAH), a syndrome caused by recurrent hypoglycaemia, affects ∼25% of patients with type 1 diabetes (T1D) and can be reversed by strict avoidance of hypoglycaemia for 3 weeks. Adjunctive treatment with GLP-1 receptor agonists has been associated with lower risk of hypoglycaemia. The aim of our study was to investigate the effect of exenatide on awareness of hypoglycaemia in people with T1D and IAH.

Methods: In this randomized double-blind, placebo-controlled cross-over trial, we included ten patients with T1DM and IAH (age 38.5 ± 4.4 years, 40% males, BMI 27.0 ± 1.5 kg/m^2, disease duration 21.7 ± 4.3 years, HbA_{1c} 55.2 ± 1.5 mmol/mol). They were treated with exenatide 5 μg BID (first 2 weeks), followed by 10 μg BID for 4 weeks or matching placebo, with a washout period of 4 weeks. At the end of each treatment period, subjects underwent a modified hyperinsulinaemic normoglycaemic-hypoglycaemic

glucose clamp (glucose nadir, 2.5 mmol/L). Blinded continuous glucose monitors were used in the final treatment weeks.

Results: Treatment with exenatide did not change median (IQR) percentage of time spent in hypoglycaemia (15.5 [4.5, 25.5] vs. 7.8 [4.4, 17.1]%, $p = 0.11$) and mean (±SEM) frequency of hypoglycaemia (15.8 ± 3.7 vs. 12.1 ± 3.5 events, $p = 0.19$). There was a significant change in body weight after treatment with exenatide when compared to placebo (-3.9 ± 0.9 vs. 0.6 ± 1.2 kg, $p = 0.047$). We found no differences in symptom scores or in counterregulatory hormone levels in response to clamped hypoglycaemia.

Discussion/conclusion: Six weeks treatment with exenatide did not affect awareness of hypoglycaemia in patients with T1D and IAH.

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New Medications for Treatment of Diabetes

ATTD19-0078

STUDY OF GLUTATHIONE STATUS AND ITS CORRECTION IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND MACROANGIOPATHY OF THE LOWER EXTREMITIES

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Background and Aims: The **aim** of the study was to evaluate the effectiveness of the antioxidant drug in patients with type 2 diabetes mellitus (T2DM) and macroangiopathy of the lower extremities for correction of glutathione status.

Method: 40 men with T2DM and macroangiopathy of the lower extremities, 20 men with T2DM without such complications and 30 - control group were involved in the study. Then 20 patients from the group with T2DM and macroangiopathy of the lower extremities additionally applied the solution of N-acetylcysteine in a daily dose of 600 mg once, intravenously, for 7 days. Methods of high-performance liquid chromatography were used.

Results: The level of reduced glutathione (GSH) decreased more in the group with macroangiopathy - by 108% comparing to 59.3% - in the group without complications. The content of oxidized glutathione (GSSG) in the T2DM group without macroangiopathy increased by 52%, and in the macroangiopathy group increased by 70%. Glutathione status in patients at addition of N-acetylcysteine in treatment had changed. So, by the third day the value of the GSH increased (by 11%) and became equal to 381 ± 38 μg/ml ($p < 0.05$); by seventh day - by 13% and became equal to 387 ± 42 μg/ml ($p < 0.05$). GSSG level by 50% decreased and became to 45 ± 13 μg/ml ($p < 0.05$); by seventh day GSSG by 79% decreased and becomes 20 ± 4 μg/ml ($p < 0.05$).

Conclusion: We can conclude that the therapy we proposed effectively affects the activation of the glutathione status in patients with T2DM and macroangiopathy of the lower extremities.

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New Medications for Treatment of Diabetes

ATTD19-0079

ETHNIC ASPECTS OF LIPID PEROXIDATION PROCESS FLOW IN PATIENTS WITH TYPE 1 DIABETES MELLITUS

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Background and Aims: Numerous researches show that data on an ethnic origin can give additional information for the personified approach in treatment of different diseases. The aim of this study was to evaluate lipid peroxidation process flow in Mongoloid and Caucasian patients with type 1 diabetes mellitus (T1DM).

Method: Biochemical parameters in 147 persons (healthy and with T1DM) both Mongoloids (ethnic group is Buryats) and Caucasians (ethnic group is Russians) living in the modern city Ulan-Ude (East-Siberia) were assessed. Spectrophotometric and fluorometric methods for the study of components of the lipid peroxidation (LPO) were used.

Results: Our study has shown higher concentration of diene conjugates (DC) (by 1.35 times; $p < 0.01$) in Mongoloid patients as well as higher levels of diene conjugates (by 2.4 times; $p < 0.001$) and ketodienes (KD) (by 2.71 times; $p < 0.05$) in Caucasian patients in compare with the corresponding control groups. The study of total radical trapping antioxidant level (TRAP) in patients with T1DM, an increase (by 1.54 times; $p < 0.001$) in this indicator in Mongoloid patients in compare with the control group was shown. In Caucasian patients with T1DM, statistically significant differences from the control group included reduced GSH values (by 1.16 times; $p < 0.05$) and increased GSSG level (1.26 times; $p < 0.001$). Integral coefficient of oxidative stress in Mongoloid patients was 1.35, in Caucasian patients was 2.32 ($p < 0.05$).

Conclusion: Noted changes in LPO–AOD system in Mongoloid patients with T1DM were less intensitive than in Caucasian pathients, that allows make a recommendation on highly individualized approach to the complex therapy.

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New Medications for Treatment of Diabetes

ATTD19-0083

LOW VERSUS HIGH CARBOHYDRATE DIET IN TYPE 1 DIABETES: A 12-WEEK RANDOMIZED CROSSOVER STUDY

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Aim: To compare the effects of a low carbohydrate (<100 grams carbohydrate/day) and a high carbohydrate diet (>250 grams carbohydrate/day) on glycemic control in adults with type 1 diabetes.

Methods: In a randomized crossover study with two 12-week intervention arms separated by a 12-week washout, 14 participants using sensor-augmented insulin pumps were included. Before randomization and study start, insulin pump settings and carbohydrate counting skills were optimized.

Results: Baseline characteristics of the 14 participants (eight females) were (mean ± SD): age 44 ± 12 years, BMI 24.8 ± 2.0 kg/m^2, HbA1c 58 ± 4 mmol/mol, daily carbohydrate intake 152 ± 43 grams/day. Daily carbohydrate intake during the two periods was 98 ± 11 grams and 246 ± 34 grams, respectively. HbA1c did not change significantly, neither between nor within the low and the high carbohydrate intervention arm (56 to 57 mmol/mol (P = 0.462) and 57 to 56 mmol/mol (P = 0.366), respectively (P = 0.421 (between-group difference)). Distribution of glucose values (% time spent in ranges), mean glucose, SD and CV assessed by continuous glucose monitoring are given in the table below.

Conclusion: Carbohydrate restriction did not change mean glucose or time spent in the normoglycemic range, whereas time spent in hypoglycemia and glycemic variability was significantly reduced.

Glucose variables and insulin use during 12 weeks of low carbohydrate diet (<100 g carbohydrates per day) and 12 weeks of high carbohydrate diet (>250 g carbohydrates per day)

	LCD (N = 14)	HCD (N = 11)	LCD vs. HCD
			P value
Distribution of glucose values assessed by CGM (% time in ranges)			
<3.0 mmol/l	0.3 (0.5)	0.7 (0.5)	**0.004**
<3.9 mmol/l	1.9 (1.8)	3.6 (2.1)	**<0.001**
3.9-10.0 mmol/l	68.6 (8.9)	65.3 (6.5)	0.316
>10.0 mmol/l	29.5 (9.0)	31.1 (7.3)	0.801
>13.9 mmol/l	5.4 (3.4)	7.9 (3.9)	0.059
Mean glucose and glycemic variability assessed by CGM			
Mean glucose (mmol/l)	8.8 (0.7)	8.9 (0.7)	0.893
SD (mmol/l)	2.9 (0.4)	3.3 (0.4)	**0.004**
CV (%)	32.7 (3.2)	37.5 (3.6)	**0.007**
Insulin doses			
Total daily dose (U)	33.6 (8.1)	43.2 (11.0)	**<0.001**
Total daily basal (U)	18.5 (5.4)	17.3 (5.4)	0.105
Total daily bolus (U)	15.1 (4.4)	25.9 (7.3)	**<0.001**

Data are mean (SD). CGM, continuous glucose monitor; CV, coefficient of variation; HCD, high carbohydrate diet; LCD, low carbohydrate diet; SD, standard deviation.

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New Medications for Treatment of Diabetes

ATTD19-0092

MECHANISMS BEHIND HYPOGLYCEMIC ACTIONS OF BUTANOL FRACTION OF AZADIRACHTA INDICA IN A TYPE 2 DIABETES RAT MODEL

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The cost and side effects of oral hypoglycemic agents for the treatment and management of type 2 diabetes (T2D) has led to increase the use of natural medicines, particularly from medicinal plants. Hence, the validation of the folkloric use of these medicinal plants. In the present study, the mechanisms behind the antidiabetic effects of the butanol fraction of *Azadirachta indica* (*A. indica*) (BFAI) were evaluated. T2D was induced by feeding 10% fructose solution *ad libitum* for two weeks followed by an intraperitoneal injection of streptozotocin (40 mg/kg body weight) and the animals were treated with a low dose (150 mg/kg) and a high dose (300 mg/kg) of BFAI for 4 weeks as a single oral dose daily. Body weight and blood glucose were determined every week. Oral glucose tolerance test was performed in the last week of treatment. Insulin homostasis and liver glycogen concentration were determine after 4 weeks of oral administration. Both doses of the fractions were significantly improved body weight, reduced blood glucose, stimulated insulin secretions, improved pancreatic β cell function (HOMA-β), decreased insulin resistance (HOMA-IR), and increased liver glycogen concentration compared to untreated diabetic rats, when high dose had a better activity. GC-MS analysis of the fraction revealed the presence of polyphenols. The results of this study suggest that, the polyphenols present in the fraction may be responsible for the antidiabetic effects which have been achieved via decreasing insulin resistance, modulating β-cell function, as well as by inhibiting of α-amylase and α-glucosidase activity.

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New Medications for Treatment of Diabetes

ATTD19-0119

COMPARISON OF PHARMACOKINETICS AND EXPOSURE-RESPONSE RELATIONSHIP OF DAPAGLIFLOZIN IN ADULT AND ADOLESCENT/YOUNG ADULT PATIENTS WITH TYPE 1 DIABETES

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Background: Dapagliflozin is approved for the treatment of adults with type 2 diabetes and is in clinical development for type 1 diabetes (T1D). We quantitatively compared the pharmacokinetics (PK) and exposure-response relationship of dapagliflozin between adult and adolescent/young adult patients with T1D.

Methods: Data from two clinical studies (70 adults [NCT01498185], 33 adolescents/young adults [NCT02325206]) of single or repeated dose (1-10 mg), oral dapagliflozin as an add-on to insulin were analysed to examine dapagliflozin PK, using a two-compartment model with first-order absorption, and its

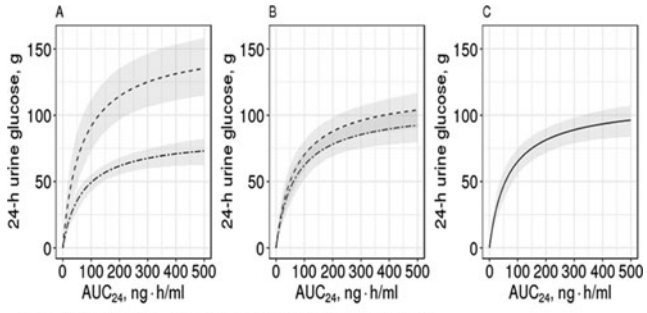

Figure 1: Simulated absolute change 24-h urine glucose based on the exposure-response model
(A) before and after normalisation for (B) blood glucose and (C) blood glucose and baseline estimated glomerular filtration rate. Median UGE response is represented by dashed lines for adolescents/young adults and by double-dashed lines for adults. Grey ribbons are 90% confidence intervals for median predictions. AUC_{24}, area under the curve from time 0 to 24 h on day 1.

exposure-response relationship (24-h urinary glucose excretion [UGE]), using a sigmoidal maximal effect model. Median 24-h blood glucose, estimated glomerular filtration rate (eGFR), sex, age and body weight were evaluated as covariates.

Results: PK model predictions fitted well with the observed data. Exposure following the same dapagliflozin dose was similar between adult and adolescent/young adult patients with T1D. The exposure-response model adequately described UGE data. The identified covariates, median 24-h blood glucose and eGFR, were consistent with dapagliflozin's mechanism of action. After normalisation of the two covariates, model-predicted UGE response was similar between adult and adolescent/young adult patients with T1D.

Conclusions: Dapagliflozin's PK and exposure-response relationship were similar between the two studies after adjusting for covariates. These results indicate that no dose adjustment was required for adolescent/young adult patients with T1D and supported the further clinical development of dapagliflozin for paediatric patients.

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New Medications for Treatment of Diabetes

ATTD19-0145

EXPOSURE-RESPONSE (HBA1C) OF DAPAGLIFLOZIN IN T1D PATIENTS

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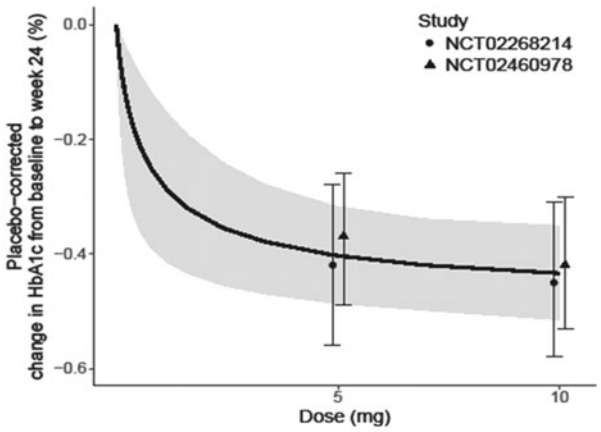
Background and Aims: Dapagliflozin has been evaluated in patients with type 1 diabetes (T1D) in two clinical trials: DEPICT-1 (NCT02268214) and DEPICT-2 (NCT02460978). This analysis used pooled data from both studies and assessed the exposure–response (ER) relationship between dapagliflozin and HbA1c reduction in patients with T1D.

Method: In both studies patients underwent double-blinded, 24-week treatment with placebo, dapagliflozin 5mg or dapagliflozin 10mg – plus adjustable insulin. Mixed-Effect Model Repeated Measures including ER maximum effect (Emax) function was used to describe longitudinal HbA1c data. The effect of several covariates was assessed.

Figure. Model-derived dose–response relationship for HbA1c reduction with 24 weeks of dapagliflozin treatment



Solid line and shaded area represent the meal model prediction with 95% CI.
Actual clinical HbA1c data are shown as data points with 95% CI.

Results: The ER model described the data well. Model predicted HbA1c mean (95% CI) reductions at week 24 (placebo-corrected change from baseline) were −0.40% (−0.50, −0.31) and −0.43% (−0.53, −0.34) for dapagliflozin 5mg and 10mg, respectively; in good agreement with the actual observations (−0.42% and −0.37% for dapagliflozin 5mg, in DEPICT-1 and DEPICT-2, respectively, and −0.45% and −0.42% for dapagliflozin 10mg). Estimated AUC50 (exposure resulting in half maximal effect) was 35.56 ng/mL*h. Insulin administration method was found to impact dapagliflozin efficacy; patients using an insulin pump were predicted to have larger HbA1c reductions than patients using multiple daily injections. This difference was observed to diminish by week 24. The maximum difference in HbA1c reduction of approximately 20% was not deemed clinically relevant.

Conclusion: A model was developed that successfully described the relationship between dapagliflozin systemic exposure and HbA1c response in patients with T1D.

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New Medications for Treatment of Diabetes

ATTD19-0152

TAURINE IN TREATMENT OF NEWLY DIAGNOSED TYPE 2 DIABETES WITH OBESITY

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Objectives: The study is aimed at investigating the effect of taurine on metabolic parameters in overweight patients with

newly diagnosed diabetes. Taurine is normally present in our tissues and known for a variety of biological actions. Considering that obesity is associated with a low-grade inflammation of adipose tissue, the antioxidant and antiinflammation effects of taurine could improve metabolic control in obesity and diabetes.

Methods: Our study is a case control study; 32 patients with newly diagnosed diabetes mellitus and obesity (BMI >30) and HbA1C ≤7% were included into the study, divided into 2 groups-experimental and control. In addition to maintaining low calorie diet 1100 kkal and 60 min physical activity per day (walking) in both groups, Taurine 1500mg were prescribed to the patients of the experimental group. BMI, waist circumference, trIglycerides, blood glucose, HbA1c were checked in both groups before and after three months.

Results: improvements were observed in both groups; average weight loss in the experimental group was 9kg and 6 kg in control group. Waist circumference decreased 5–6 cm in experimental group and an average of 4–5 cm in control group. Triglycerides were reduced in both groups. Fasting blood glucose was normalized in both groups, HbA1c was normalized in both groups, with an average of 0.5% reduced value in experimental group. Improved vision was additional benefit in experimental group.

Conclusion: taurine as a dietary supplement in addition to lifestyle changes could have additional benefits n the treatment for the newly diagnosed obese diabetes patients.

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New Medications for Treatment of Diabetes

ATTD19-0196

DYNAMICS OF MICROALBUMINURIA IN PATIENTS WITH TYPE 1 DIABETES MELLITUS AFTER INTRAVENOUS ADMINISTRATION AUTOLOGOUS BONE-MARROW DERIVED MESENCHYMAL STEM CELLS

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Microalbuminuria (MAU) is a urinary marker of the earliest stage of diabetic nephropathy. However, the effect of autologous bone-marrow derived mesenchymal stem cells (ABM-MSC) on MAU in T1DM patients is not well studied.

