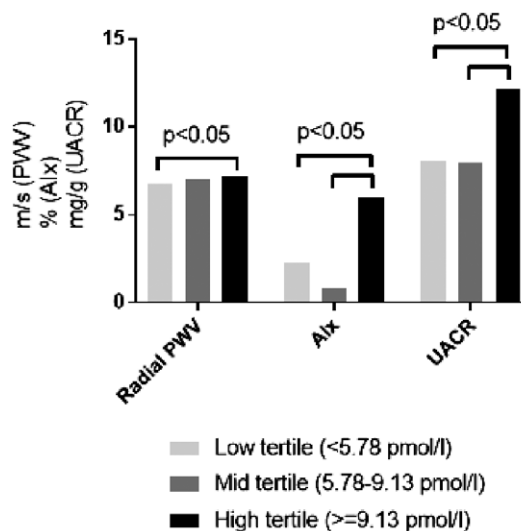


ORAL SESSIONS

Oral Session I - Diabetes Complications

O01

The role of vitamin B complex as an adjuvant therapy for diabetic nephropathy in children and adolescents with type 1 diabetes mellitus

N. Elbarbary¹, E. Abdel Rahman Ismail², M. Ahmed Zaki³, M. Zaki Ibrahim³, M. El-Hamamsy⁴¹Faculty of Medicine, Ain Shams University, Department of Pediatrics, Cairo, Egypt, ²Faculty of Medicine, Ain Shams University, Department of Clinical Pathology, Cairo, Egypt, ³Faculty of Pharmacy, Ahrum Canadian University, Department of Clinical Pharmacy, Cairo, Egypt, ⁴Faculty of Pharmacy, Ain Shams University, Department of Clinical Pharmacy, Cairo, Egypt**Background:** Homocysteine is elevated in type 1 diabetic patients with nephropathy due to several causes, including dietary deficiencies. Hyperhomocysteinemia induces renal injury and is associated with increasing urinary albumin excretion (UAE). Therefore, we performed a randomized-controlled trial of oral supplementation with vitamin B complex as an adjuvant therapy for nephropathy in pediatric patients with type 1 diabetes mellitus (T1DM) and assessed its relation to homocysteine, glycemic control, microalbuminuria and cystatin C as a marker of nephropathy.**Methods:** This trial included 80 vitamin B12-deficient T1DM patients with nephropathy, despite oral angiotensin-converting enzyme inhibitors. Enrolled patients aged 12-18 years with at least 5 years disease duration and HbA1c $\leq 8.5\%$. Patients were randomly assigned into two groups; intervention group (group A) who received vitamin B complex once daily orally. The other group (group B) did not receive any supplementation and served as a control group. Both groups were followed-up for 12 weeks with assessment of plasma homocysteine, HbA1c, cystatin C and UAE.**Results:** Both groups were well matched in baseline characteristics and laboratory parameters ($p > 0.05$). Baseline homocysteine levels were elevated in both groups compared with reference control values. After 12 weeks, supplementation with vitamin B complex for group A resulted in significant decrease of plasma homocysteine, fasting blood glucose, HbA1c, total cholesterol, triglycerides, UAE and cystatin C compared with baseline levels ($p < 0.001$) and compared with group B ($p < 0.001$). No adverse reactions were reported. Baseline vitamin B12 was positively correlated to UAE ($r = -0.877$, $p = 0.009$) and cystatin C ($r = -0.77$, $p = 0.043$).**Conclusions:** Vitamin B complex supplementation improved glycemic control and renal function through decreasing plasma homocysteine. Thus, it could be a safe and effective strategy for treatment of pediatric T1DM with nephropathy.³University of Colorado, Nephrology, Aurora, United States, ⁴Stanford University School of Medicine, Pediatric Endocrinology, Palo Alto, United States**Introduction:** There is a need for novel biomarkers and intervention strategies to prevent cardiovascular disease (CVD) in type 1 diabetes (T1D). Copeptin, a marker of vasopressin, is elevated in T1D and predicts both CVD and diabetic kidney disease (DKD) in adults. It remains unclear whether these relationships also exist in youth with T1D.**Objective:** To determine the relationships between copeptin and markers of CVD and DKD in youth with T1D.**Methods:** We assessed the cross-sectional relationships between copeptin and cardiorenal health in youth with ($n = 169$, 15 ± 2 years, 9 ± 3 years duration, HbA1c $9.0 \pm 1.6\%$, 57% girls) and without ($n = 61$, 15 ± 2 years, 59% girls) T1D. Copeptin was measured on Kryptor Compact Plus platform (ThermoFisher Scientific, MA, USA). Cardiorenal outcomes included radial pulse-wave velocity (PWV), augmentation index (AIx) corrected for heart rate 75/min and height, urine albumin-creatinine-ratio (UACR) and estimated glomerular filtration rate (eGFR) by serum creatinine and cystatin C. Generalized linear models were used to examine the relationships between copeptin and markers of cardiorenal health. Participants with T1D were stratified into tertiles of copeptin: low tertile (< 5.78 pmol/l), mid tertile (5.78-9.13 pmol/l) and high tertile (≥ 9.13 pmol/l).**Results:** Copeptin was significantly higher in youth with T1D compared to normoglycemic peers (8.91 ± 5.35 vs. 6.82 ± 2.97 pmol/l, $p = 0.004$). Participants in the high copeptin tertile had higher UACR, AIx, and radial PWV compared to those in the mid and/or low tertile in multivariable models (Fig 1), adjusting for age, sex and eGFR. The relationships remained significant for AIx and UACR after further adjustments for HbA1c and systolic blood pressure.**Conclusions:** Youth with T1D had higher copeptin concentrations than their normoglycemic peers, and elevated copeptin was associated with arterial stiffness and elevated albumin excretion.

[Figure 1]

O02

Elevated copeptin, arterial stiffness and albumin excretion in youth with type 1 diabetes

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O03

The comparative role of blood pressure (BP) and hemoglobin A1c (HbA1c) in predicting the 30 years risk of major diabetes complications in youth-onset type 1 diabetes (T1D)

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Objectives: Few studies have examined the predictive role of blood pressure (BP) in youth in predicting long duration complication outcomes in type 1 diabetes (T1D). This study thus assessed the relative strength of systolic (SBP) and diastolic blood pressure (DBP), as well as HbA1c for developing major diabetes complications using the Pittsburgh Epidemiology of Diabetes Complications (EDC) cohort of childhood onset (diagnosed age <17 years) T1D.

Methods: We studied 298 EDC participants who were first seen when aged <26 years at baseline between 1986-1988. Mean age and diabetes duration was 20 and 13 years, respectively. For this analysis, participants were followed to their 30th year of diabetes. A mean (SD) of 4.2 (2.6) BP observations per subject, obtained by a standard protocol, was analyzed. Poisson models with diabetes duration as the offset estimated the associations between complication incidence rates and updated mean HbA1c, SBP, and DBP. Major outcomes of diabetes (MOD) were defined as renal failure, blindness, amputation, major cardiovascular disease (CVD) (fatal/non-fatal myocardial infarction and stroke, and revascularization), and diabetes-related death.

Results: Both updated mean SBP and DBP were significantly associated with incidence of the composite endpoint of MOD. The two BP measures (SBP and DBP) were also associated with the development of major CVD, renal failure, and diabetes-related death, when evaluated separately. These findings remained even after adjusting for updated mean HbA1c (Table). Updated mean HbA1c was consistently associated with all composite and separate endpoints.

Conclusions: While HbA1c clearly predicts subsequent MOD in T1D youth, both SBP and DBP should also be targeted in these T1D children, as they also predict MOD overall and the important components.

Table. Poisson models for updated mean HbA1c/SBP/DBP with major complication outcomes of diabetes

Event (Total/Incident)	HbA1c(%)		SBP (mmHg)*		DBP (mmHg)*	
	β (SE)	<i>p</i> value	β (SE)	<i>p</i> value	β (SE)	<i>p</i> value
MOD (n=73/67)	0.38 (0.08)	<0.001	0.03 (0.01)	0.005	0.05 (0.01)	<0.001
Renal failure (n=25/25)	0.64 (0.12)	<0.001	0.05 (0.01)	0.005	0.07 (0.02)	0.003
Amputation (n=8/6)	0.74 (0.35)	0.004	-0.01 (0.04)	0.753	-0.01 (0.05)	0.794
Blindness (n=35/33)	0.41 (0.11)	<0.001	0.003 (0.02)	0.881	0.03 (0.02)	0.090
Major CVD (n=31/29)	0.42 (0.15)	0.004	0.04 (0.02)	0.007	0.05 (0.02)	0.020
Diabetes-related death (n=24/24)	0.34 (0.15)	0.019	0.04 (0.02)	0.038	0.08 (0.02)	<0.001

*Adjusted for updated mean HbA1c
CVD: cardiovascular disease, DBP: diastolic blood pressure, HbA1c: hemoglobin A1c, MOD: major outcomes of diabetes, SBP: systolic blood pressure, SE: standard error

[Poisson models for updated mean HbA1c/SBP/DBP with major complication outcomes of diabetes]

O04

Acute hyperglycemia may impair driving skills of young T1DM patients

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Objectives: Diabetic drivers are at a greater risk to be involved in road accidents. Acute hyperglycemia (AH) leads to cognitive impairments and has been recently found to impair sensory ability and motor response. However, no study has investigated the effects of AH on driving. We aimed to evaluate the effects of AH on type 1 diabetes mellitus (T1DM) drivers' abilities to anticipate and react toward simulated traffic hazards in comparison to euglycemic state.

Research Design and Methods: 18 T1DM drivers (24 ± 5 years of age) were asked to navigate through nine hazardous scenarios in a driving simulator during continuous euglycemic state (ES) (138 ± 34 mg/dL) and AH (321 ± 29 mg/dL) in a counterbalanced crossover design.

Driving performance was continually monitored by the driving simulator system which collects a large number of vehicle parameters (driving speed, steering wheel angle, acceleration) and other driving related parameters (location of other vehicles and obstacles) and by a mobile eye tracking system that is able to monitor the participant's eye and provide the gaze location on the virtual world.

Results

- Participants during AH were less likely to identify a hazard- Probability of identification (POI): 56.6 ± 0.5 compared to ES. POI: 68.6 ± 0.5) $p < 0.01$.
- During AH participants had a fewer number of glances on the hazard (3.2 ± 5.8) compared to ES (3.5 ± 6.7) $p < 0.05$.
- Under AH participants maintained a shorter mean headway distance (40.9 ± 20.2m) Vs euglycemia (50.5 ± 26.1m) $p < 0.01$.
- AH were associated with more breaks per Km driven: 6.7 ± 5.2 Vs 4.3 ± 3.9 ($p < 0.01$).