Materials and Methods: 5 patients (4 male,1 female) with T1DM received the ABM-MSC intravenously and 5 patients (2 male, 3 female) with T1DM were as a control group. Mesenchymal stem cells were obtained from the iliac crest of T1DM patients, cells were cultured for 3-4 weeks. The quantity of ABM-MSC infused was $95–97 \times 10^6$. We analyzed MAU in both groups of T1DM patients before and 6 months later after the ABM-MSC administration.

Results: We studied the baseline mean MAU level in T1DM patients with ABM-MSC administration, it was $12.56 + 5.56\ \mu$g/ml, 6 months after the ABM-MSC administration the mean MAU level was $-6.89 + 2.73\ \mu$g/ml ($p = 0.222$). The baseline mean MAU level in patients with T1DM of the control group was $11.09 + 2.86\ \mu$g/ml, 6 months after it was $-18.12 + 6.24\ \mu$g/ml ($p = 0.055$). So, 6 months after the mean MAU level in T1DM patients who received ABM-MSC decreased significantly compared with the mean MAU level of the control group patients with T1DM, respectively, $6.89 + 2.73\ \mu$g/ml and $18.12 + 6.24\ \mu$g/ml ($p = 0.008$).

Conclusions: Thus, the decreased MAU level in patients with T1DM after 6 months of the ABM-MSC administration compared to the control group patients with T1DM may serve a confirmation of the effectiveness of ABM-MSC administration for prevention of diabetic nephropathy in patients with type 1DM.

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New Medications for Treatment of Diabetes

ATTD19-0253

EFFECT OF ADDING DAPAGLIFLOZIN AS AN ADJUNCT TO INSULIN ON URINARY ALBUMIN-TO-CREATININE RATIO OVER 52 WEEKS IN ADULTS WITH TYPE 1 DIABETES

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Background: Dapagliflozin (DAPA), as an adjunct to insulin, was reported to improve glycemic control, reduce body weight, and was well tolerated (DEPICT-1 and 2 studies) in adults with inadequately controlled type 1 diabetes (T1D; HbA_{1c}: 58 mmol/mol - 91 mmol/mol [7.5%–10.5%]).

Methods: In this pooled post hoc analysis of the DEPICT-1 and -2 studies, the effect of DAPA on urinary albumin-to-creatinine ratio (UACR) was evaluated in individuals with T1D with baseline micro or macroalbuminuria.

Results: UACR was recorded at baseline for 548, 565, and 532 individuals treated with DAPA 5 mg, DAPA 10 mg, and

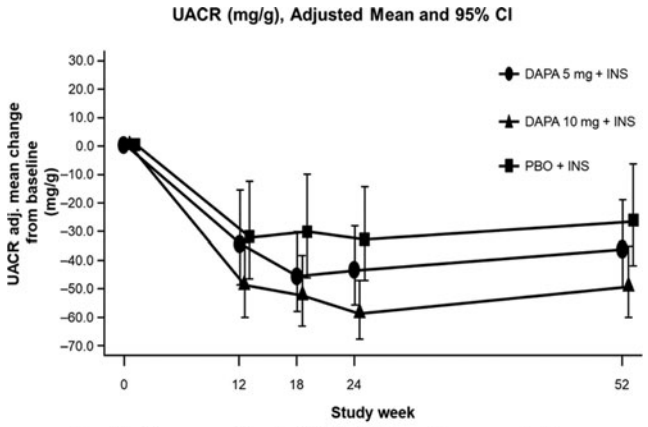

Figure: Adjusted mean percent change in UACR (longitudinal repeated measures analysis). DAPA, dapagliflozin; INS, insulin; PBO, placebo; UACR, urine albumin-to-creatinine ratio.

placebo, respectively; baseline albuminuria was found in 80, 84, and 87 of these individuals in the respective arms. Of these 251 individuals, baseline renal function measured as estimated glomerular filtration rate (eGFR) was normal in 93 (eGFR ≥90 mL/min/1.73 m^2), mildly impaired in 131 (eGFR ≥60–<90 mL/min/1.73 m^2), and moderately impaired in 27 individuals (eGFR <60 mL/min/1.73 m^2). Changes in eGFR were similar across the treatment arms (data not shown). Dose-dependent decrease in UACR was observed with DAPA treatment at weeks 12, 18, 24, and 52 (Figure). At week 52, the differences in UACR between DAPA 10 mg vs placebo and DAPA 5 mg vs placebo were −31.1% (95% CI: −49.9, −5.2) and −13.3 (95% CI: −37.2, 19.8), respectively.

Conclusion: Treatment with DAPA, as an adjunct to insulin, provided a dose-dependent benefit in reducing UACR, suggesting renoprotective effects in individuals with T1D with baseline albuminuria.

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New Medications for Treatment of Diabetes

ATTD19-0294

HDNC (1-HYDROXY-5, 7-DIMETHOXY-2 NAPHTHALENE-CARBOXALDEHYDE) FOR RAPID RECOVERY OF GESTATIONAL DIABETES (STREPTOZOTOCIN-INDUCED DIABETIC): INCISION WOUND MODEL OF RATS

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Background: HDNC (1-hydroxy-5, 7-dimethoxy-2 naphthalene-carboxaldehyde) is a bioactive compound derived from *Aegle marmelos* (Rutaceae, 'Bael'). The current study was conducted to conclude the effect of HDNC on mechanical properties and collagen content of stomach and duodenal wounds in diabetic rats (Streptozotocin-induced diabetic).

Methods: This experiment included wound creation in rumen (non-glandular part) & corpus (oxyntic) part of stomach and duodenum. These wounds were analyzed after 0, 5, 15 & 30 days post-operation.

Results: HDNC treatment found to improve the mechanical strength of healing wounds of diabetic stomach and duodenum. Breaking strength and breaking energy were also augmented in presence of HDNC. Healing process was slower in initial post-operative phase (after 5 days). However in later days wound strength enhanced drastically. Direct relation was observed between total collagen content and mechanical strength.

Conclusion: These findings point towards that the amplification of mechanical strength and collagen content in wounds of gestational diabetes has been the outcome of HDNC treatment.

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New Medications for Treatment of Diabetes

ATTD19-0302

A READY-TO-USE LIQUID GLUCAGON RESCUE PEN FOR SEVERE HYPOGLYCEMIA DEMONSTRATES REDUCED HEALTHCARE PAYER COSTS IN A BUDGET IMPACT MODEL

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Background: A ready-to-use, room-temperature stable liquid glucagon rescue pen auto-injector (GRP; Xeris Pharmaceuticals) has been developed for the rescue of severe hypoglycemia events (SHEs). GRP has a simple two-step process to administer of a full dose of glucagon, where in a simulated emergency setting 99% of users successfully (high functional efficacy). Conversely, in marketed glucagon emergency kits (GEK) only 0% to 31% of users were successful.

Objective: Model the annual value of GRP compared to GEK or no glucagon for SHE rescue treatment in people with diabetes.

Methods: To estimate the economic impact of a GRP, we developed a one-year budget impact model from a US commercial health plan perspective. Cost offsets from successful glucagon administration incorporated EMS, ED, inpatient, and outpatient utilization. Diabetes prevalence and event probabilities were estimated from publicly-available sources. Costs ($ USD) were obtained from the 2018 Medicare Fee Schedules and adjusted to represent commercial payer costs.

Results: GRP led to fewer EMS, ED, inpatient, and outpatient costs compared to GEK and no kit, resulting in total per-patient SHE costs of $2,564, $3,606, and $3,849, respectively. Health plan costs for one million covered lives were almost $9 million compared to $8.2 million following introduction of GRP.

Conclusions: The functional efficacy of GRP virtually eliminates user errors and may reduce utilization of emergency medical services (EMS), emergency department (ED), and overall inpatient and outpatient costs for SHE. A budget impact model suggests significant annual cost savings for US commercial payers can be achieved with GRP.

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New Medications for Treatment of Diabetes

ATTD19-0304

THE EFFICACY AND SAFETY OF THE SGLT2 RECEPTOR INHIBITORS IN TRIPLE THERAPY IN PATIENTS WITH UNCONTROLLED TYPE 2 DIABETES

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Objective: To assess the efficacy and safety of the SGLT2 receptor inhibitors in triple therapy in adults with type 2 diabetes.

Design: Quasi-experimental trial conducted from August 2015 to September 2018 in the Endocrinology Unit at Imbanaco Medical Center. Cali, Colombia.

Methods: A total of 65 women and 58 men with inadequate glycemic control (HbA1c >7%) with dual therapy (Group-A: Metformin 1.700mg/day plus glibenclamide 10mg/day, Group-B: Metformin 1.700mg/day plus saxagliptin 5mg/day, Group-C: Metformin 1.700mg/day plus exenatide 2mg/week subcutaneous and Group-D: Metformin 1.700mg/day plus Insulin basal-bolus), received open-label dapagliflozin (10mg/day) in triple therapy for 52 weeks. The primary efficacy end point was change in HbA1c, basal glycemia, body weight and blood pressure from baseline to week 52.

Results: All patients completed 52 weeks of follow-up. 52.8% were women (Table1). The linear trend of mean decrease at 52 weeks of HbA1c was −0.8, −1, −1, −1.1; basal glycemia was −48.9, −62.4, −40.9, −30.9; body weight was −1.6, −2.1, −3.8, −1.8; and blood pressure was −18.8/−3.9, −27.4/−10.9, −19/4.5–, −15.8/−5 in the 4 groups (A, B, C and D), respectively, (p = <0.000). A HbA1c goal of less than 7% was obtained at 12, 24 and 52 weeks for group A (22%, 25%, 31%), group B (14%, 45%, 45%), group C (14 %, 31%, 39%) and group D (15%, 32%, 26%). Episodes of hypoglycemia and urinary tract infections were infrequent.

Conclusion: SGLT2 receptor inhibitors in triple therapy produced statistically significant improvements in HbA1c, basal glycemia, body weight and blood pressure in patients with uncontrolled type 2 diabetes.

Table 1. Baseline characteristics of patients

Characteristics	Group A (n=32) (M+G+D)	Group B (n=29) (M+S+D)	Group C (n=28) (M+E+D)	Group D (n=34) (M+I+D)	p Value
Age, mean (SD) yr	52.8 ± 9.2	55 ± 8.4	55 ± 6.8	57.4 ± 5.9	0.123
Sex, no. (%)					0.410
Male	40.6 (13)	58.6 (17)	39.3 (11)	50 (17)	
Female	59.4 (19)	41.4 (12)	60.7 (17)	50 (17)	
Race no. (%)					0.731
Afrodescendant	31.2 (10)	44.8 (13)	39.3 (11)	41.2 (14)	
Hispanic	68.7 (22)	55.2 (16)	60.7 (17)	58.8 (20)	
Time of diagnosis, mean (SD) yr	5.3 ± 3.1	7.3 ± 2.9	4.5 ± 2.7	6.6 ± 3.2	**0.020***
Body weight, mean (SD) Kg	83.2 ± 9.9	80.7 ± 8.7	86.4 ± 9.6	83.9 ± 10.4	0.189
Blood pressure, mean (SD) mmHg					
Systolic	149.2 ± 22.9	154.2 ± 21.9	143.1 ± 17.6	146.1 ± 14.6	0.167
Diastolic	86.1 ± 7.4	90.1 ± 6.3	85.5 ± 8.1	86.5 ± 8	0.085
Basal glycemia, mean (SD) mg/dl	170.3 ± 49.5	173.5 ± 23.2	168.7 ± 17	151.6 ± 17.5	**0.019***
HbA1c (%)					
Mean	8 ± 0.5	8.1 ± 0.6	8 ± 0.5	8.3 ± 0.5	0.964
Median	8	7.9	8.1	8.4	

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New Medications for Treatment of Diabetes

ATTD19-0323

IMPACT OF LIXISENATIDE ON PHASE 1 AND PHASE 2 GLUCOSE-STIMULATED INSULIN SECRETION DURING AN INTRAVENOUS GLUCOSE TOLERANCE TEST IN TYPE 2 DIABETES: A MODEL-BASED ASSESSMENT

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Background: Lixisenatide, a receptor agonist of glucagon like peptide 1, has been shown to be safe and efficacious in the treatment of dysglycemia in type 2 diabetes mellitus (T2DM). Furthermore, lixisenatide has been shown to improve the overall insulin response to glycemic challenge such as intravenous glucose tolerance tests (IVGTT); both phase 1 and phase 2 of insulin secretion have shown improvements with lixisenatide injection. While models of glucose stimulated insulin secretion (GSIS) in man are available, the impact of lixisenatide on the mathematical characteristics of GSIS (e.g. gains, time constants, delays) remains to be quantified.

Method: Using data collected in two single-center, double-blind, randomized, placebo-controlled, single-dose crossover studies consisting in an IVGTT with and without a prior lixisenatide injection [Becker et al. Diab Ob Metab 2014], we quantified the impact of lixisenatide on the gains (sensitivity to glucose) of the first and second phase insulin secretion based on frequent measurements of Insulin, C-peptide, and glucose concentrations.

Results: GSIS rate was computed from regularized deconvolution of C-peptide using the C-peptide minimal model, and was then fitted by our GSIS model using glucose concentration as forcing function. Insulin secretion response and model adequacy can be seen in the figure below. GSIS sensitivity was increased

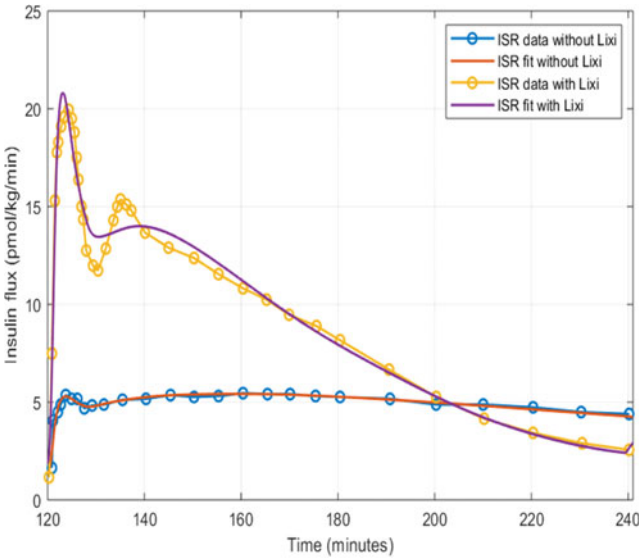

Figure 1: average insulin response to an IVGTT in patients with type 2 diabetes with (yellow circles and line) and without (blue circles and line) lixisenatide; model fits are presented in purple and red respectively.

0.53 ± 0.05 vs 0.08 ± 0.03 and 0.90 ± 0.21 vs 0.29 ± 0.09, for phase 1 and 2 respectively.

Conclusion: Using mathematical modelling of the GSIS in man with lixisenatide vs. placebo, we estimated a 6-fold increase in phase 1 of insulin response to glucose and a 3-fold increase in phase 2.

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New Medications for Treatment of Diabetes

ATTD19-0350

AZADIRACHTA INDICA INHIBITS KEY ENZYME LINKED TO TYPE 2 DIABETES IN VITRO, ABATES OXIDATIVE HEPATIC INJURY AND ENHANCES MUSCLE GLUCOSE UPTAKE EX VIVO

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The progression of secondary complications in type 2 diabetes has been linked to oxidative stress caused by hyperglycemia. Therefore, the control of hyperglycemia is the main target in the treatment of diabetes. The present study investigated the scavenging and ameliorative potentials of different fractions of *Azadirachta indica (A. indica)* ethanol stem bark extract in Fe^{2+}-induced oxidative injury in hepatic tissue as well as their ability to inhibit enzymes linked to diabetes and in enhancing muscle glucose uptake via some *in vitro* and *ex vivo* experimental models. The results revealed that the butanol fraction of the extract showed a significantly higher DPPH scavenging activity than the other fractions while the aqueous fraction showed the highest FRAP activity. All the fractions ameliorated Fe^{2+}-induced oxidative injury in hepatic tissue by significantly reducing the malondialdehyde (MDA) concentration in dose dependent manner. In addition, the activity of catalase and superoxide dimutase (SOD) were significantly improved by the butanol and dichloromethane fractions. Butanol and ethyl acetate fractions showed the highest inhibitory effect on α-glucosidase and α-amylase activities. The fractions also significantly improved glucose uptake in psoas muscle with or without insulin, the butanol fraction showed the highest activity in this regard. Gas chromatography-mass spectroscopy (GC-MS) analysis of the fractions revealed the presence of sistosterol, stigmasterol, campestrol, squalene, nimbiol among others. Molecular docking of some of these compounds with AMP-activated protein kinase (α-AMPK), α-amylase and α-glucosidase showed a positive interaction. These results suggest that the butanol and ethyl acetate fractions may have antidiabetic potentials

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New Medications for Treatment of Diabetes

ATTD19-0352

GLUCOSE RESPONSE TO LOW-DOSE GLUCAGON FOR INSULIN-INDUCED MILD HYPOGLYCEMIA AFTER 12 WEEKS OF HIGH VERSUS LOW CARBOHYDRATE DIET: A RANDOMIZED CROSSOVER STUDY

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Objective: To compare the ability of glucagon to restore plasma glucose (PG) after mild hypoglycemia in patients with type 1 diabetes on high-carbohydrate diet (HCD >250 g/day) and low-carbohydrate diet (LCD <100 g/day).

Research Design And Methods: Individuals with insulin pump-treated type 1 diabetes randomly completed 12 weeks of HCD and 12 weeks of LCD separated by a 12-week washout. After each intervention period, mild hypoglycemia was induced by a subcutaneous insulin bolus in the fasting state. When PG reached 3.9 mmol/L, 100 μg glucagon (GlucaGen®, Novo Nordisk) was given subcutaneously, and PG was measured frequently for 120 min. Friedman's test for repeated measurements was used to compare the difference in incremental peak PG after glucagon injection (primary outcome) between HCD and LCD.

Results: Four participants completed both study visits while two only completed the study visit after LCD. They were in median (IQR) 37.5 (28.5–52.5) years old, had BMI 25.0 (24.5–25.2) kg/m^2, and HbA1c 57.0 (55.0–59.8) mmol/mol. Daily carbohydrate intake during the two periods was 95 (86–97) grams and 254 (184–259) grams, respectively. Compared with HCD, the LCD had a non-inferior incremental PG peak after the glucagon bolus (1.5 (0.6–3.2) vs. 3.0 (2.2–4.2) mmol/L, $p = 0.31$).

Conclusions: No significant difference was observed in the glucose response to low-dose glucagon after 12 weeks of high versus low carbohydrate diet. The previously observed diminished glucose response to low-dose glucagon after one week of low carbohydrate diet may thus be equalized after 12 weeks. However, our study lacks statistical power to draw final conclusions.

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New Medications for Treatment of Diabetes

ATTD19-0394

EMPAGLIFLOZIN AND GABA IMPROVE B-CELL MASS AND GLUCOSE TOLERANCE IN NEW-ONSET TYPE 1 DIABETES

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While the autoimmune character of T1D is being challenged, it is currently recognized that inflammation plays a key role in its development. We hypothesized that glucotoxicity could contribute to β-cell mass destruction through participation to islet inflammation. We evaluated the potential of empagliflozin (EMPA) and GABA respectively to protect β-cell mass against glucotoxicity and to increase β-cell mass after diagnosis of T1D. In a streptozotocin-treated mice model of T1D, empagliflozin and/or GABA were delivered during seven days or three weeks. As compared to untreated T1D mice, EMPA-treated T1D mice

had decreased FFA levels and improved glucose homeostasis during tolerance tests. EMPA-treated T1D mice had a better islet density, with preserved architecture, compared to T1D mice. T1D mice showed islet with immune infiltration whereas EMPA-treated T1D mice did not. Islets from EMPA-treated mice were also less subjected to ER stress and inflammation, as shown by qPCR analysis. Furthermore, parameters of glucose homeostasis and β-cell mass were also improved, as compared to diabetic controls, when T1D mice were treated for 3 weeks with GABA and EMPA. Interestingly, T1D EMPA+GABA mice had higher glucagon levels than T1D mice, without modifications of glucagon area/islet area ratios. In conclusion, empagliflozin and GABA, used in monotherapy, have positive effects on β-cell mass preservation or proliferation through an indirect effect on islet cell inflammation and ER stress. Further research is mandatory to evaluate whether empagliflozin and GABA may be a potential therapeutic target for protection of β-cell mass after new-onset T1D.

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New Medications for Treatment of Diabetes

ATTD19-0466

GLUCAGON-LIKE PEPTIDE-2 IMPROVES GLUCOSE DYSMETABOLISM IN MICE FED A HIGH-FAT DIET BY DECREASING INFLAMMATION

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The gastrointestinal hormone glucagon like peptide-2 (GLP-2) acts through a specific G protein-coupled receptor, the GLP-2 receptor (GLP-R). The peptide is secreted in response to dietary nutrients, particularly carbohydrates and fats. It is known for its ability of influencing gastrointestinal functions and mainly for its trophic effect on the intestinal mucosa. Recent studies suggested that endogenous GLP-2 is dispensable for the regulation of glucose homeostasis under normal conditions, while it can play a beneficial role in mice fed a high-fat diet (HFD), an animal model of human obesity and insulin resistance. However, the molecular mechanisms by which GLP-2 ameliorates glucose homeostasis in HFD mice are not known. Thus, C57BL6/J HFD mice were treated once a day with intraperitoneal (i.p.) injections of Gly^2-GLP-2 (3 and 5 **m**g) or PBS (vehicle control) for four weeks and the mechanisms by which GLP-2 improves glycemic control were investigated. Fasting glucose and insulin, intraperitoneal glucose tolerance, insulin sensitivity, plasma insulin levels after i.p. glucose load, intestinal permeability to FICT-dextran by ussing chamber, plasma levels of cytokines by ELISA and adipose tissue macrophages infiltration by immunohistochemistry were examined. Gly^2-GLP-2-treated mice showed significant increase in glucose tolerance and exogenous insulin sensitivity and reduction in glucose-stimulated plasma insulin, paracellular permeability, TNF-α, IL-1β, IL-6 cytokines level and adipose tissue Mac2-expressing cells in comparison with pair-aged HFD untreated animals. In conclusion, the results of the present study suggest that Gly^2-GLP-2 may produce glucose metabolic benefits in mice with diet-induced obesity by reducing adipose tissue and systemic inflammation.

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New Medications for Treatment of Diabetes

ATTD19-0473

INCREASED TIME IN RANGE WITH SOTAGLIFLOZIN AS ADJUNCT THERAPY TO INSULIN IN ADULTS WITH TYPE 1 DIABETES DEMONSTRATED BY 24-WEEK CONTINUOUS GLUCOSE MONITORING (INTANDEM1, INTANDEM2)

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Sotagliflozin (SOTA) is a dual SGLT1 and SGLT2 inhibitor in development as an adjunct to insulin in T1D. This was a pooled analysis of the inTandem1 (NCT02384941) and inTandem2

CGM Data at Baseline and Week 24			
	Optimized insulin + placebo n=93	Optimized insulin + SOTA 200 mg n=89	Optimized insulin + SOTA 400 mg n=96
Percentage of readings in the range of 70-180 mg/dL (3.9-10.0 mmol/L)			
Baseline mean ± SD	52 ± 14	52 ± 15	51 ± 15
Week 24 mean ± SD	52 ± 15	58 ± 16	64 ± 14
LS mean change from baseline ± SE	-1.3 ± 1.8	+4.1 ± 1.8	+10.5 ± 1.7
Mean change from baseline hr/day*	-0.3 hr/day	+1.0 hr/day	+2.5 hr/day
LS mean difference from placebo (95% CI)	NA	+5.4 (+0.6, +10.1)	+11.7 (+7.1, +16.3)
P-value	NA	0.026	<0.001
Mean difference from placebo hr/day*	NA	+1.3 hr/day	+2.8 hr/day
Mean daily glucose (mg/dL)			
Baseline mean ± SD	175 ± 31	176 ± 33	178 ± 32
Week 24 mean ± SD	176 ± 32	167 ± 32	156 ± 23
LS mean change from baseline ± SE	+2.0 ± 3.6	-5.9 ± 3.6	-16.9 ± 3.4
LS mean difference from placebo (95% CI)	NA	-7.9 (-17.2, +1.3)	-18.9 (-27.9, -9.9)
P-value	NA	0.09	<0.001
MAGE mg/dL			
Baseline mean ± SD	166 ± 35	163 ± 34	158 ± 36
Week 24 mean ± SD	159 ± 32	146 ± 38	131 ± 33
LS mean change from baseline ± SE	-3.0 ± 4.2	-15.7 ± 4.2	-25.1 ± 3.9
LS mean difference from placebo (95% CI)	NA	-12.7 (-23.6, -1.8)	-22.1 (-32.7, -11.5)
P-value	NA	0.022	<0.001

CGM, continuous glucose monitoring; CI, confidence interval; LS, least squares, MAGE; mean amplitude of glucose excursion, NA; not applicable; SD, standard deviation; SE, standard error. Statistical comparisons of each SOTA arm with placebo were pre-planned and performed using a generalized linear model with repeated measures statistics; *Assuming 100% daily CGM data available for analysis, 1.0% of daily CGM time = 0.24 hours.

(NCT02421510) trials in adults with T1D treated with multiple daily insulin injections or pump therapy who were randomized 1:1:1 to placebo, SOTA 200 mg or SOTA 400 mg once daily after 6 weeks of insulin optimization. Of these, 278 patients participated in a blinded continuous glucose monitoring (CGM) sub-study. The primary endpoint of this sub-study was the percentage of time in the target glucose range (70 mg/dL-180 mg/dL). Mean daily glucose and amplitude of all glycemic excursions (MAGE) of <70 and >180 mg/dL were also assessed. Baseline characteristics were similar among groups. Compared with placebo, treatment with SOTA 200 and 400 mg significantly increased the time in range (+1.3 and +2.8 hours/day, respectively) and reduced MAGE at Week 24, while SOTA 400 mg also significantly reduced mean daily glucose (Table). In conclusion, when used adjunctively in T1D, SOTA improved the time in target glucose range compared with placebo, demonstrating efficacy in glycemic control beyond a reduction in HbA_{1c}.

These data were previously presented at the American Diabetes Association 78th scientific sessions, June 22 – 26, 2018, Orlando, Florida.

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New Technologies for Treating Obesity and Preventing Related Diabetes

ATTD19-0081

HEALTH PROMOTION PRIORITIES FOR DIABETES: RESULTS OF A DELPHI STUDY

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Background: Health promotions are interventions designed to enable people increasing control over their own health[1]. But, how to do it? This study aims at understanding healthcare professionals' views regarding how a health promotion targeting people with diabetes should be done.

Methods: A panel of five experts in diabetes and patient education participated in a 3-rounds Delphi study during February-March 2018.

In the first round they made suggestions on how to deliver health promotion contents; and also which diabetes-related topics patients and their families should know more about. In the following two rounds the experts anonymously discussed and ranked all suggested items (from 0 ''The least important'' to 10 ''The most important'') and reached consensus. The study was assessed and declared exempt by the Ethics Committee (REK Sør-Øst, Ref:2017/764C). The Data Protection Officer (Personvernombudet) at the University Hospital of North Norway approved this study (Ref:0720). Further details on the study protocol are published elsewhere[2].

Results: Regarding how to deliver information, the experts agreed that ''making sure that patients understand and use the provided information'' was the most important (average rate = 9), followed by ''using tailored information'' and ''offering information in multiple formats'' (both rated = 8,2). Regarding which topics to include, ''self-management in therapy'' was considered the most relevant topic (rated = 9,6).

The table below lists all suggested items and its rank values.

Discussion: The Delphi method was successful in providing priorities for health promotion interventions on diabetes. Further research should determine the health promotion' interests of people affected with diabetes and their families.

References

1. WHO-2016.http://www.who.int/features/qa/health-promotion/en
2. Gabarron E et al. BMC Health Services Res 2018;18:414

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New Technologies for Treating Obesity and Preventing Related Diabetes

ATTD19-0085

SWEET TALKERS: THE ROLE OF VOICE TECHNOLOGY AND VIRTUAL VOICE ASSISTANTS IN DIABETES MANAGEMENT

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Introduction: Recent advancements in voice technology present a number of novel and compelling strategies for contemporary diabetes management. Virtual voice assistants, such as Apple Siri, Google Assistant, and Amazon Alexa, offer an accessible, engaging, and highly personalized framework for diabetes care that builds on existing digital and phone-based interventions. This review aims to summarize the current state of voice technology in diabetes management, as well as speculate on upcoming and potential applications.

Methods: A rapid literature review was conducted to identify articles evaluating voice technology in diabetes care. Databases searched include PubMed, Scopus, ACM Digital Library, and IEEE Xplore Digital Library.

Findings: A number of trials and proposals have studied the role of voice technology and virtual assistants in diabetes care, with a range of interventions being evaluated. Common features include interactive elements to answer questions and provide personalized diet/exercise recommendations; verbal alerts and reminders to promote adherence; interplay with vital signs, blood sugar level, and foot health monitors; and communication with doctors and other care providers. In addition, application of voice technology has been reported to automatically calculate insulin bolus dosages from spoken descriptions of meals; expedite documentation of diabetic consultations; and enhance clinician collaboration in diabetic surgeries.

Conclusion: Voice technology and virtual assistants show promise in diabetes management, and may facilitate improved education, adherence, risk stratification, and patient-provider communication. While voice-based systems currently represent a niche role in diabetes care, research and practical adoption of the technology are progressing rapidly.

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New Technologies for Treating Obesity and Preventing Related Diabetes

ATTD19-0086

ACCU-CHEK® VIEW: MOTIVATION, INTERACTION AND REACTION UNDER THE MICROSCOPE: WHAT DRIVES THE WEIGHT-REDUCTION SUCCESS?

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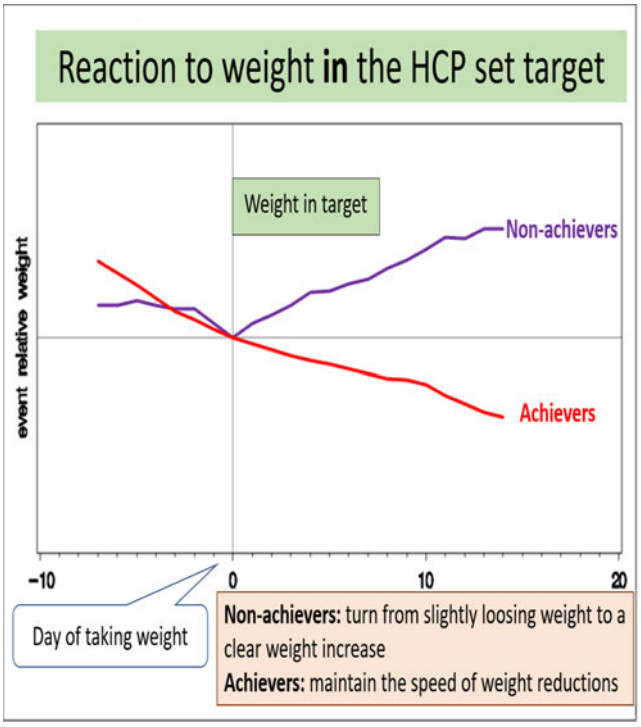
Background: Accu-Chek View (ACV) an app/web-based weight-reduction program featuring key HCP-interaction showed a favorable success-rate for 5%-weight-reduction in metabolic-syndrome patients [1]. The present analysis addresses the temporal dynamics of weight-reduction and importantly investigates how the HCP feedback interacted with the weight-goals. These analyses help understanding why compliant patients remain without success in weight-reduction.

Methods & Results: The analysis of temporal dynamics (novel chart-technique) identified a group of early-achievers (EAs, 5% weight-reduction <90 days, average-stay 8.5 months, 39% of achievers). EAs commenced with severe obesity problems (high BMI and high BP), but compliantly followed an ambitious activity program (mean 8600 steps/d) and finally reduced weight by 8.9% and BMI by 3.4.



Late 5%-achievers (LAs, >90 days) and late completers (non-achiever, >90 days) had similar baseline obesity parameters, likewise in compliance-related conduct-variables. To understand why these subgroups differed by weight-reduction, a detailed event-driven analysis of the HCP-interaction revealed the existence of complex feed-back loops. The differing response of LAs and LCs to on-target/off-target events provided the crucial hint: for on-target events LAs kept the weight-reduction speed whereas LCs showed subsequently weight-increase (Fig). Response in steps: LAs increased steps upon events markedly more than LCs. Interaction effects for BP and BG will be presented.

Conclusion: The closer analysis underlines that Accu-Chek View fosters quick success for patients with high obesity burden and high motivation for change. Patients with high program-perseverance could only succeed, when they kept a positive stance on the interaction events. This opens for new options to even better the Accu-Chek View success rate.

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New Technologies for Treating Obesity and Preventing Related Diabetes

ATTD19-0171

ESTIMATION OF CYTOKINE STATUS OF PATIENTS WITH METABOLIC SYNDROME

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Introduction: The aim of the study was to estimate cytokine profile in patients with metabolic syndrome to search for prognostic biomarkers of cardiovascular pathology.

Methods: 710 patients: 486 men and 224 women aged 19 to 65 were participated in the screening included waist circumference, arterial blood pressure, fasting blood glucose and cholesterol performed by state standard. First group: 145 patients with metabolic syndrome. Second group: 85 patients with isolated abdominal obesity. Third group: 13 patients with arterial hypertension and hyperglycemia without abdominal obesity. Cytokines leptin, TNF, CXCL16, FABP3, FABP4, PLGF, HGF, VEGF, sFASL were measured using multiplex cytokine assay.Results. Significant differences in the level of leptin (2 = 17,137, df = 2, p = 0,001) were revealed in the groups: Me of leptin in first group was 42859.61 (44513.43, 56255.95) pg/ml, whereas in second group Me was only 26210.35 (24563.49, 37371.61) pg/ml. In third group Me of leptin was 13507.43 (2018.12; 54685.41) pg/ml. FABP4 (2 = 7,0,27, df = 2, p = 0,03) was different in the groups 1 to 3 respectively: Me 17433.10 (24626.97, 34734.15) pg/ml,

Me 17077.50 (20421.11, 37066.67) pg/ml, Me 16438.45 (7957.33, 25037.47) pg/ml. Me of HGF (8,162, df = 2, p = 0.017) also was significantly different between the groups 1 to 3: Me 329.37 (331.33, 396.50) pg/ml, Me 248.28 (251.99, 357.22) pg/ml, Me 307.81 (231.94, 390.41) pg/ml, respectively. There were not found significant differences for other cytokines.

Discussion: Increased leptin and FABP4 in respondents with metabolic syndrome indicate on leptin resistance and endothelial dysfunction. HGF is associated with hypertension and hyperglycemia.

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New Technologies for Treating Obesity and Preventing Related Diabetes

ATTD19-0174

SOCIAL MEDIA USE IN AN OBESITY INTERVENTION-RESULTS FROM THE PREDIRCAM2 STUDY

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Background: A multi-center randomized-trial was designed to test telemedicine treatment for obesity supported by PREDIRCAM2 web-platform (NCT01919372). The telematic intervention included the optional use of a private group in the social media network of Facebook®. This post-hoc analysis compares the outcomes of participants who joined this private group versus those who did not.