Conclusions: Driving performance of T1DM is significantly impaired at AH state. This study provides evidence to the negative effects of AH on important driving skills such as hazard perception and speed management.

O05

Incidence and risk factors of microvascular complications among adolescent onset type 2 diabetes from a tertiary care diabetes centre in South India

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Objective: To determine the risk factors and incidence rates of microvascular complications among adolescent onset type 2 diabetes (T2DM).

Methods: From 1992 to 2017, we recruited 677 adolescent onset (diagnosed between the ages of 10 and 19 years) T2DM patients (defined by absence of ketosis, good beta-cell reserve, and good response to oral agents) from a tertiary diabetes centre in Chennai, India. We calculated the incidence rates of retinopathy (presence of at least one definite microaneurysm by retinal photography), nephropathy (urinary albumin excretion ≥ 30 $\mu\text{g}/\text{mg}$ of creatinine) and neuropathy (vibration perception threshold $\geq 20\text{V}$) per 1000 person-years by the number of new events which occurred between the first visit and the follow up visits divided by the sum of follow-up years from their respective first visit to onset date for each complication.

Results: The mean age at diagnosis and age at first visit were 16.3 ± 2.3 and 22.2 ± 3.6 years respectively. The mean duration of follow up

was 5.4 ± 4.0 years. The incidence rates of complications were as follows: retinopathy, 23.5 per 1000 person years (Confidence Interval (CI): 15.9 - 34.8), nephropathy, 27.2 (CI: 18.7-39.7) and neuropathy, 5.7 (CI: 2.1-15.2). Duration of diabetes was the major risk factor for incident retinopathy (Hazard ratio:1.21;CI:1.08-1.35; $p < 0.001$) while serum cholesterol levels was the major risk factor for neuropathy (Hazard ratio:1.02;CI:1.00-1.05; $p = 0.041$).

Conclusion: There is a high incidence of microvascular complications in adolescent onset T2DM patients in South India. This calls for early diagnosis and aggressive treatment of this group of individuals.

O06

Longitudinal changes of retinal vascular caliber in adolescents with type 1 diabetes

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Objective: To describe the longitudinal trajectories of retinovascular geometry (RVG) measures in adolescents with type 1 diabetes (T1D). RVG measures allow serial non-invasive assessment of diabetes-related vascular changes. Despite previous studies examining the significance of single RVG measures on later complications, longitudinal data on RVG measures are lacking.

Research Design and Methods: This was a longitudinal study of 163 adolescents with T1D. RVG from retinal fundal photographs was analyzed by an experienced grader using a semi-automated computer program. Parameters included vessel calibers in the "central zone": central retinal arteriolar and venular equivalents (CRAE and CRVE respectively); calibers in the "extended zone": mean width of arterioles and venules (MWa and MWv respectively); tortuosity and fractal dimensions of arterioles and venules. Generalized estimating equations (GEE) were used to explore associations between vessel calibers, diabetes duration, and HbA1C.

Results: After a median 3.1[IQR 2.1-4] years follow-up, mean calibers in central and peripheral vessel significantly increased (Table). Other retinal RVG measures (tortuosity and fractal dimensions) remained stable. In GEE analysis, longer diabetes duration was significantly associated with central (CRAE β 0.8(95% CI 0.3, 1.3) μm , CRVE 1.2(0.5, 1.9) μm), and peripheral calibers (MWa 0.4(0.2, 0.7) μm ; MWv 0.5(0.2, 0.9) μm). HbA1C was only significantly associated with peripheral venules (MWv 0.7(0.01, 1.4) μm).

Conclusions: We observed a progressive increase in both central and peripheral retinal vessel calibers in adolescents with T1D. Diabetes duration and HbA1C were positively associated with vessel calibers suggesting diabetes impairs retinal endothelial function and vascular autoregulation.

	Visit 1 Mean(SD) N = 163	Visit 2 Mean(SD) N = 158	Visit 3 Mean(SD) N = 145	Visit 4 Mean(SD) N = 102	Visit 5 Mean(SD) N = 55	p Value
Age (years)	14.4 (1.5)	15.9 (1.6)	16.7 (1.6)	17.6 (1.5)	18.8 (1.5)	<0.001
HbA1C %	8.3 (1.3)	8.6 (1.6)	8.7 (1.6)	8.6 (1.3)	8.6 (1.1)	0.04
Diabetes duration (years)	7 (3.1)	8.7 (3.1)	9.6 (3.1)	10.3 (3.1)	11.9 (3.1)	<0.001
CRAE (μm)	157 (14)	161 (14)	166 (13)	173 (10)	172 (11)	<0.001
CRVE (μm)	222 (20)	228(20)	235(18)	244(16)	242(18)	<0.001
MWa (μm)	76 (7)	79 (8)	81 (7)	85 (6)	84 (7)	<0.001
MWv (μm)	88 (9)	90 (9)	92 (10)	96 (9)	95 (8)	<0.001

* Comparison made by using ANOVA

[Trends in clinical characteristics and retinal vascular caliber]

O07

Prevalence and predictors of impaired awareness of hypoglycemia in a contemporary pediatric type 1 diabetes population - the Norwegian Childhood Diabetes Registry (NCDR)

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Objectives: To determine the prevalence and predictors of impaired awareness of hypoglycemia (IAH) in a contemporary pediatric Type 1 diabetes (T1D) population.

Methods: We conducted a nationwide population-based cross sectional study using a validated self-report questionnaire ('Clarke') to assess awareness of hypoglycemia. Parents responded in children <9 years of age. Awareness status were coupled with clinical data collected annually in the NCDR. Multiple logistic regression methods were used to identify risk factors for IAH in those aged < and ≥ 9 years separately and preliminary results are presented.

Results: 21 centers included 1329 (53% males) valid participants whose mean (SD) age was 12.7 (3.8) years, T1D duration 5.4 (3.6) years, and HbA1c 8.0 (1.1)% (64 mmol/mol). The prevalence of severe hypoglycemia (SH; loss of consciousness with or without seizures) the preceding year was 3.5%, insulin pump therapy was used by 77%, and real-time continuous glucose monitoring (RT-CGM) by 39% of the participants. The overall prevalence of IAH was 22%, but was higher in those aged <9 years (43% vs. 18%). IAH was associated with SH the preceding year, but only in those aged ≥ 9 (five-fold increase). In both age groups, IAH was associated with increased fear of hypoglycemia. Younger age and female sex predicted IAH in those aged ≥ 9 . Metabolic control, T1D duration, pump therapy and use of RT-CGM did not predict IAH.

Conclusions: The prevalence of IAH in this contemporary pediatric T1D population was similar to the prevalence in adults with T1D. Younger age, history of SH and fear of hypoglycemia were associated with IAH, whereas tighter metabolic control and T1D duration were not.

O08

Diagnostic accuracy of serologic screening tests for celiac disease in asymptomatic adults and children with type 1 diabetes

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Background: As related autoimmune conditions, celiac disease (CD) is more common in individuals with Type 1 Diabetes (T1D) and is frequently asymptomatic. The clinical performance of CD serologic testing parameters was evaluated as part of the Celiac Disease and Diabetes Dietary Intervention and Evaluation Trial (CD-DIET).

Methods: T1D patients, aged 8-45 yrs, were serologically screened for CD at multiple centers across Ontario, Canada. Patients were deemed asymptomatic on the basis of the absence of GI symptoms, weight changes, and anemia and other CD-related clinical features. Screening was conducted in 2,386 subjects using chemiluminescent (CL, BioFlash™) and/or ELISA (Celikey™) tissue transglutaminase (TTG) IgA assays, yielding 140 positives. Of these, 104 subjects had a duodenal biopsy for CD confirmation (Marsh ≥ 2). Receiver operating characteristic (ROC) curve analysis was conducted and positive

predictive values (PPV) of available screening tests for CD were evaluated.

Results: CL and ELISA data were available for 100/104 and 36/104 subjects, respectively. The area under the curve of the ROC for CL TTG was 0.918, while the PPV using the manufacturer referenced upper limit (RUL) of 30 CU was 85.9% (95%CI: 82.3-90.8%). According to our data, an optimal cut-off of 156.5 CU, or 5.2 times the RUL, showed an improved PPV of 95.8% (95%CI: 92.4-100.0%). With

respect to ELISA TTG, the PPV was 94.4% at the RUL of 8 U/ml and reached to 100% at the optimal cut-off determined by our analysis of 58.7 U/ml, which translates to 7.3 times the RUL.

Conclusion: Results from serologic CL and ELISA TTG assays that were greater than 5 times the reported upper limit showed a high PPV for biopsy-confirmed CD in asymptomatic adult and pediatric T1D patients, which may help guide diagnostic evaluation in this population.

Oral Session II - Psychological Issues and DM Care

O09

Going to school with Type 1 diabetes in urban India: factors affecting diabetes self-care practices and school support

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T1D children need a supportive, safe and non-stigmatizing school environment for diabetes self-care activities. We looked at factors affecting this in urban Indian schools, both private (PS) and Government (subsidized/free-GS).

Methods: We administered a pre-prepared questionnaire to T1D patients & parents from Aurangabad, Delhi-NCR & Kanpur, and Hyderabad (west, north, south India respectively), about diabetes self-care and attitudes of school staff.

Results: 397 responded: 204(51%) boys; 277(70%) in PS; mean age 11.7 y (3-19.9 y); diagnosis age 7.2 y (0.7-17.6 y); diabetes duration 4.5 y (0.1-15.7 y). Mothers' education was low (illiterate or primary/middle school) in 23%; medium (high school) in 25%; high (graduate or higher) in 52%; fathers' was low 13%; medium 30% & high 57%. Parental education correlated with studying in PS. Taking insulin in school (52%) had significant positive correlation with parental education ($p < 0.001$), studying in PS ($p < 0.001$) & basal insulin being analog vs. NPH ($p < 0.001$), but unaffected by age or gender. Those taking insulin at school checked BG more often ($p < 0.001$). PS more often had medical room facility ($p < 0.003$), glucometer in medical room (82/87) and help by nurse ($p < 0.001$). Non-supportive behaviors (not allowing BG checks/taking insulin; excluding from sports/excursions) did not differ significantly between PS and GS, but the rare, openly hostile schools were PS in 11/12. Hypo awareness of staff was similar in PS vs. GS ($p 0.891$). Parent visited school daily in 17%, significantly more if highly educated or if child's age is $< 6y$ ($p 0.008$).

Discussion: Schools are in general supportive. Parental education and studying in PS imply higher SES: both correlated with better self-care. PS had better infrastructure, but equal frequency of non-supportive behaviors. HCPs may need to focus on lesser-educated parents and children in GS, to improve diabetes self-care. Increased awareness to reduce prejudices is needed across societal strata.

O10

The interplay between enteroviral infection and vitamin D metabolite levels in the onset of pediatric type 1 diabetes

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Introduction: Both enteroviral (EV) infection and low vitamin D levels are putative risk factors for T1D onset. Vitamin D deficiency can lead

to an increased susceptibility to infection and viral persistence. Several viruses have an apparent greater adverse effect when host vitamin D levels are low.

Objective: We aimed to examine the interplay between enteroviral infection and vitamin D levels in the onset of pediatric T1D.

Methods: We interviewed 333 incident T1D cases and 660 controls from 2008-2011 in Melbourne, Australia. Also, in nested case control studies, enteroviral presence by reverse transcription polymerase chain reaction and vitamin D metabolites, including 25(OH)D3 and 1,25(OH)2D3 were measured.

Results: Among participants with EV, the lowest 25(OH) D3 tertile (compared to the rest) was associated with an increased likelihood of T1D onset (AOR 5.26 (95%CI 0.62, 44.50) but not for those without EV (AOR 0.74 (95%CI 0.44, 1.24); difference in effect; $p = 0.09$). For 1, 25(OH) 2D3 the differences by EV status were even more marked. The lowest tertile of 1, 25 (OH) 2D3 was associated with an AOR of 18.75 (95%CI 1.33, 264.26) vs. 0.48 (95%CI 0.28, 0.82) among EV positive vs. EV negative children; difference in effect; $p = 0.004$. Other factors, including vitamin D related gene variants, were also examined.

Conclusions: An interaction between enteroviral infection and two vitamin metabolites, 25(OH) D3 and 1, 25(OH) 2D3 was observed with regard to the onset of pediatric type 1 diabetes mellitus. The implication of this for understanding T1D pathogenesis will be discussed.

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O11

Effect of frequency of sensor use on glycaemic control in children and adolescents with type 1 diabetes on sensor-augmented pump therapy

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Introduction: In short term trials, sensor-augmented pump therapy (SAPT) with Predictive Low Glucose Management (PLGM) has reduced hypoglycaemia without deterioration in glycaemic control in individuals with type 1 diabetes by enabling automated insulin suspension when hypoglycaemia is predicted (1); however, the effect of frequency of sensor use on glycaemic control in patients on sensor-augmented pump therapy with and without PLGM is not known.

Objective: The aim of this analysis is to determine the effect of percentage time of sensor use on glycated hemoglobin (HbA1c) with and without PLGM.

Methods: We performed a 6-month multicenter randomized controlled trial using the Medtronic MiniMed™ 640G pump in children and adolescents with type 1 diabetes; a control arm with SAPT alone and an intervention arm with SAPT and Suspend before low enabled (PLGM). The sensor use was calculated as the percentage of the number of participant recordings to the number of expected total recordings in six months. The percentage of sensor wear was described in four categories; $<40\%$, 40 to $<60\%$, 60 to $<80\%$ and $\geq 80\%$.

Results: An intention to treat population of 154 subjects was analyzed. The mean sensor use in the SAPT group and PLGM group at baseline, 3 months and 6 months was 88%, 74%, 63% and 83%, 78%, 65% respectively. An increased frequency of sensor use was associated with a greater reduction in HbA1c ($p < 0.001$). For every 1% increase in sensor use, the associated HbA1c reduction was 0.006% (95% CI 0.01, 0.003; $p < 0.001$). HbA1c was not significantly different in the SAPT and PLGM group independent of the percentage of sensor use ($p = 0.209$).

Conclusion: Increasing frequency of sensor use improves glycaemic control in patients on SAPT with and without PLGM.

Reference

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O12

Acceptance to insulin pump therapy increases with group installation and group education

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Background: Pump Initiation in non-government approved setting is always a problem. We took this entirely different initiative of pump education and initiation in T1DM children.

For the first time in the history of pump we used this method.

Aim: To study the impact of Insulin Pump initiation in group education program.

Material and Methods: A 3 hours insulin pump training workshop was organized for patients to educate them about insulin pump. In this program T1DM and next to the kin were involved. In this training program 30 patients were enrolled. These patients were taught about insulin pump and hands on experience were done. Out of 30 patients 12 patients were ready to get insulin pump installed, 4 patients postponed the installation due to lack of affordability. A group installation of insulin pump was done in 8 patients at a time and they were allowed to share their experiences about pump. A follow up study of these 8 patients continued and we evaluated the level of satisfaction among the group installation group v/s individual installation group from our past records.

Results:

Result	Group installation	Individual installation
Time for convencing	1 Session	4 to 5 Sessions
Self motivated	7 out of 8	No One
Age	16 yrs to 50 yrs	4 yrs to 40 yrs
Sex	Male-2, Female-6	Male-1, Female-4
Education	Till post-graduate	Till post-graduate

[Comparison between group and individual installation]

Conclusion: Group installation is superior to individual pump installation. Peer interaction helps in strengthening the learning process and smoothens insulin pump management.

O13

Psychometric properties of the preschool diabetes behavior checklist

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Objectives: Parents of young children with type 1 diabetes (T1D) report behavioral barriers to providing diabetes care (e.g., poor cooperation with shots, refusal to eat after taking insulin). These behaviors are often a focus of clinical intervention, but no measure of T1D-specific behavior problems in young children currently exists. We aimed to evaluate the validity and reliability of the new Preschool Diabetes Behavior Checklist (PDBC), which assesses T1D-specific problem behaviors in children 2-6 years old.

Methods: The 25-item PDBC was constructed for this study by psychologists and other experts in T1D with extensive input from parents of young children with T1D. The first 97 parents of children with T1D (M = 48 months \pm 12; 59% male, A1c M = 7.4 \pm 1.0) recruited as part of a larger randomized control trial completed the PDBC as well as measures of general problem behavior and T1D adherence.

Results: Principal component analysis suggested a 19 item, 2 subscale (general adjustment to T1D and eating/mealtime behaviors) solution for this measure. The revised, 19 item PDBC demonstrated good internal reliability for the total scale ($\alpha = .74$) and subscales ($\alpha = .69-.75$). Construct validity was demonstrated by a significant correlation between the PDBC total score and a measure of general problem behaviors. Worse eating/mealtime behaviors were also associated with general problem behaviors, while worse general adjustment to T1D behaviors were associated with older age and longer T1D duration (all $p < .05$). PDBC scores were not associated with HbA1c, adherence, gender or socioeconomic status.

Conclusions: The PDBC is a brief, reliable and valid parent-report measure of young children's T1D-specific problem behaviors and could be an innovative and actionable clinical and research tool. Mealtime behaviors may be particularly relevant for this age group. The ongoing RCT will evaluate test-retest reliability, predictive utility and sensitivity to a parenting intervention.

O14

Abstract Withdrawn

O15

Psychosocial health, quality of life and glycaemic control in Haitian youth with diabetes residing in Haiti

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Objectives: Reports on psychosocial health in youth with diabetes from low-income countries and their impact on glycaemic control and quality of life (QOL) are scarce.

Methods: Cross-sectional study of youth with diabetes diagnosed at ≤ 25 years from one chronic disease clinic in Haiti from 06/17-04/18. We obtained demographics, hemoglobin A1c (A1c) and administered transculturally adapted validated questionnaires on depression, self-esteem, perceived diabetes self-management efficacy (DM-SME), and diabetes related QOL (DM-QOL). Except for depression, scores were standardized to a scale from 0-100, with higher scores indicating better metrics. We used linear regression to evaluate the association between psychometric measurements and A1c, DM-QOL and DM-SME.

Results: 85 patients (58% F, age 17.5 \pm 5.1 y, diabetes duration 3.6 \pm 3.5 y) were included. Mean most recent A1c was 11.3 \pm 2.6%. Moderate to severe depression was present in 24/84 (28.5%) and was more common in females ($p = 0.01$). Median score for self-esteem was 60 (IQR 53, 67), for DM-SME was 66 (IQR 58,75), and for DM-QOL was 54 (IQR 46,61). Despite this, 52% reported "health today" as 90-100%. In older patients, self-esteem was lower ($p = 0.004$) and

depression trended higher ($p = 0.05$). Higher A1c was predicted by younger age ($p = 0.009$) but not sex, diabetes duration, or any of the psychometric measures. Better DM-QOL was predicted by higher self-esteem ($p < 0.001$), younger age ($p = 0.04$), and marginally by absence of depression ($p = 0.07$). Better DM-SME was predicted by higher self-esteem ($p = 0.006$) and a lower depression score ($p = 0.001$).

Significance: Haitian youth with diabetes have poor diabetes control and suffer from poor mental health and low self-esteem, impacting DM-QOL. Older patients are more at risk, despite better glycemic control. High prevalence of poor glycemic control and a large burden of other adversities may have masked an association between factors of psychosocial well-being and glycemic control.

O16

Using real time continuous glucose monitoring for weaning diazoxide dose in new-born with hyperinsulinemic hypoglycaemia: a case report

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Persistent uncontrolled neonatal hypoglycaemia may cause irreversible brain damage. Hyperinsulinemia is a cause of persistent hypoglycaemia. Pharmacologic therapy is added to facilitate weaning from IV glucose. The drug of first choice is diazoxide which suppresses the insulin secretion.

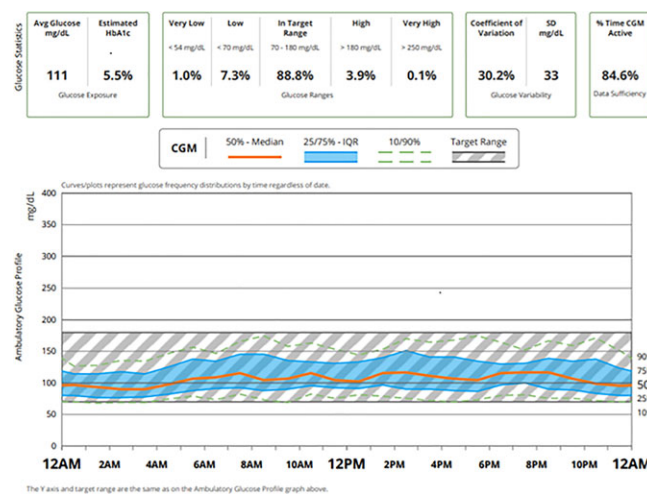
N is 1 month old term baby Girl, born at Term to non-consanguineous parents, mother has Gestation Diabetes mellitus uncontrolled during the pregnancy received Metformin 500 mg twice daily. Her weight, Height and Head circumference appropriate of her gestational age with no dysmorphic feature.