Methods: 183 participants were included in the study, 91 were randomly allocated to receive the telematic intervention and 92 to a control non-telematic intervention group. To join the private group an invitation from the research team was required. The research team continuously supervised the group. A registered dietitian posted health-related content on a weekly basis and answered to the participant's posts and comments on a daily basis.

Results: Twenty-two participants who joined the social-media private group completed the 12-month follow-up. Satisfaction evaluations revealed 63.6% of these participants considered the social media group was a motivator for behaviour change. The most frequently reported reason for not joining the group was not being a previous Facebook® user(65.4%). A larger proportion of participants who joined the private social media group lost at least 5% body weight at 9-months follow-up compared to those who did not join (80% vs. 46.5%, p = 0.0069). At 12-months follow-up this proportion difference remained although it was not statistically significant (63.6% vs. 47.6%, p = 0.181). No statistically significant differences between groups were found for HbA1c or lipids.

Conclusions: Social media guided by health-care professionals can offer networking solutions to be applied in life-style modification therapy for obesity treatment.

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New Technologies for Treating Obesity and Preventing Related Diabetes

ATTD19-0185

OURPATH - A NEW DIGITAL TECHNOLOGY FOR LIFESTYLE CHANGE IN OBESE AND TYPE 2 DIABETES POPULATIONS; A SERVICE EVALUATION OF REAL-WORLD DATA

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Background: The purpose of this service evaluation was to analyse the efficacy of OurPath, a UK-based digital lifestyle change programme, between commercial enrolments (self-paid) and NHS referrals (free to the user). Male uptake rates were further analysed, as men have historically been underrepresented in traditional commercial weight-loss programmes.

Method: Participants were either self-referred (commercial) or referred by a GP (NHS) to the digital behaviour change programme OurPath. OurPath combines a private online social network, daily structured educational content, health coaching, digital weighing scales, and an activity tracker. Participants underwent a core 3-month intensive lifestyle change intervention, with follow up data obtained after 3 and 6 months.

Results: For individuals with 3-month outcome data, a higher proportion of males took part in the programme following NHS referral (41% male; n = 342) compared with the commercial programme (12% male, n = 694). Participants had a mean starting BMI of 34kg/m^2 (commercial = 35 kg/m^2 ± SD 7.5; NHS = 34 kg/m^2 ± SD 6.0). Clinically significant weight loss at 3 months was achieved for both the commercial (−7.1%; p < 0.01) and NHS (−7.5%; p < 0.01) populations. Users with available 6-month data showed a further increased weight loss from baseline (commercial = −8.6% n = 186; NHS = −9.2%, n = 155).

Conclusion: With ongoing challenges of male attendance at traditional weight-loss programmes, a digitally delivered intervention may offer an attractive and scalable solution. This service evaluation demonstrates both a clinically significant mean weight loss for all participants at 3 and 6 months, as well a significantly higher male uptake ratio when referred by an NHS GP.

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New Technologies for Treating Obesity and Preventing Related Diabetes

ATTD19-0213

GLYCEMIA NORMALIZATION IN PATIENTS WITH OBESITY AND TYPE 2 DIABETES MELLITUS USING TECHNOLOGIES PROVIDING MAXIMUM INCRETIN EFFECT (BILIOPANCREATIC DIVERSION VS LIRAGLUTIDE 3.0 MG)

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Background and Aims: To compare glucose-lowering and weight reduction capacity of biliopancreatic diversion (BPD) vs GLP-1 agonist liraglutide 3.0 mg (models of maximum incretin effect) for 16 weeks.

Method: 31 patients with type 2 diabetes and long history (≥10 years) of obesity were divided into 2 groups: BPD-group (n = 13) and LIRA-group (n = 18), where liraglutide 3.0 mg in dose-escalation manner was added to baseline glucose-lowering therapy. Anthropometric parameters, mixed meal test, HbA1c and insulin resistance (IR) by hyperinsulinemic euglycemic clamp (M-value) and HOMA-IR were measured before and 16 weeks after the intervention. With the stabilization of glycemia (≤6.5 mmol/l at fasting state, ≤8 mmol/l postprandial) the initial glucose-lowering therapy was canceled.

Results: Both BPD and liraglutide 3.0 mg provided target HbA1c in 16 weeks (Table 1). BPD led to elimination of glucose-lowering therapy in 84.6% patients due to a more significant weight reduction and decrease in IR. In LIRA-group previous glucose-lowering therapy was cancelled in 72.2% patients, mainly receiving baseline mono- and two-component therapy. The most significant difference between interventions was achieved in BMI (Δ–7.13 kg in BPD vs Δ–1.81 kg in Lira, $p < 0.05$) and M-value (Δ2.71 in BPD vs Δ0.36 in Lira, $p < 0.05$).

Conclusion: BPD is more effective in reducing body weight but similar in glucose-lowering effect comparing with adding liraglutide 3.0 mg to the initial glucose-lowering therapy in patients with obesity and type 2 diabetes. Liraglutide 3.0 mg glucose-lowering effect is more prominent in patients initially receiving mono- and two-component therapy.

Support: Grant No. 17-15-01435 Russian Science Foundation.

Table 1. Anthropometric, metabolic parameters and glucose-lowering therapy before and 16 weeks after intervention

	BPD (n=13)		Liraglutide (n=18)	
	Baseline	16 weeks	Baseline	16 weeks
Type 2 DM duration (yrs)	7,50 [5.00; 9.50]		6.90 [4.50; 8.90]	
Glucose-lowering therapy (%)				
MET	84.6	15.4	61.1	22.2
SU	46.2	0	50	0
iDPP-4	61.5	7.7	22.2	0
INS	14.4	0	16.6	0
SGLT-2i	30.7	0	11.1	5.6
BMI (kg/m^2)	39.3 [34.93; 43.45]	30.72 [28.65; 36.63]*	41.0 [34.9; 44.9]	37.42 [33.1; 41.8]*
HOMA-IR	10.19 [5.13; 14.61]	3.2 [1.27; 4.43]*	12.9 [6.6; 31.0]	6.42 [3.80; 10.73]*
M-value (mg/kg/min)	1.34 [0.97; 1.97]	4.32 [3.09; 5.24]*	2.13 [1.18; 2.69]	2.38 [1.23; 3.07]*
HbA1c (%)	8.1 [7.35; 9.0]	6.1 [5.9; 6.6]*	7.70 [7.42; 8.85]	6.3 [5.85; 7.25]*
Fasting blood glucose (mmol/l)	9.85 [7.98; 13.37]	6.36 [5.86; 7.12]*	9.78 [7.8; 11.6]	6.3 [5.38; 6.72]*
2h blood glucose (mmol/l)	13.77 [11.64; 16.65]	6.59 [5.58; 8.30]*	12.05 [9.84; 14.57]	6.48 [5.42; 9.25]*

*- p<0.05 baseline vs 16 weeks after intervention

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New Technologies for Treating Obesity and Preventing Related Diabetes

ATTD19-0297

APP ENGAGEMENT AND WEIGHT LOSS IN A MOBILE HEALTH STUDY (MDIAB)

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Purpose: The purpose of this study was to evaluate the association of app engagement with change in weight and BMI as part of the mobile health technology for the prevention of type 2 diabetes (mDiab) trial.

Methods: The mDiab app included 12 weeks of video lessons administered to 267 obese participants who received the app as part of the intervention group. Additionally, participants received coach calls who summarized the weekly lessons and presented feedback on their tracked diet, physical activity and weight loss behaviours. App engagement was divided into four groups - no engagement, only videos, only coach calls, video and coach calls.

Results: Within a 3-4 month period, participants who viewed the video lessons showed a significant decrease in weight and obesity. Those who attended coach calls also showed a similar trend but this did not reach statistical significance. The participants who both attended the calls and saw the videos showed a significant decrease in weight and BMI however there was no synergistic effect (Table 1).

Table 1: Association of app engagement with weight loss and obesity

Dependent variable: Engagement	Difference in weight	Difference in BMI
Reference category: Participants who did not engage		
Participants who attended only coach calls	-0.897	-0.302
	[-2.14,0.35]	[-0.76,0.16]
Participants who viewed only videos	-2.410**	-0.800*

Dependent variable: Engagement	Difference in weight	Difference in BMI
	[-4.10,-0.72]	[-1.43,-0.17]
Participants who did both	-1.282*	-0.468*
	[-2.47,-0.10]	[-0.91,-0.03]
* p<0.05, ** p<0.01, *** p<0.001		

Conclusions: Engagement with the mDiab app resulted in decreased weight and BMI with the strongest effect seen for the video lessons.

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New Technologies for Treating Obesity and Preventing Related Diabetes

ATTD19-0393

RESPONDER ANALYSIS APPROACH FOR ACCU-CHEK® VIEW DATA: TEMPORAL DYNAMICS, HCP INTERACTION - HOW TO UNDERSTAND INDUCED FEEDBACK LOOPS

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Background: The app/web-based weight-reduction program ACCU-CHEK VIEW showed a favorable success-rate in metabolic-syndrome patients [1]. Interaction with HCPs through personalized goal setting and messages induced complex feedback loops bearing upon the temporal dynamics of success and failure. The present analysis presents approaches and results for disentangling the behavioral patterns.

Methods & Results: A novel chart technique helped to identify subgroups with distinct baseline characteristics and specific weight-reduction dynamics. Detailed HCP-interaction event-driven analysis revealed that a positive stance to both in-target and off-target events was key for success. Graphs and tables will present the spectrum of identifiable subgroups, reaching from early program drop-outs to highly compliant unsuccessful patients contrasted to those with early or late achieved and maintained weight reduction.

Conclusion: The analysis revealed a plausible composition of the population of metabolic syndrome patients. The analysis of interactions may open up the road for further improving success rates by focusing in detail on feedback loops for compliant patients.

[1] J.H.Arens, W.Hauth, J.Weissmann(2018): ''Novel App- and Web-Supported Diabetes Prevention Program to Promote Weight Reduction, Physical Activity, and a Healthier Lifestyle: Observation of the Clinical Application'': JDST(Vol 12) pp 831-838.

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New Technologies for Treating Obesity and Preventing Related Diabetes

ATTD19-0405

UTILISING A DIGITAL LIFESTYLE INTERVENTION TO IMPROVE WEIGHT AND GLYCAEMIC CONTROL IN PEOPLE LIVING WITH TYPE 2 DIABETES; A SERVICE EVALUATION OF REAL-WORLD DATA

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Background: The purpose of this study was to evaluate the real-world efficacy of OurPath, a digital lifestyle change programme, aimed at improving weight and HbA1c levels for people living with type 2 diabetes (T2D).

Method: Participants, who had already been diagnosed with T2D, were recruited by practice and specialist nurses working in the NHS. Each participant was referred to OurPath to take part in a 3-month digital lifestyle intervention that integrates tracking technology with daily education on nutrition, exercise, mental wellbeing, peer group support and personalised health-coaching from a registered dietitian. The study was funded by the Solent Diabetes Association.

Results: 79% of participants enrolled on OurPath following referral (n = 190), and a further 79% completed the 3-month programme (n = 150); data is reported for these completed participants (n = 119). Participants had a mean BMI of 35.1 kg/m^2 (+- SD 6.7) at baseline. Participants with 3-month outcomes data achieved a clinically significant mean weight loss (-6.6%, $p < 0.01$, n = 112) and HbA1c reduction (13.6mmol/mol, $p < 0.01$, n = 50). 40% of participants with 3-month HbA1c data achieved a HbA1c level of <48mmol/mol. Participants with available 6-month weight data showed a further decrease in mean weight (-8.3%, $p = 0.02$, n = 51).

Conclusions: Participants referred to the OurPath programme achieved both clinically significant mean weight loss at 3 and 6 months, and also achieved a clinically significant mean reduction in HbA1c. As a result, digital platforms like OurPath could offer an effective and scalable solution to the T2D epidemic.

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Other

ATTD19-0095

STUDY DESIGN FOR AN OBJECTIVE ASSESSMENT OF MEALTIME BOLUS INSULIN BEHAVIOUR AND ASSOCIATED FACTORS

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Background and Aims: Current diabetes management using basal/bolus insulin regimens requires a high level of patient engagement. One-third of patients with type 1 diabetes (T1D) or type 2 diabetes (T2D) reported insulin omission/nonadherence at least once in the past month. We aimed to objectively estimate the average number of days per month with a missed bolus dose in patients with T1D or T2D using continuous glucose monitoring (CGM) and a connected insulin pen.

Methods: This was a 12-week, multicenter, single-arm, outpatient, exploratory study with 2 study periods in subjects with T1D (age ≥21 to ≤65 years) or T2D (age ≥35 to ≤65 years); 68 subjects and 50 completers were planned. Subjects followed a prescribed insulin regimen using insulin lispro 100 U/mL injected via an investigational pen (which captured bolus insulin doses), and glucose was monitored via a commercially available CGM device (blinded during Study Period 1 and unblinded during Study Period 2). Patient reported outcomes (PRO) evaluations assessed potential behaviours related to short-term glycaemic control.

Results: Expected outcomes include average missed or suboptimal bolus doses (MSBD) per day and month, percent time in range (blood glucose >3.9 and ≤10 mmol/L), and PRO results.

Conclusions: Using a connected insulin pen and a CGM device will allow for an assessment of MSBD, subject characteristics, and the relationship of MSBD to short-term glycaemic control. The MSBD metric may be important in the management of insulin pen users.

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Other

ATTD19-0096

A PRAGMATIC RANDOMIZED CONTROL TRIAL EVALUATES ONE DROP WITH INHALABLE VS. INJECTABLE INSULIN

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Objective: Digital therapeutics and innovative pharmaceuticals may deliver better outcomes together than alone. We conducted a pragmatic RCT to assess One Drop's digital therapeutics platform ([OD] mobile app, glucometer, and coaching) with Afrezza inhalable insulin vs. OD and injectable insulin.

Methods: We randomized 265 adults with type 2 diabetes (T2D) to one of two interventions. Chi-square and Mann-Whitney U tests assessed baseline group differences. Multiple imputation by group corrected for missing data. ANCOVA intent-to-treat (ITT) and per protocol (PP) models tested effects on 3-month A1c.

Results: The enrolled sample (n = 119) was 50 ± 11 years old, 53% female, 61% White with T2D for 14.5 ± 8 years and an A1c 9.3% ± 1.6%. Age and days between A1c differed by group and were covariates. Both groups experienced significant A1c improvements ($p < .008$-04). A significant group by baseline A1c interaction required examining effects by baseline A1c levels. In ITT, a lower baseline A1c was associated with a better effect from OD and Afrezza than OD and injectable insulin. In PP (n = 80), 3-month A1c trended lower in OD and Afrezza ($Mean_{Diff}$ -.47% to -.73%; $p < .09$ to .19) vs. OD and injectable insulin.

Conclusion: OD with Afrezza was associated with −.94% absolute A1c improvement; an absolute −.52% better A1c than OD with injectable insulin and an absolute −.39% better A1c than Afrezza without OD (i.e., based on a −.55% A1c effect). While speed and external validity are trial strengths, power to identify group differences was limited. Multiple methods are needed to fully understand the effects of digital therapeutics with pharmaceuticals.

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Other

ATTD19-0142

PREVENTION OF SEVERE HYPOGLYCEMIA BY USE OF THE ELECTROENCEPHALOGRAPHY (EEG) BASED ALARM DEVICE, HYPOSAFE SUBQ

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Objective: Hypoglycemia is associated with characteristic changes of the electrical activity of the brain with highly varying glucose thresholds for the onset of these changes. The objective of our current study is to test the subcutaneous electroencephalography (EEG)-based alarm device, hyposafe™ SubQ using the brain as a biosensor to prevent severe hypoglycemia.

Methods: 8 patients with type 1 diabetes and impaired hypoglycemia awareness were included in a 3-month pilot study. EEG was recorded continuously and analyzed real-time using an automated EEG algorithm. Daily use of the device was recorded.

Results: 7 patients completed the study with a total of 659 recording days. Median daily use was 22.3 hours (range: 19.1–23.0) for 97 days (range: 60–109). One patient withdrew due to discomfort. The hyposafe™ SubQ detected a total of 16 events of hypoglycemia-related EEG changes in 5 patients, all during daytime. The alarm was triggered at a median blood glucose level of 2.4 mmol/L (range: 1.9–3.0). In all cases, the patients were able to take preventive actions to avoid severe hypoglycemia. No false negatives were reported, as no patients reported a need for external assistance for recovery. The patients experienced a median false detection rate of 2.9/week (range: 0.3–8.9) during daytime and 0.2/week (range: 0.0–2.0) during nighttime.

Conclusions: 7 patients used the hyposafe™ SubQ over a 3-month period with high compliance. Hypoglycemia-related EEG changes were detected in time for the patients to take preventive action and avoid severe hypoglycemia. No false negative and few false positives were detected, especially at night.

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Other

ATTD19-0150

LIPOPEROXIDATION IS NEGATIVELY ASSOCIATED WITH VASCULAR FUNCTION IN T1DM BUT NOT WITH GLUCOSE CONTROL OR VARIABILITY

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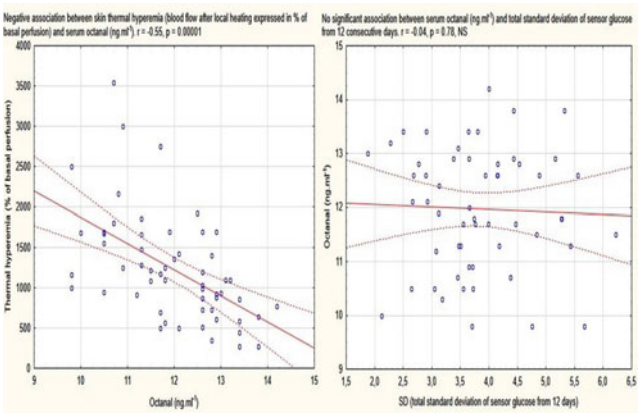
Background: Oxidative stress contributes to vascular complications in diabetes and may be induced by glucose variability (GV). Increased GV is typical for Type 1 diabetes (T1DM) and it would be useful to identify patients at risk for vascular complications using biomarkers and/or tests of vascular function. To contribute to the development of such test(s), we evaluated skin microvascular function, glucose variability and reactive aldehydes. Reactive aldehydes originate in lipoperoxidation and reflect the levels of oxidative stress.