Admitted to Neonatal Intensive Care Unit due to asymptomatic hypoglycaemia (Blood Glucose 1.5 mmol/l) at 2 hours of age. Started Intravenous Dextrose and enteral feeding of Expressed breast milk total. Glucose infusion Rate titrated reached 12 mg/kg/min and showing hypoglycaemia attacks at day 10 of life.

Critical sample taken and showed non-ketotic hyperinsulinaemia with hypoglycemia.

Started Diazoxide (3 mg/kg/day increased gradually up to 10 mg/kg/day and chlorothiazide (7 mg/kg/day. Glucose polymer added to feed (EBM). Discharged day 31. One week after discharge started hyperglycaemia up to 12 mmol/l. Admitted to hospital to prevent Ketoacidosis, and to wean Diazoxide without hypoglycaemia. Dexcom G5 inserted and the dose weaned gradually till stopped based on Dexcom G5 glucose monitoring finding (Fig 1) that showed glucose trends with in target range with no evidence of hypoglycaemia.

Conclusion: Continuous Glucose Monitoring with real time glucose monitoring as in Dexcom G5 allow safe weaning of diazoxide dose in a baby with persistent hypoglycaemia due to hyperinsulinism. The use of CGMS gives insight about dose titration to avoid hypoglycaemia or severe iatrogenic hyperglycaemia



[Fig (1) The average Glucose values as tracked by Dexcom G5 over 14 days]

Oral Session III - Diabetes Care

O17

Primary care contact during the prodrome for childhood-onset type 1 diabetes (T1D): a national matched case-control study using pseudoanonymized-linked data to explore earlier opportunities for diagnosis

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Objectives: To evaluate contact with primary care during the prodrome of childhood-onset T1D, to explore opportunities for an earlier diagnosis to reduce the risk of ketoacidosis (DKA) at onset.

Methods: Contact with primary care in the 12 months prior to diagnosis was compared following pseudoanonymized linkage between cases (≤ 15 years) diagnosed between January 2000 & October 2015, from a prospectively collected national Welsh diagnostic diabetes (Brecon Group) dataset & controls without T1D, identified from primary care health records held in the SAIL Databank (matched for age, gender & primary care provider, on a 1:3 ratio). Read codes of symptoms, diagnoses & prescriptions for medication were grouped to form variables relating to a diagnosis of T1D. Conditional logistic regression modeling was used to compare the event of a symptom associated with T1D & those that presented in DKA.

Results: The study population comprised 1345 T1D cases (19% presented in DKA) & 4035 controls. During the 12 months prior to diagnosis, cases were 6.5 times more likely to have at least one primary care encounter compared to controls ($p < 0.001$) & had more encounters (median 4 v 3). One to 30 days prior to diagnosis, seven symptoms (blood testing, constipation, fungal or respiratory tract infections (RTI), urinary, vomiting & weight) were more likely to occur in T1D. Boys were 1.3 times more likely to present in DKA ($p = 0.047$). Children with a primary care encounter relating to urinary conditions 181 to 366 days prior to diagnosis were less likely ($p < 0.037$) to present in DKA whereas those relating to antibiotics, constipation, urine & vomiting, a month prior to diagnosis were more likely (p values vary from <0.001 to 0.049) to present in DKA.

Conclusions: There are likely opportunities in primary care for an earlier diagnosis of T1D in childhood. These data may be used to create a predictive diagnostic tool, as a potential aid for primary care health professionals.

O18

Inequalities in glycaemic control in children and young people with type 1 diabetes - a national population-based cohort study in England and Wales

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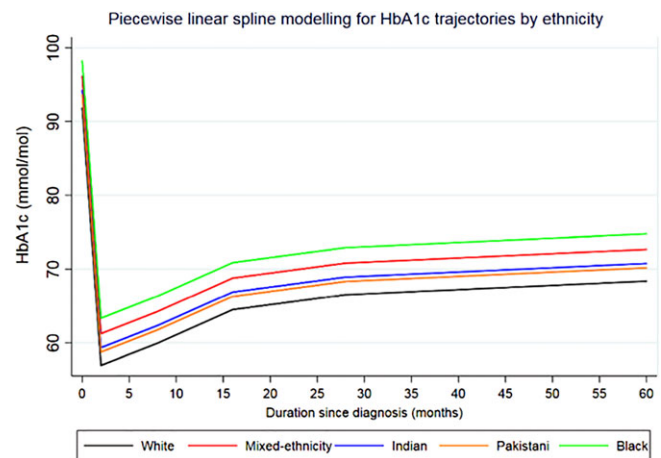
Objectives: To investigate ethnic and socioeconomic (SES) differences in glycaemic control in children and young people (CYP) with type 1 diabetes.

Methods: We undertook a longitudinal population-based cohort study of 20,777 CYP <19 years old and included in the National Pediatric Diabetes Audit (>95% of diabetes cases in England/Wales) attending 178 diabetes clinics between 2011-2015. Piecewise linear spline multilevel models were used to analyze ethnic differences in glycaemic control (HbA_{1c}) trajectories up to 5 years post-diagnosis (156,679 HbA_{1c} datapoints, mean 7.5 datapoints/subject), adjusting for sex, age and SES. The best fitting model allowed for changes in slopes at 2, 8, 16 and 28 months post-diagnosis. Ethnicity was self-identified and SES based on area-level indices of deprivation (grouped into quintiles).

Results: Mean age at diagnosis was 9 years, 47% of CYP were female and 78% were White. Mean HbA_{1c} at diagnosis was 97 mmol/mol. On average, HbA_{1c} decreased by 35 mmol/mol during the first two months, followed by a gradual increase (0.5 mmol/mol/month between 8 to 16 months, 0.6 mmol/mol/month between 16 to 28 months and 0.1 mmol/mol/month thereafter).

After adjustment for all covariates, mixed-ethnicity (mean difference 4 mmol/mol, 95% CI 3-6), Pakistani (2 mmol/mol, 1-3), Indian (2 mmol/mol, 1-4), and Black (6mmol/mol, 5-8) CYP had higher HbA_{1c} at diagnosis compared to White CYP (Figure). Compared to CYP in the poorest SES quintile, CYP in all other quintiles had on average lower HbA_{1c} at diagnosis with a dose-response relationship (-6 mmol/mol, 95% CI -6 to -5 for the richest SES quintile). Ethnic differences in HbA_{1c} trajectories remained constant during follow-up.

Conclusion: Large ethnic and socioeconomic inequalities in glycaemic control persist from diagnosis onwards. This is of concern as poor glycaemic control tracks into adulthood increasing risk for acute and chronic outcomes across the lifecourse.



O19

Effect modifiers of a behavioral intervention in adolescents with type 1 diabetes: the FLEX study

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The Flexible Lifestyles Empowering Change trial (FLEX) was an 18-month randomized trial to promote self-management and improve blood glucose control in 258 youth ages 13-16 with type 1 diabetes (T1D). The intervention used integrated motivational interviewing and problem-solving skills training tailored to patients' individual needs. The primary outcome, change in Hemoglobin A1c (HbA_{1c}), was not significant. This study aimed to identify subgroups that predicted treatment success, based on HbA_{1c} ($\leq 9.0\%$ vs $>9.0\%$), sex (female vs male), age (13-14 vs 15-16 years), and T1D duration (<5 vs ≥ 5 years) at baseline. Linear mixed models were fit to test whether the intervention effect was different by subgroups, with a random effect for participants and fixed effects for subgroup, site, timepoint, randomization status, and two- and three-way interactions between subgroup, timepoint, and randomization status.

The intervention effect was stronger for participants with high versus low HbA_{1c} at the 12-month time-point (p -for-interaction = 0.03), but

not at 18-months. The intervention effect was stronger for females vs. males at the 12 and 18-month time-points (p -for-interaction = 0.03 and 0.04, respectively; Table). The intervention effect did not differ based on T1D duration or age.

Youth with T1D who had high HbA_{1c} at baseline or were female benefited most from FLEX. Future interventions may be further tailored to these subgroups or modified to address other subgroups.

	Study time-point	Control* mean (SD)	Intervention mean (SD)	Model-estimated intervention effect on HbA _{1c} (p-value)
High HbA _{1c} (>9.0%)	12-months	10.33 (1.31)	9.91 (1.49)	-0.44 (.03)
High HbA _{1c} (>9.0%)	18-months	10.21 (1.46)	10.1 (1.66)	-0.15 (0.44)
Low HbA _{1c} (≤9.0%)	12-months	8.62 (1.09)	9.00 (1.08)	0.30 (0.21)
Low HbA _{1c} (≤9.0%)	18-months	8.87 (1.24)	9.15 (1.80)	0.22 (0.36)
Female	12-months	9.85 (1.63)	9.45 (1.13)	-0.50 (0.03)
Female	18-months	9.86 (1.74)	9.63 (1.43)	-0.34 (0.13)
Male	12-months	9.46 (1.29)	9.77 (1.63)	0.13 (0.54)
Male	18-months	9.46 (1.20)	9.93 (2.00)	0.26 (0.20)

The interaction p -value between HbA_{1c} group and intervention 0.03 at 12-months. The interaction p -value between sex and intervention was 0.03 and 0.04 at 12- and 18-months, respectively. All other interaction p -values were NS.

[Table: Intervention effects on Hemoglobin A1c (HbA_{1c}) at 12- and 18-months by HbA_{1c} group and sex]

O20

Basal to total insulin ratio and its association to HbA_{1c}, BMI-SDS and treatment modality in children with T1D from the international SWEET database

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Aims: This study aimed to investigate the ratio of daily basal insulin dose to daily total insulin dose (BD/TD) and association to metabolic control, BMI-SDS, and treatment modality in children with type 1 diabetes (TD1) from the international SWEET database.

Methods: Cross-sectional study among subjects with T1D ≤18 years and ≥2 years diabetes duration from the international SWEET database (March 2018). Variables included: Region, gender, age, diabetes duration, treatment modality (injection or pump), HbA_{1c}, daily basal insulin dose, daily total insulin dose, BMI-SDS, and occurrence of severe hypoglycemia and ketoacidosis events. WHO growth charts were used for BMI-SDS calculations. Hierarchic linear regression models were applied with adjustment for age, gender, diabetes duration, HbA_{1c}, BMI-SDS and treatment modality.