Methods: We studied 56 T1DM patients (age 32 ± 8 yrs, HbA1c 62 ± 12 mM/M or 7.8 ± 1.5% DCCT, DM duration 14 ± 6



yrs). Reactive aldehydes with C-chain length from 6 to 12 (hexanal to dodecanal) and malonyl dialdehyde (MDA) were measured by mass spectrometry. Mean blood glucose (MBG) and GV (SD, CV, MAGE, CONGA) was calculated from 12 days of masked continuous glucose monitoring. Skin microvascular reactivity (MVR) was measured by laser-Doppler during occlusion (PORH) and heating (TH).

Results: MVR during PORH was negatively associated with octanal and MDA ($p = 0.0003$ and $p = 0.017$, respectively). Similarly, TH was negatively associated with octanal, nonanal, decanal and MDA ($p < 0.0001$, $p = 0.021$, $p = 0.048$ and $p = 0.001$, respectively). No associations were found between reactive aldehydes and glucose control or variability. MVR was not associated with glucose parameters as well.

Conclusion: In our cross-sectional observational study, higher levels of reactive aldehydes were associated with impaired skin MVR. MBG, HbA1c and GV were not associated with lipid peroxidation or MVR. Other than simple glycemic mechanisms are probably more important in the process of lipoperoxidation and vascular damage in T1DM.

Support: AZV 15-26705A.

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Other

ATTD19-0159

DPP-4 INHIBITORS (LINAGLIPTIN) IMPACT ON KLOTHO SERUM LEVEL IN PATIENTS WITH TYPE 2 DIABETES

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Cardiovascular complications are the main cause of death in type 2 diabetes (T2D) patients. The development of early cardiovascular risk markers and search for the ways of risk elimination is an urgent public heath priority. Klotho protein level appears the earliest marker of cardiovascular and renal lesion in T2D patients.

We compared the effect of linagliptin on Klotho serum level in T2D patients in a prospective, randomized, double-blinded, placebo-controlled study.

Materials and methods: The study involved 42 T2D patients with nephropathy (microalbuminuria, GFR ≥60 ml/min). The study group (n = 22) received 5 mg a day of linagliptin (DPP-4 inhibitor). The control group (n = 20) received placebo and other types of hypoglycemic drugs (except SGLT2 inhibitors). The follow-up period was 3 years. We measured GFR level and cardiovascular markers: Klotho serum level (ELISA), Echo data, sphygmography («Sphygmocor», Australia) at the baseline and at the end of follow-up period.

Results: We found significant difference between the groups in: Klotho level ($p = 0.0027$), GFR ($p = 0.0412$), heart valves calcification ($p = 0.043$), vessel augmentation (stiffness) index ($p = 0.0011$), LVMMI ($p = 0{,}0048$), creatinine/microalbuminuria ratio ($p = 0.013$).

Conclusion: The long term DPP-4 inhibitors (linagliptin) nephroprotective effect in the study group can be associated with the drug impact on Klotho level resulting in cardiovascular risk decrease (lower cardiovascular calcification and left ventricular hypertrophy) compared to the control group.

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Other

ATTD19-0160

EFFECT OF OSTHOLE ON ADVANCED GLYCATION END PRODUCTS-INDUCED RENAL TUBULAR HYPERTROPHY AND ROLE OF KLOTHO IN ITS MECHANISM OF ACTION

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Background and Aims: Osthole has been widely reported to have pharmacological activities such as anti-cancer, anti-inflammation and anti-hyperlipidemic effects. Klotho was identified as an anti-senescence protein in a variety of tissues. Loss of klotho has been associated with chronic kidney disease. In the current study, we undertook to investigate the molecular mechanisms of osthole and exogenous klotho against AGE-induced renal tubular hypertrophy.

Method: Cell viability was elucidated by MTT assay. Protein expression was measured by Western blotting. mRNA level was analyzed by real-time PCR. Cellular hypertrophy growth was evaluated by hypertrophy index. Relative cell size was detected by flow cytometry.

Results: We found that raising the ambient AGE concentration causes a dose-dependent decrease in klotho synthesis. Osthole significantly increased AGE-inhibited klotho mRNA and protein expression. Osthole and exogenous klotho treatments significantly attenuated AGE-induced Janus kinase 2 (JAK2)-signal transducers and activators of transcription 1 (STAT1) and STAT3 activation. Moreover, protein levels of suppressor of cytokine signaling 1 (SOCS1) and SOCS3 were augmented by osthole and exogenous klotho. The abilities of osthole and exogenous klotho to reverse AGE-induced cellular hypertrophy were verified by the observation that osthole and exogenous klotho inhibited $p21^{Waf1/Cip1}$/collagen IV/RAGE expression, total protein content, and cell size.

Conclusion: We found that osthole attenuated AGE-induced renal tubular hypertrophy via induction of klotho expression and

suppression of the JAK2-STAT1/STAT3 signaling. These results also showed that klotho might be used as a unique molecular target for the treatment of diabetic nephropathy.

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Other

ATTD19-0162

ARE FOUR TIMES DAILY INJECTION OF INSULIN USING A SMART BLOOD GLUCOSE METER AS EFFECTIVE AS INSULIN PUMP THERAPY IN PEDIATRIC PATIENTS WITH DIABETES?

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Introduction: In the Netherlands the healthcare cost are increasing and cost efficiency decisions about effective use of advanced and generally more expensive devices is increasingly needed. Therefore, the question arises whether four times daily injections in combination smart glucose meter (meter with bolus advice function similar to the boluswizard) is as effective as insulin pump therapy in pediatric patients with diabetes in the clinical practice.

Objective: The objective of this study was to evaluate whether patients on a four times daily regime with a smart glucose meter have a comparable HbA1c compared with insulin pump users.

Methods: Single center retrospective observational cross-sectional database analysis

Results: 175 patients in the clinic were evaluated of which 48% used an insulin pump, 42% used a smart meter and (9%) used a basic blood glucose meter. Initial results show that the average HbA1c of patients on an insulin pump was 65.8 mmol/mol (SD = 10.0). The HbA1c of patients on MDI and a smart meter the average HbA1c was also 65.8 mmol/mol (SD = 14.8). Considering a 5 mmol/mol difference in HbA1c as clinically relevant it is shown with a two one-sided test procedure that the groups are indeed equal ($p < 0.01$). Further analysis will be performed to control for potential confounders.

Conclusion: This database study has shown that with 4 daily injections of insulin with a smart meter can achieve equal results compared to pump therapies.

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Other

ATTD19-0176

ADJUST: IMPACT OF BLINDED CONTINUOUS GLUCOSE MONITORING USE ON CLINICAL DECISION AND GLYCEMIC CONTROL OF PEOPLE WITH TYPE 2 DIABETES UNDERGOING INSULIN THERAPY

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Introduction: In people with type 2 diabetes (T2D) without adequate glycemic control for an extended period of time, blinded continuous glucose monitoring (CGM) can provide detailed information about daily glycemic profile, facilitating therapeutic support.

Material and Methods: We recruited 102 individuals with T2D undergoing insulin therapy, aged less than 66 years old and HbA1c ≥7.5%. Participants performed a 7 days blinded CGM (iPro2) each four month, for one year. Retrospective data was also collected. Laboratory analysis, anthropometric measurements, CGM interpretation, and GHQ and DTSQ questionnaires were performed.

Results: 90 participants, aged 56.9 ± 0.8 years, diabetes duration of 16.9 ± 0.8 years and BMI of 31.0 ± 0.5 kg/m2 completed the protocol.

HbA1c at study enrollment was 9.4 ± 0.1% (worse than clinical records showed from one year before (9.1 ± 0.1%, $p = 0.003$)). With the intervention, a decrease in HbA1c was achieved already at 4 months (8.4 ± 0.1%, $p < 0.0001$), and maintained by one year (8.1 ± 0.1%, $p < 0.0001$). Successive blinded CGM enabled therapeutic changes to be translated into more targeted support.

Furthermore, we observed a significant increase in time-in-range (70-140 mg/dL; 25.4 ± 1.8 vs 32.6 ± 1.9%, $p < 0.01$), especially due to lower exposure time above 140mg/dL (73.2 ± 2.0 vs 66.1 ± 2.0% $p < 0.05$) with no difference in exposure time below 70mg/dL (1.4 ± 0.3 vs 1.0 ± 0.2% $p = 0.6$).

After one year, there was an increase in self-reported diabetes treatment satisfaction ($p < 0,05$) and a decrease in perceived hyperglycemia exposure ($p < 0,001$).

Discussion: In people with T2D and worsening metabolic control, clinical decision based on the interpretation of blinded CGM provided a significant improvement in clinical outcomes, effective shared decision-making, and patient satisfaction with treatment.

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Other

ATTD19-0199

PLASTIC PLANT POLLUTION AND PREVALENCE OF PRE-DIABETES AND TYPE 2 DIABETES MELLITUS

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Worldwide, millions of people are working daily in a dusty environment in various occupational allied industries. Plastic production is markedly increasing and its pollution is an emerging global health concern. This study aimed to investigate the occurrence of pre-diabetes and type 2 diabetes mellitus among non-smoking plastic industry workers. 278 non-smoking plastic industry workers were recruited. The mean age for the participants was 38.03 ± 10.86 years and Body Mass Index was 25.52 ± 3.15(kg/m)^2. The plastic industry workers had been exposed to plastic plant pollution for about 8 hours daily, six days in a week. Subjects with HbA1c less than 5.7% were considered non diabetics; HbA1c 5.7%-6.4% were pre-diabetics; and

subjects with HbA1c more than 6.4% were considered diabetics. In plastic industry workers the prevalence of pre-diabetes was 176 (63.30%) and diabetes mellitus was 66 (23.74%) however, 36 (12.95%) plastic plant workers were normal. The prevalence of pre-diabetes and type 2 diabetes mellitus among plastic industry workers was significantly increased with duration of working exposure in plastic industry.

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Other

ATTD19-0203

WHOLE-EXOME SEQUENCING FOR MONOGENIC DIABETES IN RUSSIAN CHILDREN REVEALS HIGH FREQUENCY OF GENETIC VARIANTS IN MODY-RELATED AND UNRELATED GENES

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Using whole-exome sequencing, we identified the frequency and the spectrum of genetic variants causative of monogenic diabetes in 93 Russian children with non-type 1 diabetes mellitus. Genetic variants were screened in a total of 35 genes: 13 genes causative of MODY (*HNF4A*(MODY1), *GCK*(MODY2), *HNF1A*(MODY3), *PDX1*(MODY4), *HNF1B*(MODY5), *NEUROD1*(MODY6), *KLF11*(MODY7), *CEL*(MODY8), *PAX4*(MODY9), *INS*(MODY10), *BLK*(MODY11), *ABCC8*(MODY12), *KCNJ11*(MODY13)), and 22 genes causative of transient or permanent neonatal diabetes, including the ones related to specific syndromes (*EIF2AK3, RFX6, WFS1, ZFP57, FOXP3, AKT2, PPARG, APPL1, PTF1A, GATA4, GATA6, GLIS3, IER3IP1, LMNA, NEUROG3, PAX6, PLAGL1, SLC19A2, SLC2A2, SH2B1, SERPINB4, MADD*). Overall, 50 out of 93 patients (55 %) had genetic variants in the target genes. Of all 50 positive patients, 42 (84 %) had genetic variants in MODY-related genes. The majority of these patients – 35 out of 42 – had genetic variants in *GCK* (MODY2). We analyzed the relationship of the detected genetic variants to the patients' diabetic phenotypes. Among 42 detected genetic variants, 25 have been reported previously to be linked to monogenic diabetes and 17 were novel ones. Thus, our results together with the results of other studies show that a higher mutation detection rate may be achieved by increasing number of genes tested. In this regard, one more advantage of WES should be mentioned: DNA sequencing data may be easily stored for further analysis of newly discovered candidate genes. Ethnic differences play an important role in determining epidemiology of monogenic diabetes, especially of MODY.

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Other

ATTD19-0218

ASSESSMENT OF LONGEVITY OF THE COATED CONVATEC INFUSION SET WITH LANTERN TECHNOLOGY

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Objective: Current insulin infusion sets are approved for 2-3 days of wear; however, glucose sensors are approved for 10 days of wear. A commonly reported reason for discontinuing use of diabetes technology within 1 year is not wanting to wear devices on two sites of the body. Any attempt to create a combined glucose sensor and infusion set for closed-loop control requires a set with greater longevity. The coated ConvaTec Infusion Set with Lantern Technology is a new infusion set with multiple slits intended to reduce foreign body response and occlusion from bending or kinking, thereby enabling greater longevity.

Research Design And Methods: A pilot safety and extended wear tolerability study will be performed at Stanford University. The study will enroll 24 adult subjects on tethered insulin pump therapy using insulin aspart or lispro. Each participant will place the set and wear it for 10 days or until set failure to establish a maximum length of infusion set wear when 80% of sets are still functional (excluding accidental ''pull-outs'').

Results: Infusion set failures are based on: (1) Presence of serum ketones with hyperglycemia; (2) Unexplained hyperglycemia, unresolved with correction dose; (3) Signs of infection at the infusion site; (4) Pump occlusion alarm; and (5) Adhesive failure.

Conclusions: The duration of wear established in this pilot study will be used to perform a masked, randomized controlled crossover study comparing time to failure of the coated ConvaTec Infusion Set with Lantern Technology against commercially available infusion sets without coating and slits.

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Other

ATTD19-0223

NOCTURNAL HYPOGLYCEMIA IN DIABETIC CHILDREN: EFFECT ON AUTONOMIC HEART RATE REGULATION

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Background: Hypoglycemia is the most common complication in insulin treated diabetes. Nocturnal hypoglycemia can be fatal in rare cases, and there is evidence, that sympathoadrenal stimulation contributes to cardiac arrhythmia. On the other hand, disturbed autonomic function has already been seen in children with type 1 diabetes and is associated with hypoglycemia unawareness.

Objective: To determine heart rate variability (HRV) in children with type 1 diabetes during episodes of nocturnal hypoglycemia.

Patients and Methods: In 25 (11f, 14m) children with type 1 diabetes (mean age 13.5 y, range 8.1–17.5) continuous glucose monitoring was performed for 5 days, and simultaneously, holter ECG (Schiller) was recorded during each night. HRV parameters (RMSSD, LF and HF = low and high frequency component) were analyzed for different 15min intervals during nocturnal hypoglycemia (< 3.7mmol/l): before hypoglycemia, at the start of hypoglycemia, before nadir, after nadir, at the end of hypoglycemia and after hypoglycemia.

Results: 41 episodes of nocturnal hypoglycemia were observed, 33 with ECG recording. HRV changed significantly during these episodes: RMSSD and HF (both representing parasympathetic activity) decreased continuously from the time interval before hypoglycemia to the time interval after nadir, while LF (representing sympathetic activity) and heart rate increased in these intervals ($p = 0.04$).

Conclusion: We could document short term and immediate changes in HRV during episodes of nocturnal hypoglycemia. As these represent reactions in the autonomic modulation, we could demonstrate intact sympathoadrenal counterregulation to hypoglycemia in our patients. HRV reactions to hypoglycemia occur prompt and therefore may be utile for hypoglycemia detection in the future.

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Other

ATTD19-0246

PAN-EUROPEAN ECONOMIC ANALYSIS TO IDENTIFY POTENTIAL COST SAVINGS FOR THE HEALTH CARE SYSTEMS AS A RESULTS OF INTEGRATING TELEMEDICINE INTO DIABETES MANAGEMENT

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Background and aims: Self-monitoring of blood glucose supported by the mobile diabetes-app OneTouch Reveal® can improve HbA1c. We aimed at analysing costs savings related to the HbA1c reduction based on the integration of telemedical features into diabetes management.

Material and methods: Data from a randomized controlled study, analysing the influence of the colour-based glucose meter and the mobile diabetes-app OneTouch Reveal® on glycaemic control, were used to assess the 10-year risk of patients for a fatal myocardial infarction (MI). On the basis of the risk assessments, cost savings - also related to a 5 % reduction of hypoglycaemic episodes - for the health care systems of five European countries (France, Germany, Italy, Spain and UK) were modelled.

Results: An HbA1c reduction of 0.92 % in insulin-treated T2DM patients over six month that was observed in the randomised trial, was associated with a 1.2 % decreased 10-year risk for fatal MI. In our model this decrease led to cost savings of € 16.37 (France), € 15.22 (Germany), € 23.11 (Italy), € 13.49 (Spain) and € 7.24 (UK) per patient-year. Considering all insulin-treated T2DM patients in the respective countries, this 1.2 % reduction of MI resulted in annual savings of € 8.1 million (France), € 29.1 million (Germany), € 15.6 million (Italy), € 11.9 million (Spain) and € 2.9 million (UK).

Conclusion: Improving metabolic control and thus risk for comorbidities like MI by combining the colour-based glucose meter with the mobile diabetes-app OneTouch Reveal® has the potential to reduce costs for European health care systems.