Results: A total of 19,687 patients with T1D (48.7% females) with median age 14.8 [11.5; 17.2] years and median diabetes duration 6.0 [3.9; 9.0] years were included. Median HbA_{1c} was 7.9 [7.2; 8.9] %, median BMI-SDS was 0.55 [-0.13; 1.21] and 49% was on pump treatment. Lower BD/TD was significantly associated to male gender, younger age, shorter diabetes duration, pump therapy (all $p < 0.001$), and no ketoacidosis events ($p < 0.01$). After adjustment, lower BD/TD (<0.5 versus ≥0.5) was related to lower HbA_{1c} and BMI-SDS ($p < 0.001$). After stratifying for treatment modality, the significant linear relation prevailed in pump therapy. When dividing BD/TD in three groups (<0.3, 0.3-< 0.6, ≥0.6), still the same linear relations between BD/TD and HbA_{1c} and BMI-SDS (comparing <0.3 to 0.3-< 0.6 and <0.3 to ≥0.6) prevailed ($p < 0.001$).

Conclusion: Lower BD/TD are associated with HbA_{1c}, and BMI-SDS in children with T1D, particularly in patients on pump treatment. These findings might be relevant in diabetes treatment recommendations to optimize treatment strategies for children with T1D.

O21

Real world use of hybrid closed loop therapy in pediatric patients with type 1 diabetes: a clinical observation study

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

Methods: Patients from a pediatric clinic starting the 670G for their routine T1D clinical care participated in this observational study. Data on HCL use and glycemic outcomes were obtained from device downloads and chart review during routine clinical care.

Results: The sample included 49 patients (15.3±3.3 yrs.; 51% M) with T1D for 6.4±4.2 yrs using the 670G. HbA_{1c} decreased from 8.9+1.5% prior to starting HCL mode to 8.4±1.3% at the first clinic follow-up (78±37 days after starting HCL; $p = 0.002$). Patients spent an average of 58±25% of each week in HCL mode, wore the sensor 67±23% of each week and checked BG 4.8±2.4 times/day. System exits from HCL mode to standard pump mode occurred 0.86±0.44 times/day, primarily due to hyperglycemia. Sensor glucose time in target range (70-180 mg/dl or 3.9-10 mmol/l) was 58±16% with 1% of sensor glucose values <70 mg/dl (3.9 mmol/l). Increased time spent in HCL mode was correlated with a lower mean sensor glucose and standard deviation of glucose, and increased time in target range. Increased sensor use and number of BG checks/day were also correlated with more time in auto mode (Table).

Conclusions: HCL use may improve glucose control for pediatric patients with T1D. However, hyperglycemia is a barrier to time in HCL mode for youth. Consistent sensor use is essential and frequent BG checks (4-6/day) are important to increasing time in HCL.

	% time HCL	r	p -value
% time sensor values 70-180 mg/dl (3.9-10 mmol/l)	0.66		<0.001
% time sensor glucose >250 mg/dl (>13.9 mmol/l)	-0.58		<0.001
% time sensor glucose <55 mg/dl (<3.0 mmol/l)	-0.21		0.16
% time sensor glucose 55-69 mg/dl (3.0-3.9 mmol/l)	0.12		0.43
Mean sensor glucose	-0.60		<0.001
Standard deviation of sensor glucose	-0.53		<0.001
# BG checks/day	0.35		0.02
% sensor wear	0.95		<0.001

[Pearson correlations between percent time in HCL and glucose variables and behavior]

O22

The Australasian Diabetes Data Network (ADDN): national benchmarking across the age spectrum

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Introduction: The ADDN Registry is a national longitudinal prospective database that offers a unique opportunity for the long-term surveillance of diabetes outcomes in both youth and adults with T1D across Australia and New Zealand. The ADDN benchmark report provides a contemporary real-world snapshot of treatment patterns and outcomes on more than 12,000 people with T1D.

Methods: Inclusion criteria were diagnosis of T1D with a follow-up visit from 01/01/2017 to 31/12/2017. Outcome measures were HbA1c, Body Mass Index and/or Standard Deviation Scores (BMI-SDS) and insulin regimen: twice daily injection (BD), multiple daily injection (MDI), continuous subcutaneous insulin infusion (CSII) or other.

Results: 4791 (49% female) pediatric patients and 1760 (48% female) adult patients from 13 tertiary diabetes centers in NSW, QLD, SA, VIC, WA and New Zealand met the inclusion criteria. In youth (aged < 18.0 years) mean (\pm SD) age was 12.1 ± 3.9 and T1D duration 4.8 ± 3.8 years. Mean BMI SDS was 0.6 ± 0.9 and HbA1c $8.3 \pm 1.4\%$, with 28% achieving a HbA1c of <7.5% (58 mmol/mol). Overall, 39% were treated with CSII, 38% MDI and 17% with BD regimens. In adults (aged ≥ 18.0 years at visit) mean age was 39 ± 16 , and T1D duration 17.6 ± 13.1 years. Mean BMI was 26.8 ± 5.5 and HbA1c $8.4 \pm 1.7\%$, with 14% achieving a HbA1c of < 7.0% (53 mmol/mol). Overall, 20% were treated with CSII, 57% MDI and 5% with BD regimens.

Conclusions: The majority of people with T1D in ADDN do not currently meet the recommendations for glycaemic control or healthy weight. By providing diabetes centers an opportunity to compare their own care practices and outcomes through benchmarking with other centers, ADDN has a pivotal role in driving change in clinical practice and improving patient outcomes.

O23

Supporting students with type 1 diabetes at school is associated with better glycaemic control and other benefits

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Aim: To understand the characteristics and consequences, including association with glycaemic control, of parents feeling supported or not supported in the management of their child with Type 1 Diabetes (T1D) at school.

Methods: An anonymous on-line survey (SurveyMonkey) was conducted in 2017 and open to any Australian parent of a child with T1D at school. Responses of being well supported in school with few

deficiencies were assigned to the supported (S) group. Responses with significant support deficiencies were assigned to the not supported (N) group. Difference between the groups was then tested for significance by chi square analysis.

Results: 394 respondents from all Australian states, all school levels and private / public school models participated. The S group comprised 216 (55%) responses. The S group had 45% students with HbA1c <7.5% compared to 34% in N group ($p = 0.04$). The N group had 19% students with HbA1c >9% compared to 3% in S group ($p < 0.001$). The S group were characterized by a Diabetes Management Plan (65% vs 49%) ($p < 0.001$), staff well trained in complex T1D care (30% vs 13%) ($p < 0.001$), and adequate Government funding (16% vs 3%) ($p < 0.001$). The N group reported school staff with direct student responsibility having inadequate T1D knowledge (88% vs 34%) ($p < 0.001$).

The S group reported less discrimination (8% vs 51%) ($p < 0.001$) and confidence in the school managing exercise (67% vs 24%) ($p < 0.001$). The N group reported inadequate hypoglycaemia supervision (31% vs 5%) ($p < 0.001$), more parents feeling a nuisance for advocating for their child (41% vs 9%) ($p < 0.001$) and more parents changed jobs to support their child at school (53% vs 24%) ($p < 0.001$).

Conclusion: Parental perception of feeling supported with their child's management in school is associated with better outcomes with improved glycaemic control and other moral benefits including less discrimination and burden on families.

O24

Use of real-time continuous glucose monitoring (RT-CGM) and bolus-calculator gave better metabolic control - the Norwegian Childhood Diabetes Registry (NCDR)

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Objectives: To assess the use of RT-CGM and bolus calculator in a nationwide, population-based cohort of children and adolescents with type 1 diabetes (T1D) in Norway in relation to HbA1c and acute complication.

Methods: The Norwegian Childhood Diabetes Registry (NCDR) is a nationwide population based registry covering all pediatric departments and 98% of all children with T1D in Norway. Standardized examinations from 98% of all Norwegian with T1D, age 0-17y in 2017 were reported to NCDR.

Assessing the use of real-time continuous glucose monitoring (RT-CGM) and bolus-calculator is part of the standardized annual examination. Only reported use of bolus calculator more than 50% of the time was included. Severe hypoglycemia (SH) is defined as having seizures and/or unconsciousness. DKA is defined as pH < 7.3 or bicarbonate <15 mmol/l, ketonemi and ketonuria.

Results: The study population included 2741 individuals (54.4% boys) with T1D. Mean age 12.9y, mean diabetes duration 5.3y, 73% on insulin pump. 49.6% reported using CGM, an increase from 32.8% in 2016. 44.5% reported using bolus calculators, an increase from 39.9% in 2016. 26% reported using both CGM and bolus calculator, 50.4% boys. More boys used CGM than girls, 53.5% vs. 47.0%, and bolus calculator, 50.5% vs 49.5%. In both gender the age group 10-14y had the highest proportion of only CGM (41.1%), only bolus calculator (45.5%) and both together (42.9%). Patients not using CGM or bolus calculator had mean HbA1c 8.1% (65 mmol/mol). HbA1c was significant lower ($p < 0.001$) in patients using:

- (1) Bolus calculator HbA1c 7.7% (65 mmol/mol),
- (2) CGM HbA1c 7.7% (61 mmol/mol),
- (3) CGM + bolus calculator HbA1c 7.5% (58 mmol/mol).

It was no difference in SH (3.3%) or DKA (2.5%) between the patients using CGM and/or bolus calculator, or not using.

Conclusion: An increasing number of children with T1D in Norway use CGM and bolus calculator. The use of CGM and bolus calculator gives better metabolic control.

Oral Session IV - DM in Developing Countries and Nutrition

O25

Ratio of glycated albumin to glycated hemoglobin identifies hemoglobin glycation phenotype in each diabetic and non-diabetic subject

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Objectives: To clarify that ratio of glycated albumin (GA) to glycated hemoglobin A_{1c} (A1C), GA/A1C ratio, was individually consistent as glycation gap (G-gap) in both diabetic and non-diabetic subjects, if using A1C in either IFCC or KO500 A1C standardizing method not containing non-glycated hemoglobin, A1C_{IFCC} and A1C_{KO500}, respectively.

Methods: An individual mean GA/A1C ratio in each T1D subject (n = 544) was obtained over time, that in each NDF subject (n = 433) at the time of registration. The internationally standardized NGSP A1C (A1C_{NGSP}) value was certified by Japan Diabetes Society calibrator set (Lot 5) with assigned A1C_{KO500} value for traceability in Japan. A1C_{NGSP} value was converted to A1C_{KO500} value by the equation according to Lot5 and to A1C_{IFCC} value by the international master equation.

Results: Correlations between glycation gap and GA/A1C_{NGSP}, GA/A1C_{KO500} or GA/ A1C_{IFCC} ratio in T1D were inverse, $r = -0.86$, $r = -0.98$ and $r = -0.98$, respectively, while those in NDF were also highly inverse, $r = -0.95$, $r = -0.995$ and $r = -0.99$, respectively. Correlations between GA/A1C_{KO500} and GA/ A1C_{IFCC} ratios in T1D and NDF were higher ($r = 0.99$ and $r = 0.999$, respectively) than those between GA/A1C_{NGSP} and GA/A1C_{KO500} ratios ($r = 0.91$) and between GA/A1C_{NGSP} and GA/ A1C_{IFCC} ratios ($r = 0.91$) in T1D and those between GA/A1C_{NGSP} and GA/A1C_{KO500} ratios ($r = 0.97$) and between GA/A1C_{NGSP} and GA/ A1C_{IFCC} ratios ($r = 0.75$) in NDF. GA/A1C ratios showed significant correlations between T1D and NDF with paternal predominance.

Conclusions: An individual GA/A1C ratio more accurately identified hemoglobin glycation phenotype using Z-score of GA/A1C_{KO500} or GA/ A1C_{IFCC} ratio than that of GA/A1C_{NGSP} ratio in Japanese T1D subjects or NDF subjects. The GA/A1C ratio Z-score will be epidemiologically comparable between each population regarding prediction of complications, type of diabetes, ethnicity, heredity and so forth, while G-gap cannot apply to such comparison between populations.

O26

Hemoglobin A1c trajectory over the first 3 years of type 1 diabetes diagnosis

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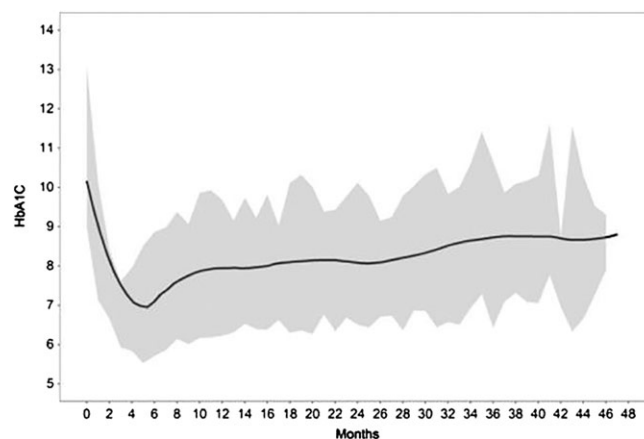
Objective: A majority of pediatric patients with type 1 diabetes (T1D) do not meet the ISPAD HbA_{1c} target. The purpose of this study is to characterize the HbA_{1c} trajectory over time following T1D diagnosis and to identify opportunities to intervene to maintain tight glycaemic control.

Methods: We reviewed HbA_{1c} data from pediatric patients (age 3-21 years) diagnosed with T1D at Stanford University between June 2014 to December 2016 (n = 272) to evaluate HbA_{1c} trajectory over time.

We used local regression scatter plot smoothing techniques (LOESS) for this purpose (Figure 1).

Results: HbA_{1c} distribution increased at 6-, 12-, and 18-months post diagnosis. HbA_{1c} declined in children with new onset T1D from $11.0 \pm 2.0\%$ at diagnosis to $7.3 \pm 1.6\%$ at 6 months post-diagnosis (Figure 1), consistent with decreased insulin requirements after initial glycaemic stabilization. However, as the need for exogenous insulin increases, the mean HbA_{1c} rises to 8.0% by 1 year post-diagnosis. At 18 months post-diagnosis, the mean HbA_{1c} increases to 8.2% and remains stable, which is consistent with Stanford's SWEET registry HbA_{1c} data.

Conclusions: Our data indicate that individuals with new onset T1D have an inflection point in their glycaemic control 6 months post diagnosis. Clinical resources should focus on robust diabetes education and timely multi-disciplinary clinical interventions in the first year after diagnosis to maintain lower HbA_{1c} and improve long-term outcomes.



[Figure 1. Mean HbA_{1c} (line) and standard deviations for each time point following diagnosis of T1D.]

O27

A study of islet antibodies (GAD, IA2 and ZnT8) in Indian type 1 diabetic patients

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Introduction: Type 1 Diabetes (T1D) is characterized by auto-immune destruction of beta cells in pancreatic islets. There are limited reports on islet antibodies on Indian T1D patients. We planned a study to measure islet antibodies in Indian T1D patients.

Objective: To study plasma C-peptide concentrations, Islet antibody status of clinically defined Indian T1D patients.

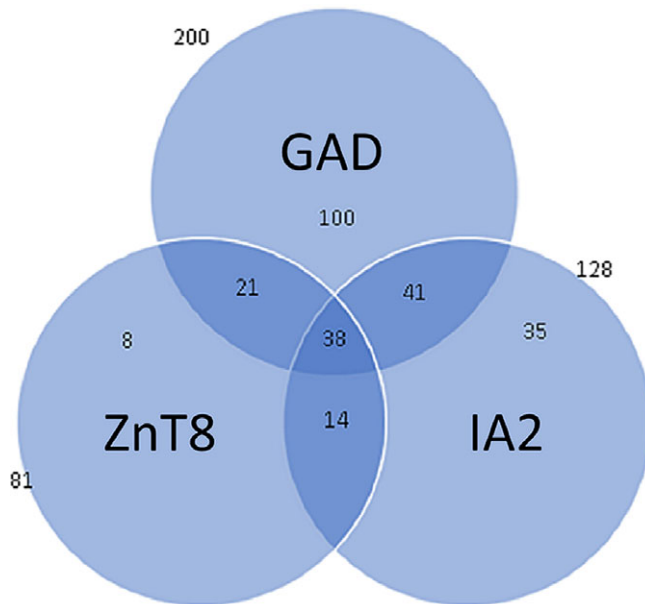
Methods: Random plasma blood samples were collected from 357 (42% male) young patients attending Diabetes Unit, KEM Hospital, Pune. Patients were clinically defined as T1D (diagnosed <30years of age, ketosis at presentation or subsequently, and clinical dependence on insulin treatment). Islet Antibodies [Glutamic acid decarboxylase (GAD), Islet Antigen-2 (IA2), Zinc Transporter Protein (ZnT8)] were measured using ELISA-kits. We studied associations of antibody positivity with age at diagnosis, duration of diabetes using multivariate logistic regression.

Results: Median age at diagnosis was 9.8years (19% <5years and 11% ≥18 years) and median duration of diabetes was 4.1 years (31% <1year & 16% >15years). Median C-peptide was 22.8pmol/l (41% undetectable, 16% >200 pmol/l). GAD was the most prevalent (58 %

compared to IA2 (37%) and ZnT8 (24%); 74% had at least 1 antibody and 11% had all 3 antibodies. 16% had either IA2 or ZnT8 antibody in absence of GAD.

Prevalence of antibodies decreased with duration of diabetes: GAD [<1 year (76%), 1-5 yrs (62%), >5 years (42%)]. GAD prevalence was higher in those diagnosed older [<9.8 years (53%), ≥ 9.8 years (63%)] but not for IA2 and ZnT8. Antibody prevalence was not influenced by C-peptide level and there was no interaction between age at diagnosis and duration of diabetes.

Conclusion: This is the 1st comprehensive report of islet immunity in Indian T1D patients. GAD antibody was more prevalent and ZnT8 least prevalent. In clinical practice, C-peptide and GAD will help to confirm T1D diagnosis in Indians.



[Islet antibodies (GAD, IA2, ZnT8) among 357 Indian T1D Patients]

O28

Providing free insulin pumps to T1D children: challenges and opportunities- insights from our KT1DP initiative

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Background: Type 1 diabetes (T1D) management demands strong commitment and enthusiasm. Despite the best efforts, some still fail to achieve targets with MDI, making them potential candidates for insulin pump therapy (IPT). In India, the lack of a reimbursement policy or free governmental supply is a major barrier in providing affordable IPT. We initiated Kesavadev trust T1D Project (KT1DP) to provide free insulin pumps and accessories to deserving T1D children consulting our diabetes clinic.

Objectives: Challenges and opportunities associated with implementing this humanitarian project were evaluated.

Methods: A brief survey among our multidisciplinary diabetes care team appraised the challenges faced while implementing KT1DP and the feasible recommendations. Clinical improvements achieved by the beneficiaries (n = 5; age: 17.4 ± 3.29 years; T1D duration: 6.62 ± 3.11 years; IPT duration 11.25 ± 5.91 months) were evaluated.

Results: HbA1c improved ($11.13 \pm 0.66\%$ vs $8.47 \pm 1.55\%$, p = 0.026), and patients met with lesser events of hypoglycemia and no events of DKA. Major challenges: i) unlike educated patients, the extent of awareness, training, and support to be provided to this group was high; ii) with the availability of free resources, irresponsible

nature and tendencies of the participants to misuse the supplies seemed to be high.

Conclusions: In developing countries where even insulin is unavailable, IPT is a farfetched dream. Policy-makers should recognize the significance of such life-saving modalities and take steps to foster reimbursement policies. The demand of extra time and resources to manage, especially the uneducated beneficiaries, will remain a major challenge. Another underlying risk will be bearing the responsibility of any mishaps arising from the inappropriate use of the technology. Beneficiaries should be educated on the advantage they are at with regard to obtaining such a costly treatment at no cost, which is essentially meant for 'providing a life'.

O29

Six months of gluten-free diet lowers insulin requirement but does not influence residual beta-cell capacity in children with recent T1D onset

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Objectives: Recent evidence suggests a potential role of gluten in type 1 diabetes (T1D) pathogenesis but the data on this matter are scarce. The aims of this one year study were to test whether the gluten-free diet (GFD) instituted shortly after T1D onset can decelerate the decline in beta-cell capacity and influence T1D management in T1D children without celiac disease. Here we present the preliminary results at 6 months.

Methods: Thirty-five children (24 boys, 11 girls, mean age 11.6 ± 3.4 years) with recent T1D onset (maximum 6 weeks) were prospectively recruited into this intervention study. The intervention group (n = 19) started with strict GFD whereas the control group (n = 16) remained on standard gluten-containing diet. The change in residual beta-cell function was tested by decline in C-peptide area under the curve (AUC) in mixed-meal tolerance tests performed at months 1 and 6. Secondary outcomes included the differences in HbA1c and insulin dose adjusted A1c (IDAA1c). All intervention effects and p-values were adjusted for baseline imbalances in gender, age at T1D onset, HbA1c, insulin dose, C-peptide AUC and IDAA1c in regression models. The adherence to the diets was tested every three months by immunoreactive gluten in stool samples.