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Other

ATTD19-0308

FRAMEWORKS FOR EVALUATING MHEALTH TECHNOLOGIES LACK PATIENT FOCUS

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Introduction: There are many attempts to create multi-level frameworks for mHealth evaluation. However, due to the complex environment of mHealth technologies, there has been no consensus on a standard. With the aim of providing input for a consensus, we performed a review of different mHealth assessment frameworks.

Methods: Literature searches were performed in Google Scholar, Google and PUBMED for publicly available

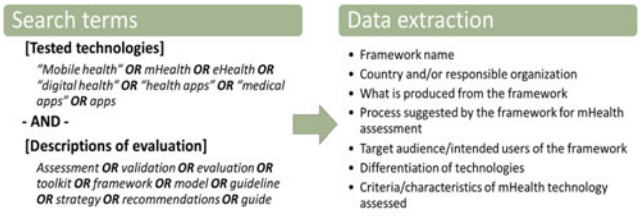

Figure 1. Descriptions of search terms used in the scientific and gray literature search, and extracted data types for mHealth frameworks.

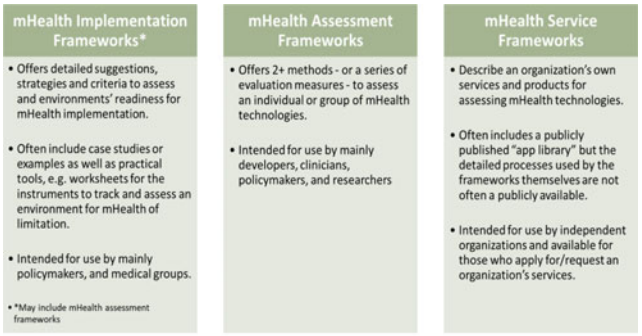

Figure 2. Definitions and descriptions of the three main types identified mHealth frameworks

descriptions of mHealth assessment efforts and strategies. Exclusion criteria included descriptions of single method ''frameworks'', e.g. questionnaires. Search terms and data extraction strategy described in Figure 1.

Results: Three main types of frameworks were identified: implementation frameworks (n = 20), assessment frameworks (n = 28), and service frameworks (n = 13). Developed definitions are described in Figure 2. The most commonly covered areas were security (n = 18), privacy (n = 17), usability (n = 16), and user experience (n = 16). Target audiences included developers, policy-makers, researchers, and health professionals.

Discussion: While user experience was considered a common priority for frameworks, with the most frequent users of mHealth being individual citizens, surprisingly few frameworks focused on this stakeholder group.

Conclusion: Stakeholder-specific frameworks spanning a diversity of target audiences have both advantages and disadvantages, but overall, create a fragmented mHealth assessment landscape. It is clear that one framework cannot be expected to assess all the different aspects of mHealth. Actions are needed to coordinate these efforts to utilize all stakeholders' expertise. As citizens are the most experienced and prevalent mHealth users, they must be involved in the development and have easy access to resulting framework(s).

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Other

ATTD19-0322

ASSOCIATION OF THE FABP2 GENE RS1799883 POLYMORPHISM WITH CARBOHYDRATE METABOLISM DISORDERS IN THE REPUBLIC OF TATARSTAN

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The aim of the study: to investigate the possible association of the *FABP2* gene rs1799883 polymorphism with different disorders of carbohydrate metabolism in residents of the Republic of Tatarstan (RT).

The study involved 225 patients (aged 38-76) with a single history of hyperglycemia and 95-with confirmed diagnosis of type 2 diabetes (T2DM). All patients underwent an oral glucose tolerance test. The patients were divided into groups: 1-impaired glucose tolerance, 2–impaired fasting glycemia (IFG), 3–functional hyperinsulinism, 4-newly T2DM. DNA was isolated from leukocytes, followed by analysis of gene polymorphisms with real time PCR (TestGen). The control was taken from the 1000 genomes database (European population).

The frequency distribution of alleles and distribution of genotypes of the A/G polymorphism of the *FABP2* gene in the control and study groups corresponded to the Hardy-Weinberg distribution ($p > 0.05$). The A allele is associated with an increased risk of developing T2DM (OR = 1.32, 95% CI [0.99-1.78]); the GG genotype is associated with a reduced risk of disease (OR = 0.72, 95% CI [0.49-1.06]). It was found that the chance of developing a disorder significantly increases in the carriers of the AA (OR = 5.52, $p = 0.02$) in the group with IFG. A significant correlation of the rs1799883 of the *FABP2* with the level of insulin and C-peptide ($r = 0.16$, $p = 0.04$, $r = 0.15$, $p = 0.05$,respectively) was obtained.

The association of the *FABP2* gene with the risk of developing T2DM in RT has been proved. Apparently, the A/G polymorphism of the *FABP2* is mostly associated with the insulin resistance in the group of patients with early carbohydrate metabolism disorders.

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Other

ATTD19-0328

IMPORTANCE OF IDENTIFIABILITY ANALYSIS IN RELIABLE INDIVIDUALIZED MODEL FOR USE IN ARTIFICIAL PANCREAS SYSTEMS

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Objective: To show the importance of robust identifiability analysis on personalized glucose forecasting.

Background: Standard methods for model identification usually assume population values or direct identification without analysis of parameter identifiability. Neither of these methods produces a reliable patient-specific set of parameter values since the impact of the model structure or the amount and quality of the available data is not exploited.

Method: The Subcutaneous Oral Glucose Minimal Model is derived from the well-known minimal model of glucose-insulin kinetics that has been extensively used in Artificial Pancreas Systems. SOGMM has 13 parameters of which 2 are a priori known. Model individualization included correlation analysis among parameters, global parameter ranking, and structural and

practical identifiability analysis to define a final unique set of 5 parameters. Data from 2 clinical trials (NCT02137512 and NCT02558491), were used for analysis and parameters identification. Our method was compared to the identification of all 11 model parameters, using the same optimization procedure. Data from 6 subjects was separated in 6 hour non-overlapping intervals and 2 steps forecast was used to assess quality of fit via root mean square error (RMSE).

Result: Average RMSE value was improved: 18.8 ± 16.75mg/dL vs 27.5 ± 27.46mg/dL. Maximum errors in glucose forecast over all cases were 32.9mg/dL vs. 102.2mg/dL.

Conclusion: Methods not accounting for robust identifiability lack the precision of parameter estimation necessary for accurate forecast. On the contrary, robust identifiability analysis can be associated not only with a reduction of computational burden, but also with an improvement in the accuracy of glucose predictions.

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Other

ATTD19-0331

CHANGES OF INSULIN SENSITIVITY AND EXPOSURE TO HYPOGLYCEMIA ACROSS THE MENSTRUAL CYCLE IN WOMEN WITH TYPE 1 DIABETES FREE-CYCLING OR USING ORAL CONTRACEPTIVE

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Background: Women with Type 1 Diabetes (T1D) face additional challenges in achieving successful glycemic control due to changing insulin requirements throughout the menstrual cycle. Insulin sensitivity (SI) is a key metabolic parameter mediating insulin action on glucose homeostasis. Our purpose is to assess the impact of menstrual cycle phases on SI and exposure to hypoglycemia, comparing free-cycling (FC) women to those using oral contraceptives (OCP).

Methods: Twelve women with T1D (8[4] FC[OCP]) using continuous glucose sensor (CGM) and insulin pump were studied for 3 menstrual cycles. Cycle phases were determined based on dates of menses and ovulation kits. SI was calculated using a Kalman filter-based algorithm, from CGM, meal, and insulin pump data. Exposure to hypoglycemia was quantified using the low blood glucose index (LBGI). SI and LBGI were compared between the last 5 days of a cycle (late luteal phase [LL]) and the first 3 days of the following one (early follicular phase [EF]). Total daily insulin (TDI) was also compared between the phases.

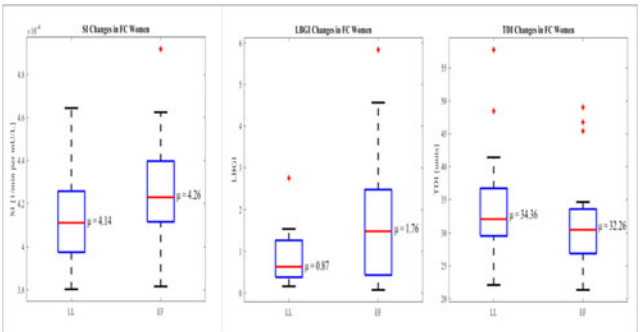

Figure. Changes of insulin sensitivity (SI), low blood glucose index (LBGI), and total daily insulin (TDI) from late luteal (LL) to early follicular (EF) menstrual cycle phase in free-cycling (FC) women with type 1 diabetes. On each box, the central mark is the median, the edges of the box are the 25th and 75th percentiles, the whiskers extend to the most extreme datapoints the algorithm considers to be not outliers, and the outliers are plotted individually.

Results: SI significantly increased from LL to EF in FC women (p = 0.006); this was accompanied by an increase in LBGI (p = 0.03), despite a decreased TDI (p = 0.044) [see Figure]. In women using OCP, SI and LBGI did not show a statistically significant increase, with TDI remaining unchanged.

Conclusions: These preliminary results suggest that the initial phase of the menstrual cycle is characterized by increased SI, which – in absence of adequate therapy adjustment – may lead to higher exposure to hypoglycemia. This phenomenon seems to be mitigated through the use of OCPs.

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Other

ATTD19-0346

THE OCCURRENCE OF OBSTRUCTIVE SLEEP APNEA SYNDROME IN PATIENTS WITH DIABETIC FOOT AND IT'S POSSIBLE ASSOCIATION WITH LIMB ISCHEMIA AND WOUND HEALING.

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Aim: The aim of our study was to assess in patients with DF (diabetic foot) the occurrence of Obstructive Sleep Apnea Syndrome(OSAS)and its association with peripheral arterial disease(PAD)and impact on DF healing.

Methods: We included into our study 38 patients with DF whose completed screening and sleep disability questionnaires and underwent ApneaLink screening test for the OSAS detection. Patients were divided into 2 groups-group A (OSAS positive) and group B (OSAS negative). During the follow-up periods (6-9 months and 12-15 months) macrovascular and microcirculation status (transcutaneous oxygen tension-TcPO2) and DF healing were assessed.

Results: OSAS was detected in 79% of studied patients (30/38–group A),of whom 30% had the severe form of OSAS(9/30).Trends to higher incidence of PAD (50%vs.25%;p = 0.18) and to lower values of TcPO2 (38.7 ± 12.9 vs.50.8 ± 10.8 mmHg;p = 0.14) with higher frequency of patients with TcPO2 bellow 40mmHg (50%vs.12.5%;p = 0.096) were found in group A compared to group B. Patients from group A had significantly larger defects(p = 0.03) as at the begging of this study, as after 6-9 months(p = 0.002and 0.001) and 12–15 months(p = 0.001and 0.0009). The presence of OSAS had no impact on the DF prognosis. Patients with severe OSAS were significantly older(p = 0.03), had more sleep abnormalities(p = 0.01), larger DF ulcers at the end of the study(p = 0.08) and higher occurrence of new DF ulcers(p = 0.09)

Conclusion: The incidence of OSAS including it's severe form is probably higher in patients with DF compared to general diabetic population. Patients with OSAS had higher occurrence

of PAD and lower TcPO2 values. OSAS has probably no clinical impact on the DF prognosis but could negatively influence DF characteristics.*VZ 00023001*

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Other

ATTD19-0349

CRASH: CONVERSATIONS AND REACTIONS AROUND SEVERE HYPOGLYCEMIA: A GLOBAL STUDY

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Background and Aims: There is little known about the experience of persons with diabetes (PWD) and their caregivers' (CG) knowledge of a severe hypoglycemic event (SHE), and the use of glucagon to treat such an event. The CRASH (Conversations and Reactions Around Severe Hypoglycemia) cross-sectional survey was developed to address this research gap.

Method: Medical research panels were used to identify and recruit 400 participants (200 PWD and 200 CG, evenly divided between type 1 and type 2 diabetes) in each of six countries: Canada, Germany, China, Spain, UK, and US. All participants were age ≥18 years old. Inclusion criteria for PWD included self-report of insulin therapy and having had experienced a SHE within the past 3 years. CG inclusion required self-report of caring for a PWD ≥4 years old on insulin therapy, who had experienced a SHE within the past 3 years. Participants completed a 30-minute online survey that examined their understanding of a SHE and its treatment, their actions during the SHE, and finally, what precautionary actions occurred after the SHE in terms of prevention and emergency preparedness. Descriptive analyses were conducted. Management and impact of a SHE were analyzed by subgroups including: diabetes type, participant type, age, glucagon use.

Results: Data from 400 UK participants were analyzed. Findings describe symptom recognition, knowledge and use of self-management strategies and professional emergency medical assistance.

Conclusion: Results provide much needed insights of the impact SHE (both personal and societal perspectives) and current glucagon treatment have on PWD and their CG.

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Other

ATTD19-0368

USING TWINE OPEN-SOURCE SOFTWARE TO CREATE SERIOUS AND ENTERTAINING DIGITAL GAMES – ENHANCING DOCTOR AND PATIENT MANAGENT OF DIABETES

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Background: Diabetes management is a complex learning process for patients and an area of low confidence amongst junior doctors. Serious digital games allow healthcare professionals to simulate clinical interactions in a safe environment. Many facets of diabetes management, such as carbohydrate counting, also lend themselves to gamification. Our work utilises Twine open-source software to create digital games that facilitate patient and healthcare professional education in diabetes management.

Method: Three serious digital games with virtual patients were developed using Twine open-source software, Wacom Intuous Pro, Autodesk SketchBook, Camtasia Studio, and simulated patient videos. Chalk-talk explanations of key concepts are integrated into these cases. A prototype was piloted by a small cohort of medical students and junior doctors and evaluated using the Kirkpatrick model. A detective-themed game was also developed using the aforementioned technology to enable diabetic patients to engage in aspects of management in a safe environment.

Results: Pilots with senior medical students and junior doctors have demonstrated high levels of engagement, as well as significant improvements in confidence and knowledge ($p < 0.05$). Larger cohort analysis will subsequently be performed, with a view to incorporating games into undergraduate and postgraduate curriculums. The utility of our patient-orientated game will be tested in a similar way.

Conclusion: Twine software can be used to create serious digital games that enhance the confidence and knowledge of medical students and junior doctors in diabetes management. It may also represent an opportunity to create games that enable patients to practise diabetes management in a safe and engaging environment.

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Other

ATTD19-0372

DDP-4 INHIBITORS VERSUS SULPHONYLUREAS AND CARDIOVASCULAR OUTCOMES: A META-ANALYSIS OF OBSERVATIONAL COMPARATIVE STUDIES

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Introduction: Dipeptidyl peptidase IV inhibitors (DPP4i) and sulphonylureas are commonly prescribed antidiabetic treatments, particularly after the failure of metformin monotherapy. Although DPP4i have demonstrated non-inferiority versus to placebo in clinical trials, their relative effectiveness in reducing cardiovascular events compared to sulphonylureas was evaluated in observational studies.

Aims: To evaluate the risk of mortality (all-cause and cardiovascular) and major cardiovascular adverse events (MACE) in patients treated with DPP4i versus sulphonylureas.

Material and methods: A literature search was conducted in PUBMED, EMBASE and Cochrane Library aiming to identify observational, comparative studies. The outcomes evaluated were all-cause mortality, cardiovascular mortality and MACE. Odds ratios (ORs) and its 95% confidence intervals were calculated using a Mantel-Haenszel random-effects model. A sensitivity analysis was conducted restricting the results to studies using metformin as baseline antidiabetic therapy.

Results: Thirteen observational studies were included in this meta-analysis. Compared with sulphonylureas, DPP4i reduced the risk of all-cause mortality [OR 0.72 (95% CI 0.64 - 0.81); $p < 0.001$; $I^2 = 72.9\%$], cardiovascular mortality [OR 0.36 (95% CI 0.18 - 0.70); $p = 0.003$; $I^2 = 69.3\%$] and MACE [OR 0.81 (95% CI 0.66 - 0.98); $p = 0.032$; $I^2 = 83.7\%$]. The results did not significantly change when the analyses was restricted to studies where the baseline therapy was metformin.

Conclusions: According to the available post-marketing observational data, DPP4i reduce the risk of overall mortality and MACE compared to sulphonylureas.

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Other

ATTD19-0373

SAFETY PROFILES OF ANTIDIABETIC DRUGS (AD): A DISPROPORTIONALITY ANALYSIS IN THE PORTUGUESE PHARMACOVIGILANCE SYSTEM (PPS) DATABASE

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Introduction: Safety profile of AD is recognized as a component of the treatment of diabetic patients. Databases of spontaneously reported adverse drug reactions (ADR) offer the possibility of exploring data aiming at safety signals generation.

Aims: To investigate possible associations between Ads and the occurrence of given ADR through disproportionality analysis in the PPS.

Material and Methods: ADR's received from 1st January 2008 to 31st December 2017 were collected. Insulin ADRs were excluded. ADR's were coded according to MedDRA PT (Preferred Term) and drugs according to the ATC classification (4th level). Associations between drugs and ADRs were assessed through case/non case methodology. Disproportionality was measured using reporting odds ratio (ROR) and 95% CI.

Results: 33.125 ADR reports were identified. Of these, 413 were due to AD. 262 (63.4%) reactions were serious. Statistically significant associations were found: a) alpha-glucosidase inhibitors/ abdominal pain (ROR 9.67, 95%CI 2.48–37.66); b) DPP4 inhibitors/acute pancreatitis(ROR 21.99, 95%CI 2.55–189.93); c) GLP1 agonists and vomiting (ROR 3.40, 95%CI 1.38–8.37); d) metformin/lactic acidosis (ROR 76.87, 95%CI 4.66–1269.03); d) SGLT2 inhibitors/candida infection (ROR 51.53, 95%CI 2.79–950.10), diabetic ketoacidosis (ROR 84.80, 95%CI 4.83–1487.81), pollakiuria (ROR 15.16, 95%CI 1.56-147.13) and urinary tract infection (ROR 15.16, 95%CI 1.56-147.13); e) sulfonylureas/hypoglycaemia (ROR 44.79, 95%CI 14.35–139.80).