Results: There was no effect of GFD on C-peptide AUC at 6 months. Mean decrease in C-peptide AUC was 234 pmol/L and 472 pmol/L in GFD and control group, respectively (NS). Children on GFD had significantly lower mean insulin dose by 0.2 U/kgBW/day (p < 0.01), by 12.4% lower HbA1c (p = 0.06) and by 19.4% lower IDAA1c (p < 0.005) compared to control group. The adherence to GFD was excellent, immunoreactive gluten was found in stool of only one patient who was excluded from analysis.

Conclusions: Our results suggest that GFD leads to lower doses of insulin to maintain similar levels of HbA1c without significant differences in residual beta-cell capacity in children with T1D six months after T1D onset.

O30

Clinical characteristics of type 1 diabetes mellitus among children and adolescents in Mexico

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Objectives: Determine demographic and clinical features of children and youth supported by member associations of the Federación Mexicana de Diabetes, with supplies and other resources provided by the International Diabetes Federation Life for a Child Program.

Methods: Analysis of the 2017 Annual Clinical Data Sheets of 306 subjects from five centres across Mexico.

Results: Two hundred and eighty-eight subjects were diagnosed with type 1 diabetes (T1D), nine with type 2 diabetes (T2D), three with other causes, and six had "neonatal diabetes" with onset <6 months of age (two were siblings both diagnosed at birth). Genetic testing has not yet been conducted.

Further analysis was done on the 2882 type 1 subjects. Age at diagnosis was 1.2-22.6 years (peak onset was 8 years), with 23.7% <5 years, 44.3% 5-<10 years, 27.9% 10-<15 years, 4.2% >15 years. 54.2% were female. Duration since diagnosis was 5.3 (0.1 - 20.6) years, with subjects 10.7 ± 4.2 (mean \pm SD) years of age at check-up.

In the T1D subjects, 1.0% were receiving 1 injection per day, 6.6% were receiving 2 injections per day, 12.9% 3 injections, and 79.4% 4 or more injections. Mean \pm SD insulin usage was 0.91 ± 0.35 Units/kg. Mean blood glucose tests per week was 39. Mean/median HbA1c for those with duration ≥ 6 months were 8.8/8.4% (73/68 mmol/mol) and were higher in adolescents. Creatinine levels were normal in all subjects (n = 193). Elevated BMI SD, fasting triglycerides (≥ 150 mg/dl), and total cholesterol (≥ 200 mg/dl) were common: 8.0%, 10.6%, and 14.0% (n = 288, 216, and 222) respectively.

Conclusions: Children with diabetes in less-resourced families are achieving reasonable glycaemic control despite limited resources. Some youth however have adverse vascular risk factor profiles. Further attention is needed to prevent, screen for, and treat chronic complications. Monogenic cases appear to be occurring and genetic testing is indicated.

O31

Decline of beta-cell function in T1D patient from India

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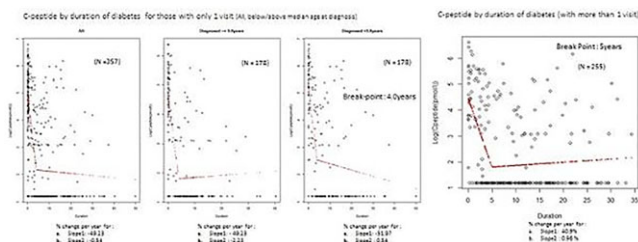
Introduction: Type 1 Diabetes (T1D) is a result of autoimmune destruction of β -cells in the pancreas. There is little information on the rate of fall of C-peptide (a marker of β -cell mass) with time. Recent studies in the UK have shown a bi-phasic loss of C-peptide in European T1D patients.

Objective: To investigate C-peptide concentrations in Indian T1D patients over time in a cross-sectional and longitudinal analysis.

Methods: Random plasma blood samples were collected from 357 patients [508 Observations (1 in 357, >1 in 153)] attending Diabetes Unit, KEM Hospital, Pune. These patients were clinically defined as T1D (diagnosed <30 years of age, ketosis at presentation or subsequently, and clinical dependence on insulin treatment). C-peptide was measured on Cobas-e411 using Cobas C-peptide kit. Non-parametric regression modeling was used to explore the association between duration and log-C-peptide. Segmented regression was done to model the pattern revealed.

Results: Non-parametric regression suggested a 2-phase (1st phase: log-linear decline, 2nd phase: a flatten-out) shape of log-C-peptide over duration of T1D. Segmented regression determined the optimal breakpoints as 4.0 years (cross-sectional data) and 5.0 years (longitudinal data) from diagnosis. In the first phase, C-peptide declined by 49% /year (Cross-sectional data), 41%/year (Longitudinal data); in the 2nd phase by 0.54% per year (Cross-sectional data), 0.96% (Longitudinal data) suggesting a stable period with no further decline. Analysis for those diagnosed \leq /> 9.8years (median age at diagnosis) revealed no difference in the slopes of decline.

Conclusion: Our results replicate results in T1D patients from the UK (B.Shields et al, Diabetes Care in press), and reinforces the importance of understanding the mechanisms involved in β -cell destruction.



[Figure 1: Segmented regression of C-peptide by duration of diabetes]

O32

Retrospective case reviews of children with type 1 diabetes following low carbohydrate diets, less than 40% daily energy requirement (EAR) against the advice of the multi-disciplinary team from Young Diabetes Connections (YDC) Network, and Queen Mary's Hospital London

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Introduction: Low Carbohydrate diets (LCD) are becoming popular in pediatric Type 1 diabetes to decrease HbA1c.

Objectives: Review of patients on LCD with those who ceased it.

Methods: Case notes review of 6 patients (m = 6)

Results: A, 1.3 yrs, started LCD 60-109g/day, 22-29% EAR weight 11.3 kg (0z), height 80.6 cm (1z), HbA1c 42-51 mmol/mol. Weight rose 18.2 kg (3.495z), height 93.4 cm (1.978z). At 3.34 yrs at 45% EAR weight 16.98 kg (1.06z) height 101.2 cm (0.79z), HbA1c 53 mmol/mol. B, 3.2 yrs, started LCD 20 g/day, 7% EAR. HbA1c down 60 to 48 mmol/mol. After 6 months weight static 14.8 kg (0.08z), height 98.4 cm (0.26z) to 99.4 cm (-0.25z). At 4.5 yrs on 40 g/d 11% EAR weight 17.5 kg (0.01z) height 103.8cm (0.0z), HbA1c 53 mmol/mol. C, 6 yrs, started LCD 61-114 g/day, 13-28% EAR. HbA1c 38 to 54mmol/mol, weight 22.2 kg (0.638z), 120 cm (1.037z). 11 months on weight 25.98 kg (0.83z), 128cm (1.164z). 20 months on LCD growth slowed weight 27.1kg (0.598z), height 132.2 cm (1.14z) HbA1c 45 mmol/mol.

D, 8 yrs started LCD 111 g/day 25% EAR. HbA1c down 75 to 67 mmol/mol, growth slowed, weight static at 31 kg (1.03z) height 138.9 cm (1.75z) to 140.4 cm (1.51z). Off LCD growth improved, weight 40.2 kg (1.04z) height 151 cm (1.52z) HbA1c stable at 56 mmol/mol.

E, 10 yrs started LCD, 81 g/day (26% EAR). HbA1c down 79 to 40 mmol/mol in 6 months, but weight dropped, 39.3 kg (0.93z), to 38.36 kg (0.61z), height; 148.5 cm (1.18z), 150.2 cm (1.08z). Now growth slowing weight 39.4 (0.5z) height 152 cm (0.9z). HbA1c stable 61 mmol/mol.

F, 17 yrs, 180 cm weight 92 kg (2z) started LCD 100 g/day 13% EAR to loose weight HbA1c dropped from 66 to 59 mmol/mol, but weight up 99 kg (3z). 21 months on LCD he lost 7 kg keeping his HbA1c stable.

Conclusions: This data shows the impact of LCD on growth which is greater at younger ages with prolonged restriction, <40% EAR. Here we show that increasing carbohydrates leads to improved growth with stable HbA1c. Long term growth data over years is needed to assess their impact.

Oral Session V - Diabetes Epidemiology

O33

Pediatric insulin injection technique: findings on glycemic control, needle use and disposal from the worldwide insulin injection technique survey

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Introduction: The Insulin Injection Technique Questionnaire survey of 13,289 patients included 898 (6.8%) subjects in the pediatric age range (≤ 18 years).

Objectives: To understand how children and adolescents around the world inject insulin and dispose of their used sharps.

Methods: We grouped these younger patients based on age: Group 1 (G1), 0-6 years, $n = 85$; Group 2 (G2), 7-13, $n = 423$; Group 3 (G3), 14-18, $n = 390$. Their injection technique was assessed through a questionnaire and nurse assessment.

Results: There were higher HbA1c values in adolescents (G3) - 9.3% compared to 8.6% and 8.4%, respectively, in G1 and G2 ($p < 0.05$). Between 38.5% and 66.7% of pediatric patients use 4mm pen needles. However, many patients use needles longer than the recommended 4 mm (33.3% in G1, 45.9% in G2 and 61.5% in G3). Skipping injections (any) was reported by 30-35% in Groups 1 and 2, and by 58% of Group 3 ($p < 0.05$). Nearly half the patients in each group disposed of their used needles into the ordinary rubbish. Most did so after recapping, but 1-2.5% did not even recap; they discarded the unprotected sharp directly into the rubbish. Up to a third of patients are not receiving site inspections every clinic visit; a proportion could not recall ever having injection site examination (8.6% in G1, 6.2% in G2 and 11.6% in G3). The percentages of patients who had not received any injection training in the last 12 months were 21.2% to 26.8% in the three groups.

Conclusion: Pediatric patients in all age groups should use 4 mm pen needles or 6 mm syringes (inserted at a 45° angle). Patients 6 years old or younger should always inject into a raised skin fold regardless of which device is used. These education-based interventions should result in fewer intramuscular injections and possibly less hypoglycemia. Professionals should inspect injection sites and provide targeted, individualized instruction on a regular basis.

O34

Pediatric insulin injection technique: findings on lipohypertrophy from the worldwide insulin injection technique survey

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Introduction: The Insulin Injection Technique Questionnaire survey of 13,289 patients included 898 (6.8%) subjects in the pediatric age range (≤ 18 years).

Objectives: To understand the complications experienced by insulin-injecting children and adolescents around the world, especially lipohypertrophy.

Methods: We grouped these younger patients based on age: Group 1 (G1), 0-6 years, $n = 85$; Group 2 (G2), 7-13, $n = 423$; Group 3 (G3), 14-18, $n = 390$.