Conclusions: The number of ADR reports to AD was found to be low (1.25% of the database), a limitation of this study. SGLT2i pre-marketing safety concerns were confirmed, as well as metformin and sulfonylureas known risks. The association between DPP4i and pancreatitis deserves further research.

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Other

ATTD19-0374

EMPOWERMENT LADDER: THE PATH EXPERIENCED BY ACTIVATED LEADERS WITH DIABETES AND OTHER NONCOMMUNICABLE DISEASES (NCDS)

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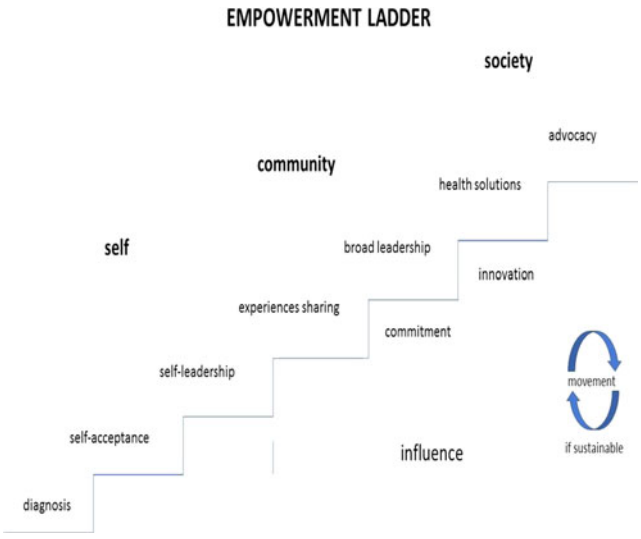
Introduction: Structured leadership training has potential to bring individuals with chronic conditions to a higher conscience and desire to promote social change.

Objective: Identify the steps that these individuals climb from an initial acceptance stage to a social active role, when offered an opportunity.

Method: Young Leaders in Diabetes Training (YLDT), a program that has been offered annually for 10 years has contents including: diabetes management, health education, fundraising, communication, interpersonal relationship, leadership skills, self-confidence, resilience, advocacy, storytelling, among others. Programs/movements that shared lessons with YLDT: IDF's Young Leaders in Diabetes Programme and Blue Circle Voices;



NCDAlliance's Our Views Our Voices; and Medtronic Foundation's Bakken Invitation.

Results: a) stage 1: The ladder starts with focus on the self, including self-acceptance followed by self-leadership steps, where a self-pity turns into a positive mindset; b) stage 2: Focus on the community, individuals intentionally share own experience, followed by a more strategic leadership, influencing or tutoring others to become leaders; c) stage 3: Focus on the society, individuals translate their passion into initiatives to play a broader social role, aiming to improve access and life quality to others living with the same condition. 47 (50% of who started YLDT) progressed from Stage 1 to 2, whereas the others left to optimize their own treatment. 19% of the remaining 47 progressed to Step 3 (9 individuals), developing broader awareness, advocacy or education initiatives.

Conclusion: Although not everybody climbs fully this multistep ladder, structured training programs favor individuals' growth from self-pity to active leadership.

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Other

ATTD19-0385

THE PREVALENCE OF DIABETES MELLITUS TYPE 2 AND METABOLIC DISORDER IN PSORIATIC ARTHRITIS PATIENTS: DATA OF THE RUSSIAN PSORIATIC ARTHRITIS REGISTRY (RU-PSART)

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Objectives: to assess Psoriatic arthritis (PsA) patents' (pts) prevalence of metabolic disorders

Methods: 294 (M/F133/161) pts with PsA, diagnosed according to CASPAR criteria, age 41.2 ± 1.9 (Min 21 Max 72) yrs, PsA duration 6.1 ± 5.3 (0; 31) yrs. According to Disease Activity index for Psoriatic Arthritis (DAPSA), remission (REM) ≤4, low (LDA) ≤14, moderate (MDA) ≤28 and high disease activity (HDA) >28.

Results: 71 patents had Psoriasis Area Severity Index (PASI) 3.1 ± 7.0 (0; 60), most of pts had mild Ps.

291 pts underwent Body Mass Index (BMI) assessment. 37% were overweight, 19% had 1st degree obesity, 8% had 2nd degree obesity, 3% pts had 3rd degree obesity, 31% pts had normal BMI, 2% had body weight deficit. Type 2 diabetes mellitus had 15.7%, metabolic syndrome 14.8%, hyperlipidemia 12.0%. 7% with diabetes had PASI <10, 2.8% had PASI >10. 5.6% pts with metabolic syndrome had PASI <10, 1,4% had PASI >10. 11 pts with hyperlipidemia had PASI <10. 19 pts with normal BMI had HDA and 11 - MDA. After 6 months of treatment 4 pts had REM. Among pts with 1st and 2nd obesity degree, 18 pts had HDA, 12 - MDA. After 6 months of treatment, no one achieved REM. Pts without obesity had DAPSA change median 13.1 (0; 46.5), pts with 1st and 2nd degree – 19.9 (4.2; 95.8) ($p < 0.05$).

Conclusions: Most of pts with PsA had mild Ps and higher BMI than normal. The presence of metabolic disorders did not correlated with the severity of Ps. The treatment on pts without obesity showed to be more effective.

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Other

ATTD19-0386

USE OF HBA1C POINT-OF-CARE DEVICE AT BASIC HEALTH UNITS IN BRAZIL, AS PART OF HEALTHRISE BRAZIL

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Background: In the Brazilian public primary healthcare, it may take months for people with diabetes mellitus (DM) to have access to glycated hemoglobin (HbA1c) tests, and even longer to receive and bring to the physician their results, because blood sampling and tests are not always available near where they live.

Methods: We conducted a demonstrative study from June to October of 2018, in Vitória da Conquista, northeast Brazil. People with DM had their HbA1c tested using a POC device in BHU near their homes. Cases of high HbA1cs were immediately seen by a physician or a nurse in order to assess the need for treatment adjustments and education for healthy habits. Finally, a second test was scheduled for after 90 days.

Results: We tested HbA1c in 166 patients with DM using POC. The mean age was 62.7 years (95%IC: 60.7 – 64.6) and 95 (59%) were female. Until now, 47 (28%) have tested HbA1c at least twice. In these, 37 (79%) had inadequate glycemic control in the first measurement (HbA1c > 7.0%). However, in the second measurement 33 (89%) presented a decrease in values, with Hb1Ac being less than 7.0% in 03 (9%).

Conclusion: HbA1c POC testing has shown to be promising in to qualify the care of individuals with DM and we keep studying its cost-effectiveness in Brazilian primary care.

This research is part of HealthRise, in partnership with the Medtronic Foundation, Abt Associates and the Institute for Health Metrics and Evaluation. This project was funded by Medtronic Foundation.

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Other

ATTD19-0420

LIFESTYLE CHANGES AND GLYCEMIC CONTROL IN TYPE 1 DIABETES MELLITUS: A FACTORIAL DESIGN APPROACH

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Type 1 diabetes (T1D) is a challenge, for patients and caregivers, as hypoglycemia and ketoacidosis are acute complications. Incidence of T1D has been increasing globally over the past three decades. Reports from Pakistan draw attention to non-adherence of T1D patients to dietary advice (58.5%), physical activity (42.3%) and insulin regimen (88.1%). Use of mobile applications help to increase medication adherence and self-monitoring of blood glucose (SMBG). A wearable wrist e-device (Fitbit App) tracks step count by recording data in mobile application. HbA1c levels acts as an indicator for the glycemic control and correlates with complications. A factorial design approach will be taken to study the lifestyle change for self-management of T1D. A randomized controlled trial will enroll T1D patients of >14 years in four groups. All groups will keep a log book per advice from routine care given by endocrinologists, nurses, and nutritionists. First group will follow routine care, to be compared to second group with step count e-device, third group with e-messages as reminders for maintaining log-book, and fourth group for step count by e-device plus daily e-messages. Log book data will be obtained at a monthly interval and HbA1c as a main outcome will be measured three times, at baseline, three and six months to study the time trends. Expected results will increase adherence to SMBG, insulin therapy, and blood glucose levels; optimizing HbA1C levels, and reduction in acute complications in low income settings. (Figure shows the factorial design approach).

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Other

ATTD19-0423

IMPACT OF ERRORS IN CARBOHYDRATE ESTIMATIONS ON BLOOD GLUCOSE CONTROL IN TYPE 1 DIABETES

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TABLE I: MINIMUM AND MAXIMUM GLUCOSE VALUE AND THE PERCENTAGE IN DIFFERENT GLUCOSE RANGES (MEAN ± STANDARD DEVIATION)

BA: Bolus Advisor					
	BGmin	*BGmax*	*Target*	*Hypo*	*Hyper*
MU0	**98.0±10.2**	**199.1±16.8**	93.7±6.5	**0.0±0.0**	6.3±6.5
MU0*	94.8±13.9	200.8±16.5	**93.8±6.6**	0.1±0.2	**6.2±6.4**
MU15	92.3±18.4	199.6±16.9	93.0±8.0	0.1±0.3	6.9±7.8
MU15*	90.5±11.9	206.0±19.7	91.1±8.6	**0.0±0.0**	8.9±8.6
MU25	88.3±21.2	203.8±18.4	91.7±9.2	0.1±0.4	8.2±8.8
MU25*	78.5±16.2	205.6±20.8	91.7±8.0	0.2±0.6	8.1±7.6
MU50	73.2±21.3	221.5±32.9	86.6±10.4	0.3±0.8	13.1±9.8
MU50*	60.6±21.2	241.0±43.4	84.9±9.2	1.1±1.7	14.1±8.1
PID: Proportional-Integral-Derivative Controller					
	BGmin	*BGmax*	*Target*	*Hypo*	*Hyper*
MU0	89.6±13.7	**198.9±28.5**	**92.1±13.3**	**0.0±0.0**	**7.9±13.3**
MU0*	**90.6±11.1**	199.5±26.1	91.6±15.1	**0.0±0.0**	8.4±15.1
MU15	87.4±17.5	202.6±27.0	91.0±15.4	0.0±0.1	9.0±15.3
MU15*	88.0±13.1	210.7±29.3	88.2±15.9	**0.0±0.0**	11.8±15.9
MU25	83.9±19.0	205.4±26.9	89.8±15.4	0.1±0.3	10.1±15.2
MU25*	80.2±15.9	205.8±27.3	91.4±12.4	0.1±0.2	8.4±12.2
MU50	69.7±19.6	228.1±52.3	83.9±15.8	0.7±1.1	15.4±15.2
MU50*	61.1±21.9	226.0±41.6	83.7±15.6	0.9±1.0	15.4±15.1
RL: Reinforcement Learning Based Algorithm					
	BGmin	*BGmax*	*Target*	*Hypo*	*Hyper*
MU0	91.2±11.5	**189.4±13.9**	96.7±4.3	**0.0±0.0**	3.3±4.3
MU0*	**91.4±11.1**	191.6±12.9	**96.8±4.2**	**0.0±0.0**	**3.2±4.2**
MU15	89.8±12.2	192.3±15.9	96.2±5.2	**0.0±0.0**	3.8±5.2
MU15*	82.5±18.7	199.4±17.5	93.3±8.6	0.1±0.4	6.6±8.3
MU25	86.1±14.0	196.6±22.0	94.0±9.7	0.0±0.1	6.0±9.6
MU25*	78.5±15.2	199.3±22.9	93.7±10.0	0.1±0.2	6.2±9.9
MU50	71.4±17.6	214.2±36.1	88.7±13.7	0.4±0.8	10.9±13.0
MU50*	62.8±20.3	222.8±42.5	87.0±13.6	0.7±0.7	12.3±13.3

MU*x*: meal announcement (MA) under MU*x* with numerical value, MU*x**: MA under MU*x* with categorical value (Small, Medium, Large)

Background and Aims: Many diabetic patients need external insulin to maintain blood glucose levels. Different algorithmic approaches aim to define optimum insulin delivery and are incorporated into bolus advisors, basal-bolus advisors and the artificial pancreas. Independently of the algorithm used, the bolus dose is calculated from the carbohydrate (CHO) content of the meal, as entered manually by the patient (meal announcement, MA). This study investigates the procedure for MA, and related errors (meal uncertainty, MU) in estimating the insulin dose and in glucose control.

Method: Three algorithms were analysed for insulin adjustment under various MU conditions. A bolus advisor, a proportional-integral-derivative (PID) controller, and a reinforcement learning (RL)-based algorithm were considered. Four MU conditions were investigated: accurate CHO announcement (MU0), accurate CHO announcement ±15% (MU15), ±25% (MU25) and ±50% (MU50). The amount of CHO was announced in two ways: i) as a numerical value, ii) as categorical values of three different levels (SML: small, medium, and large). The experiments were conducted using the educational version of the UVa/Padova simulator on 11 virtual adult subjects.

Results: The results (Table 1) indicate that, at low errors of CHO estimation, the mode of announcement of the CHO level has low impact on the quality of the algorithm. As the error increases, more intelligent algorithms must be employed.

Conclusion: The finding suggests that patients can give categorical CHO estimations to the algorithm, if they are capable of keeping the overall error of CHO estimation low. This approach requires less effort from the patient and may therefore improve quality of life.

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Other

ATTD19-0432

DISTURBANCES IN INTRAVENTRICULAR CONDUCTION IN TEENAGERS WITH TYPE 1 DIABETES - A PILOT STUDY

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Cardiac autonomic neuropathy may occur in adolescent patients with type 1 diabetes (T1D). Body Surface Potential Mapping (BSPM) is a multi-electrode synchronous method for examining electrocardiographic records on the patient's body surface that allows the assessment of changes in the heart conduction system.

The aim of the study was to visualize and evaluate changes in the intraventricular area in adolescents with T1D.

Patients and methods: Inclusion criteria: age >12 years, T1D duration >3 years, HbA1c >8%. Exclusion criteria: diagnosis of autonomic neuropathy, heart defect. The 87-electrode Fukuda Denshi HPM 7100 system was used to generate BSPM images. Data were processed into map plotting to illustrate differences in ventricular activation time (VAT, isochron line).

Results: 33 teenagers (20 boys) at the age of 15.0 ± 2.1 years, with DM1 lasting an average of 6.8 ± 4.1 years were included. Mean HbA1c was 9.6 ± 2.0%. Hypoglycaemia did not occurred in any child during the test. ECG abnormalities were not present. The distribution of isolines on the mean map plotted for T1D patients only initially resembles the course of isolines on the map of healthy subjects (N = 30). After proper start of stimulation, the isolines in the area of ventricles reach higher time values, which indicates problems in the propagation of the activation.

Conclusions:

1. The times of significant ventricular stimulation in T1D indicate a delayed and inconsistent propagation of activation in the heart conduction system over the left and right ventricle.

2. The observed changes occured mostly outside the area of classic ECG registration.

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Other

ATTD19-0472

USE OF TECHNOLOGICAL INTERVENTIONS IN PATIENTS WITH TYPE 2 DIABETES BY PRIMARY CARE PHYSICIANS AND ENDOCRINOLOGISTS IN THE UNITED STATES

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Background and Aims: Determining when technological interventions (eg, insulin delivery devices [IDDs], continuous glucose monitoring (CGM) systems, smart phone applications) are appropriate to optimize treatment in patients with type 2 diabetes (T2D) can be challenging. This study assessed T2D diabetes technology (DT) practice trends among primary care physicians (PCPs) and endocrinologists (ENDOs) in the United States.

Method: An online survey to assess the perspectives and use of DT (eg, IDD) was conducted in a sample of PCPs and ENDOs nationwide. To participate in this survey, at a minimum, PCPs treated ≥20 T2D patients/month, ≥25% receiving insulin; ENDOs treated ≥80 T2D patients/month, ≥50% receiving insulin. Respondent demographic results were analyzed by descriptive statistics.

Results: Participants included 102 PCPs and 100 ENDOs. Fifty percent of ENDOs and 48% of PCPs report prescribing a traditional or wearable tube-free patch insulin pump when patients failed to achieve HbA1c targets with basal therapy plus ≥3 prandial injections of insulin/day. Participants ranked requiring fewer injections, glucose data versus insulin dosing graphical representation, and objectively capturing insulin dosing data as the most useful technologies of IDDs. Most important perceived features of an IDD were ease of use, flexible dosing, and large insulin reservoirs. Patients' blood glucose control motivation, health literacy and/or cognitive ability, and previous good adherence were considered the strongest predictors for success with DT.

Conclusions: PCPs and ENDOs who are highly focused on diabetes management report using IDDs when patients taking a basal injection plus ≥3 prandial injections of insulin are not achieving their HbA1c target.

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Other

ATTD19-0475

TRANSCUTANEOUSLY REFILLABLE, 3D-PRINTED BIOPOLYMERIC ENCAPSULATION SYSTEM FOR THE TRANSPLANTATION OF ENDOCRINE CELLS

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The success of β cell transplantation hinges on the achievement of a suitable implantation site for long-term cells survival and function. While autologous cell transplantation abrogates the issue of transplant rejection, poor graft vascularization, and lack of cell retention and mechanical support have limited the effectiveness of encapsulation approaches. Transplanted cells

require a vascularized environment providing adequate oxygen level and nutrients.

To address this need, we developed a three-dimensional printed polylactic acid (PLA) cell encapsulation termed *neovascularized implantable cell homing encapsulation (NICHE)*. The NICHE houses cells distributed in microwells and connected to the surrounding tissues by 100 μm square microchannels. The NICHE is designed for subcutaneous implantation and prevascularization prior to transcutaneous cell loading. For this, the NICHE is coated and filled with a platelet-rich plasma (PRP) hydrogel capable of releasing growth factors to enhance vascularization. NICHE subcutaneous vascularization was assessed in mice, rats, pigs and rhesus macaques. In a following study using immunocompromised mice, 4-weeks prevascularized NICHEs were transcutaneously loaded with 2,000 IEQ human islets. Insulin release was detected for 12 weeks. Additional islets (2,000 IEQ) were then loaded producing an increase in insulin levels ($\sim$10 μIU/ml) for additional 10 weeks, demonstrating viability of the transplant. The NICHE was later adopted to transplant Leydig cells in castrated Rag-/- mice. Cells maintained viability and testosterone secretion achieving plasma concentration between 1.5ng/ml to 2.2ng/ml for the time of analysis (7 weeks). We are currently developing the NICHE2 for allo- or xenografts, which allows for local, constant, and sustained immunosuppression.

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Other

ATTD19-0481

HYPOGLYCEMIA AND DIABETIC KETOACIDOSIS STRATIFIED BY AGE AND GLYCEMIC CONTROL: A REAL-WORLD STUDY OF OVER 30,000 ADULT PATIENTS WITH TYPE 1 DIABETES IN US

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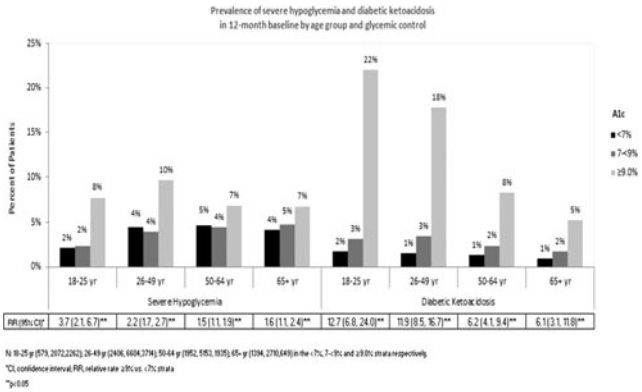
Background and Aims: The burden of disease among adult patients with type 1 diabetes (T1D) is infrequently assessed. We evaluated acute and microvascular complications among adult T1D patients stratified by age and glycemic control in a US Electronic Health Record database.

Method: Retrospective observational study of patients classified as having T1D (identification period: 7/1/2014–6/30/2016, first diagnosis as index date) using a validated algorithm, with ≥24 months of disease duration, ≥18 years old, not pregnant during baseline (12 months prior to index date); with ≥1 insulin prescription and ≥1 A1C measure in baseline. Baseline demographic characteristics, acute complications (severe hypoglycemia [SH], diabetic ketoacidosis [DKA]), and microvascular complications (neuropathy, nephropathy and retinopathy) were stratified by age-group (18-25, 26-49, 50-64, 65+) and glycemic control (A1C <7%, 7-<9% and ≥9%).

Results: 31,430 adult T1D patients were included. Older patients had lower A1C compared with younger patients ($p < 0.001$).



N: 18-25 yr (579, 2072,2262); 26-49 yr (2406, 6604,3774); 50-64 yr (1952, 5353, 1935); 65+ yr (1194, 2710,649) in the <7%, 7-<9% and ≥9.0% strata respectively.
*CI, confidence interval; PR, relative rate ≥9% vs. <7% strata
**p<0.05

Patients with poor (≥9%) glycemic control had the highest prevalence of SH (4.2%, 4.0%, 8.3%) and DKA (1.3%, 2.8%, 15.8%) in the <7%, 7-<9% and ≥9% strata, respectively; $p < 0.001$. Stratified prevalence suggested interaction between age and glycemic control: Younger patients with poor glycemic control had higher relative rates of SH and DKA than comparable older patients, $p < 0.001$ (Figure). Patients with poor glycemic control also had higher prevalence of neuropathy and nephropathy ($p < 0.001$).

Conclusion: This real-world study in over 30,000 adult T1D patients showed that individuals with A1C≥9% had a two-fold and a twelve-fold increased prevalence in SH and DKA respectively compared to A1C<7%; higher relative rates were observed in younger patients.

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Other

ATTD19-0483

A DEEP NEURAL NETWORK FOR PREDICTING BLOOD GLUCOSE

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Background and Aims: Timely recognition of upcoming hypo- and hyperglycemic events is crucial for the safety of individuals with T1D. To this end, we introduce a deep neural network based on long-short term memory (LSTM) to allow the accurate prediction of subcutaneous glucose concentrations, by minimizing the time lag and root mean square error (RMSE) between predicted and actual concentrations.

Method: A sequential model with one LSTM layer, one bidirectional LSTM layer and several fully connected layers was used to predict blood glucose levels for different prediction horizons (PHs). Two rounds of pre-training - with both *in silico* data and real patient data - were introduced to generate a ''global model''. The model was then further trained and tested on 26

TABLE I: PREDICTION RESULTS OF DIFFERENT METHODS

PH = 15 minutes				
Methods	*RMSE*	*CC*	*Time Lag*	*Fit*
ARIMA	12.256	0.972	10.192	76.425
SVR	11.694	0.973	9.808	77.565
LSTM	**11.633**	**0.974**	**9.423**	**77.714**
PH = 30 minutes				
Methods	*RMSE*	*CC*	*Time Lag*	*Fit*
ARIMA	22.924	0.903	22.885	55.923
SVR	22.135	0.904	20.769	57.644
LSTM	**21.747**	**0.909**	**20.385**	**58.523**
PH = 45 minutes				
Methods	*RMSE*	*CC*	*Time Lag*	*Fit*
ARIMA	32.588	0.806	37.885	37.463
SVR	30.628	0.812	34.423	41.595
LSTM	**30.215**	**0.818**	**32.692**	**42.563**
PH = 60 minutes				
Methods	*RMSE*	*CC*	*Time Lag*	*Fit*
ARIMA	40.841	0.698	52.885	21.694
SVR	37.422	0.709	47.885	28.893
LSTM	**36.918**	**0.722**	**46.346**	**30.079**

retrospectively analysed datasets from 20 real patients. Cross validation was used to prevent over-fitting during the pre-training and training phases. Only continuous glucose monitoring (CGM) measurements were used as input.

Results: As shown in Table 1, the LSTM method outperforms the classical methods - in all the PHs and with respect to all the evaluation criteria. In comparison with ARIMA and SVR, the LSTM method can simultaneously decrease RMSE and Time Lag, while correlation coefficient (CC) and fit are both increased.

Conclusion: Deep learning approaches have been used to predict blood glucose concentrations on the basis of the available glucose data. The results are promising with respect to evaluation criteria. We are investigating the inclusion of additional information related to therapy, lifestyle and patient characteristics.

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Other

ATTD19-0486

OBESE PATIENTS WITH TYPE 2 DIABETES: OUTCOMES AFTER LAPAROSCOPIC SLEEVE GASTRECTOMY

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Objective: to evaluate metabolic results in short, medium and long term of obese patients with T2DM after laparoscopic sleeve gastrectomy (LSG).

Design: Observational and retrospective analysis.

Patients and Methods: obese patients with T2DM operated by LSG in our hospital, between 01/2009 and 07/2016 were included. We analyzed demographic data, average time of diagnosis of T2DM, pre and post-surgical pharmacological treatment, BMI and evolution (complete or partial remission, improvement, without changes and recurrence of DMT2) at 1, 3 and 5 years post LSG (Criteria ASMBS 2012). Statistical analysis was performed with SPSS 19.0.

Results: 166 patients were evaluated. 60.8% (n = 101) women, average age 49.1 ± 12.8 years. Initial average BMI was 46.4 ± 7.7 kg / m2 (range 33–69). Average time of diabetes was 5.9 years (1–28). Average preoperative HbA1c was 7.5 ± 0.9%. In the preoperative, 75% (n = 125) were treated with oral agents (OA) and 13.2% (n = 22) with insulin. Average follow-up was 65 ± 10 months. Complete remission was observed in 78.3%, 76.2% and 71.4% at 1, 3 and 5 years respectively; 7.2% partial remission, 10% improved and 11.4% recurrence of T2DM at 5 years. Patients previously treated with insulin and / or with more than 5 years of diagnosis had lower frequency of complete remission at 5 years ($p = 0.0004$ and $p = 0.0001$ respectively).

Conclusion: this work reveals the significant role of LSG in the treatment of T2DM in obese patients, since more than 70% support complete remission in the long term.

ATTD 2019 Read by Title

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Artificial Pancreas

ATTD19-0281

A PROTOTYPE OF ARTIFICIAL PANCREAS FOR GLUCOSE HOMEOSTASIS

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Artificial Pancreas

ATTD19-0434

ROLE OF INSULIN EXCIPIENTS IN CONTINUOUS SUBCUTANEOUS INSULIN INFUSION (CSII) PERFORMANCE

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Blood Glucose Monitoring and Glycemic Control in the Hospitals

ATTD19-0015

OPTIMAL GLYCAEMIC CONTROL DURING CAESAREAN SECTION PROVIDED BY SENSOR-AUMENGED PUMP THERAPY WITH PREDICTIVE LOW-GLUCOSE SUSPEND FUNCTION

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Blood Glucose Monitoring and Glycemic Control in the Hospitals

ATTD19-0461

THE BETA-CELL FUNCTION AND GLUCOSE PROFILE OF NEWLY DIAGNOSED ACROMEGALIC PATIENTS WITH NORMAL GLUCOSE TOLERANCE USING CONTINUOUS GLUCOSE MONITOR SYSTEM

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Clinical Decision Support Systems - Advisors

ATTD19-0040

PNEUMOCOCCAL VACCINATION RECOMMENDATION PRACTICES AWARENESS

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Clinical Decision Support Systems - Advisors

ATTD19-0043

ANTIHYPERGLYCEMIC AND ANTIOXIDANT EFFECTS OF CITRULLUS LANATUS (WATERMELON) SEEDS AND MORINGA OLEIFERA LEAVES IN ALLOXAN-INDUCED DIABETIC WISTAR RATS

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Clinical Decision Support Systems - Advisors

ATTD19-0452

A SCHEME TO RECYCLE THE USED INSULIN PUMPS TO NEEDY WILLING TYPE 2 AND TYPE 1 DM PATIENTS IN INDIA AND DEVELOPING COUNTRIES A THOUGTH

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Closed-loop System and Algorithm

ATTD19-0087

BOLUS WIZARD SETTING SHOULD BE MORE AGGRESSIVE WHEN SWITCHING TO HYBRID CLOSED LOOP IN TYPE 1 DIABETES PATIENTS

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Closed-loop System and Algorithm

ATTD19-0318

IN-SILICO EVALUATION OF TRUST REGION POLICY OPTIMIZATION FOR T1DM CLOSED-LOOP CONTROL

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Closed-loop System and Algorithm

ATTD19-0419

NEW AUTONOMIC UNIVERSAL CLOSED GLYCEMIC CONTROL SYSTEM

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Closed-loop System and Algorithm

ATTD19-0462

HYPOXIA-SENSITIVE SYNTHETIC NANOVESICLES FOR CLOSED LOOP GLUCOSE RESPONSIVE RELEASE OF INSULIN

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Glucose Sensors

ATTD19-0046

STUDY: USE OF FLASH GLUCOSE SCANNING IN TYPE 1 DIABETES IN CHILDREN- A SERVICE EVALUATION OF (LIBR(E): ASSESSMENT OF TECHNOLOGY EFFECTIVENESS (LIBREATE- STUDY)

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Glucose Sensors

ATTD19-0088

SAME HBA1C LEVEL AND DIFFERENT TIME IN RANGE IN TYPE 1 DIABETES PATIENTS: WHY IT MATTERS?

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Glucose Sensors

ATTD19-0156

A MUELLER MATRIX BASED PHASE SENSITIVE NONINVASIVE BLOOD GLUCOSE MEASUREMENT

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Glucose Sensors

ATTD19-0313

A REAL-LIFE EXPERIMENTAL PILOT PROJECT OF BLOOD GLUCOSE MONITORING IN ARCTIC WINTER CONDITIONS

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Glucose Sensors

ATTD19-0422

NASCENT MEMS AND NANOTECHNOLOGY BASED HARDWARE TECHNOLOGIES FOR NEXT-GENERATION GLUCOSE SENSING AND INSULIN PUMPING

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Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0272

YAGI: A FREE REAL-TIME MULTI-SENSOR AND CROSS-PLATFORM SHARING SYSTEM OF BLOOD SUGAR GRAPHS, TREATMENTS AND STATISTICS

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Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0307

GOAL-SETTING AND PATTERNS OF APP USE: SELECTED RESULTS FROM THE "TAILORING TYPE 2 DIABETES SELF-MANAGEMENT" RCT

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Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0314

THE STATUS OF WEARABLES IN ACTUALIZING PERSONALIZED MEDICINE FOR DIABETIC PATIENTS IN QATAR

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Informatics in the Service of Medicine; Telemedicine, Software and other Technologies

ATTD19-0407

HOW CAN DIABETES EDUCATORS INCORPORATE DIGITAL THERAPEUTICS AND INSULIN TITRATION INTO THERAPEUTIC SELF-MANAGEMENT EDUCATION AND SUPPORT FOR PEOPLE WITH TYPE 2 DIABETES

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Insulin Pumps

ATTD19-0090

REAL TIME GLUCOSE VALUES WITH TREND ARROWS ARE IMPORTANT IN DECISION MAKING IN TYPE 1 DIABETES PATIENTS

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Insulin Pumps

ATTD19-0103

INACCURATE SENSOR TRACING LEADING TO HYPOGLYCEMIA IN A HOSPITALIZED PATIENT WHILE USING THE 670G HYBRID CLOSED LOOP (HCL) SYSTEM

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New Insulin Analogues

ATTD19-0048

SAFETY AND EFFICACY OF INSULIN DEGLUDEC/ LIRAGLUTIDE FIXED-RATIO COMBINATION IN OAD FAILURE TYPE 2 DIABETES PATIENTS IN A TERTIARY CARE CENTRE IN EASTERN INDIA

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New Medications for Treatment of Diabetes

ATTD19-0033

MANAGEMENT OF PATIENTS WITH TYPE 2 DIABETES AT HIGH CARDIOVASCULAR RISK: VIRTUAL SIMULATION IMPROVES CLINICAL DECISIONS

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New Medications for Treatment of Diabetes

ATTD19-0080

AN IMPACT ASSESSMENT AND OVERVIEW OF 20 ANTI-DIABETIC MEDICINAL PLANTS: THE NIGERIAN RESEARCH RECORDS

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New Medications for Treatment of Diabetes

ATTD19-0183

ALTERATIONS IN PANCREATIC HISTOLOGY, INSULIN SECRETION AND OXIDATIVE STATUS IN DIABETIC RATS AFTER TREATMENT WITH HIGH DOSE AND LOW DOSE OF CRASSOCEPHALUM RUBENS

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New Medications for Treatment of Diabetes

ATTD19-0344

DAPAGLIFLOZIN USE IN TRIPLE THERAPY FOR TREATING TYPE 2 DIABETES IN THE ENDOCRINOLOGY UNIT AT IMBANACO MEDICAL CENTER. CALI, COLOMBIA

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New Medications for Treatment of Diabetes

ATTD19-0348

HOT WATER-INFUSION OF PHRAGMANTHERA INCANA REDUCES BLOOD GLUCOSE, IMPROVES MUSCLE GLUCOSE UPTAKE AND ABATES OXIDATIVE STRESS IN A TYPE 2 DIABETES RAT MODEL

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New Technologies for Treating Obesity and Preventing Related Diabetes

ATTD19-0056

CAPACITY BUILDING FOR NURSES' KNOWLEDGE AND PRACTICE REGARDING PREVENTION OF DIABETIC FOOT COMPLICATIONS

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Other

ATTD19-0165

INSULIN-TRANSFECTED MESENCHYMAL STEM CELLS FROM HUMAN WHARTON'S JELLY OF UMBILICAL CORD AS AN ALTERNATIVE INSULIN SECRETING BIOIMPLANT

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Other

ATTD19-0212

FGF-23/KLOTHO/SCLEROSTIN IMBALANCE IS AN EARLY BIOMARKER OF CARDIOVASCULAR DISEASE AND DECREASING OF RENAL FUNCTION IN DIABETIC CKD STAGE 2-3A PATIENTS

L. Milovanova[1], *M. Taranova*[1], *S. Milovanova*[1], *M. Lebedeva*[1], *V. Kozlov*[1], *O. Li*[1], *M. Brovko*[1], *D. Zubacheva*[1], *V. Zabadaev*[1], *A. Kuchieva*[1]

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Other

ATTD19-0389

MANAGEMENT OF HYPERGLYCEMIA AND ITS IMPACT ON MATERNAL AND FETAL OUTCOMES IN PATIENTS WITH GESTATIONAL DIABETES

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ATTD19-0412

TRANSITION FROM SENSOR AUGMENTED INSULIN PUMP TO SULFONYLUREA THERAPY IN 4-MONTH-OLD PATIENT WITH KCNJ11 MUTATION

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Other

ATTD19-0445

A REAL WORLD RETROSPECTIVE ANALYSIS OF ELECTROLYTES CHANGE AND NONGLYCEMIC PARAMETERS WITH CONCOMITANT USAGE OF SGLT2I AND DIURETICS IN T2DM PATIENTS

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Other

ATTD19-0446

A RETROSPECTIVE CASE STUDY OF 12 WEEKS TO ASSESS GLYCEMIC AND NON-GLYCEMIC CHANGES WITH SGLT2I FROM DATA BASE OF 6 TYPE 2 DIABETIC PATIENTS

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