Results: Nurses found lipohypertrophy in 41.3%, 45.2% and 47.3% of patients in G1, G2, and G3, respectively. Of those with lipohypertrophy, 40.8% of G1 patients always inject into it; in G2 14.9% do and in G3, 8.8%. More than a third of patients do not perform their rotation

correctly (leaving 1 cm space between successive injections). From 21.1% to 32.5% of patients reuse their needles. Excessive reuse (using a single needle more than 5 times) was reported in 9.4% to 21.8% of patients, with a trend to higher reuse with age. A majority of patients (59.4% to 70.0%) reported that their injections were painful and pain was associated with needle reuse ($p < 0.05$). Incorrect site rotation and excessive needle reuse were associated with the presence of lipohypertrophy ($p = 0.01$ for the former and $p = 0.05$ for latter). Unexpected hypoglycemia was common, ranging from 23.8% to 48.1%, and glucose variability even more so (61.0% in G1, 45.9% in G2 and 52.5% in G3). Both were associated with lipohypertrophy ($p < 0.05$).

Conclusion: All patients should avoid injecting into lipohypertrophy whenever present. When switching to healthy tissue, frequent BGM should be performed and patients should decrease their insulin dose initially by up to 20% to avoid hypoglycemia. They should rotate sites correctly and use needles only once to avoid lipohypertrophy. These education-based interventions should result in a lower prevalence of lipohypertrophy, fewer unexpected hypoglycemic reactions and less glycemic variability.

O35

Longitudinal changes in markers of etiologic diabetes type in older children: SEARCH for diabetes in youth study

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Introduction: The SEARCH for Diabetes in Youth etiologic diabetes type, determined using measures from the baseline visit at mean duration 0.8 (SD 0.6) yr, is based on the presence/absence of ≥ 1 positive diabetes autoantibody titers (DA) and the degree of insulin sensitivity, estimated using an equation validated against hyperinsulinemic euglycemic clamps including waist circumference, HbA1c and triglyceride levels. Insulin resistance (IR) was defined as values for insulin sensitivity $< 25^{\text{th}}$ percentile, insulin sensitive (IS) $\geq 25^{\text{th}}$ percentile, in the 1999-2004 NHANES cohort of multiracial non-diabetic youth age 12-20 yr. Four mutually exclusive groups were described: DA+/IS; DA+/-IR; DA-/IS; DA-/-IR.

Objectives: To explore longitudinal changes in DA and insulin sensitivity over a mean of 7 yr among SEARCH participants ≥ 12 yr old at their baseline visit ($n = 861$).

Methods: Measures were collected at fasting study visits. Longitudinal changes in insulin sensitivity index were assessed by calculating the difference between baseline and cohort visits and compared across the 4 etiologic groups using a one-way ANOVA.

Results: Mean age (SD) was 15.0 (2.2) yr at baseline and 21.9 (3.0) yr at follow up with 7.7 (1.9) yr diabetes duration. The majority (87.5%) of DA+ at baseline remained. IA2 (82.3%) was most stable followed by GAD65 (67.7%) and ZnT8 (58.0%); Of those DA- at baseline, 2.6% became DA+, 85.7% due to change in GAD65.

Insulin sensitivity decreased in all groups, greatest in the baseline IS groups: absolute change in index DA+/IS -0.48, DA+/-IR -0.27, DA-/IS -0.50, DA-/-IR -0.28. (DA+/IS and DA+/-IR vs DA-/IS or DA-/-IR, $p < 0.005$; DA+/IS vs DA+/-IR, $p = 0.854$).

Conclusions: In a contemporary cohort of youth with diabetes, DA status is fairly stable, while insulin sensitivity decreases over time,

particularly in groups that were IS at baseline. We are exploring factors associated with worsening of insulin sensitivity and potential associations with diabetes complications.

O36

Worldwide differences in pediatric type 1 diabetes: comparing 5 regions within the international SWEET registry

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Method: An analysis of the SWEET data set was carried out at Ulm University. The SWEET database from February 2018 was analyzed based on the following inclusion criteria: Type-1-diabetes, 2015 to January 2018; age <21 years with analysis of the most recent documented year of treatment.

For the statistical analysis, we used multivariable linear and logistic regression model.

Result: SWEET centers were stratified into 5 regions Europe (EU), Asia/Middle East/ Africa (A/ME/AF), Australia/New Zealand (Aus/NZ), North America/Canada (NA/C), South America (SA) with a total of 32607 patients. Centers in these regions were 45 in EU, 17 in A/ME/AF, 4 in Aus/NZ, 5 in NA/C, 3 in SA.

The adjusted mean HbA1c was found to be 7.9% (95% CI 7.67-8.19) for EU, 9.7% (9.26-10.16) for A/ME/AF, 8.2% (7.33-9.08) for Aus/NZ, 8.6% (7.78-9.35) for NA/C, 8.2 (7.15-9.21) for SA. p-value < 0.001.

The severe hypoglycaemia prevalence was defined as at least one episode during the year of observation. The prevalence noted for different regions were 2% EU, 9% A/ME/AF, Aus/NZ 2%, 3%NA/C, 1% SA respectively (p < .0001).

The insulin dose per kg was highest for the Asian/ME/African region with 0.91 IU/kg (0.83-0.98) and lowest for the Australia/NZ region with 0.77 IU/kg (0.62-0.91) (p = 0.0543 for comparison of all regions). The adjusted frequency of SMBG per day for Europe was 5.76 (5.38-6.1), Asian/ME/African region 3.29(2.62-3.9), Australia/NZ 4.59 (2.3-6.8), North America/C 5.11 (3.9-6.2) and South America 3.62 (1.9-5.3) (p < 0.001).

Percentage of pump users was highest in NA/Canada- (82%) and lowest in South America (2%, p < 0.001 for comparison of all regions).

Conclusion: Based on our analysis of the SWEET data including centres from different continents, we found dramatic differences in diabetes care and outcomes. The aim for equal care for each child remains a challenge for SWEET and also for other international initiatives.

O37

Cognitive skills in Danish school children with type 1 diabetes are similar to background population - a population-based cohort study

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Objectives: To determine if children diagnosed with type 1 diabetes perform worse in math and reading tests compared to their peers, and

to investigate the association between glycemic control, diabetic ketoacidosis (DKA), severe hypoglycemia, and test-scores among children with type 1 diabetes.

Methods: Population-based prospective cohort study from 2010-2015 with all Danish school children attending grades 2, 3, 4, 6, and 8 involving n = 631,620 children of which n = 2,031 had a confirmed diagnosis of type 1 diabetes. Main outcome was standardized test-scores (z-scores) in math and reading. Test-scores were obtained in math (n = 524,764) and reading (n = 1,037,006). Linear regression models compared outcomes with/without adjusting for socioeconomic characteristics. Case-sibling analysis was also performed.

Results: No differences in z-scores were found between children with type 1 diabetes and the background population of children (unadjusted z-score difference: 0.00; 95% CI -0.04, 0.05; p = 0.88 / adjusted for socioeconomic factors: 0.02; 95% CI -0.03, 0.06; p = 0.45). This was confirmed in a case-sibling analysis. A strong association was found between HbA1c and z-scores. A 10 mmol/mol increase in HbA1c was associated with a decrease in the z-score of -0.14 (95% CI -0.17, -0.10, p < 0.001), but adjusting for socioeconomic variables reduced this association considerably (-0.06, 95% CI -0.1, -0.02, p = 0.005). Especially children with a HbA1c>80 mmol/mol did not have different test-scores than the background population. No association was found between DKA, severe hypoglycemia and test-scores.

Conclusion: Type 1 diabetes does not adversely affect test-scores in Danish school children. Socio-economic factors are more important than HbA1c for variation in test-scores. Families affected by type 1 families should ease worries on school performance.

O38

DKA at onset of pediatric type 1 diabetes across the world: results from a Joint International Project

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Objectives: To evaluate worldwide geographic variability and time trends of DKA rate at onset of pediatric type 1 diabetes between 2006-2016.

Methods: An international collaboration conducted a retrospective longitudinal study on DKA at type 1 diabetes onset in children aged 0.5-14y. Population-based registries were used to obtain data from 13 countries, Auckland -NZ, Australasian Diabetes Data Network (ADDN), Austria, Czech Republic, Denmark, Germany, Italy, Luxembourg, Norway, Slovenia, Sweden, SEARCH-US, Wales. Age, date of diabetes, gender, presence of DKA (defined as pH < 7.30 or HCO < 15) were collected at diabetes onset. Two registries (ADDN and Wales) were reporting DKA as yes or no only. Since data presented here do not use a common definition of DKA, future efforts directed at harmonizing such definitions are needed. Temporal trends in DKA rates were estimated using logistic regression, and ORs for annual changes were obtained overall and for each country.

Results: During the study period 58,584 newly diagnosed cases fulfilled inclusion criteria; 52.9% males; median age 9.0y. The sample size varied across the countries from 191 to 19,098. The overall mean DKA rate was 29.1%, lowest in Sweden and Denmark, highest in Italy and Slovenia (Table 1). The overall DKA rate significantly changed over time, with females having a higher risk of DKA at onset (OR 1.05, 95%CI 1.01-1.08), and an increasing trend observed in males (OR 1.01; 95%CI 1.004-1.02). In most countries there was no change, while a considerable increasing trend was found in USA.

Conclusions: DKA rate varies hugely across the world, albeit generally unacceptably high and showing a slight increase between 2006-2016. Efforts focused at reducing the rate of DKA at onset of type 1 diabetes are warranted.

Countries	Type 1 diabetes cases (n)	Total DKA cases (n)	Average DKA Rates (%)	95%CI	Odds Ratios for annual change	95%CI
Auckland-NZ	670	176	26.3	22.9-29.6	1.035	0.982-1.091
ADDN-AU	4,428	1,101	24.9	23.6-26.1	1.026	1.003-1.049
Austria	1,502	572	38.1	35.6-40.6	1.002	0.968-1.038
Czech Rep.	2,175	614	28.2	26.3-30.1	0.984	0.951-1.019
Denmark	3,084	637	20.7	19.2-22.1	1.024	0.996-1.053
Germany	19,098	5,114	26.8	26.2-27.4	1.016	1.006-1.026
Italy	10,019	4,146	41.4	40.4-42.4	0.974	0.961-0.987
Luxembourg	191	74	38.7	31.8-45.6	1.031	0.935-1.137
Norway	3,331	735	22.1	20.7-23.5	1.015	0.989-1.042
Slovenia	471	190	40.3	35.9-44.7	1.042	0.986-1.102
Sweden	6,457	1,261	19.5	18.6-20.5	1.022	0.966-1.082
SEARCH-US	5,485	2,021	36.9	35.6-38.1	1.107	1.072-1.144
Wales	1,673	419	25.0	23.0-27.1	0.989	0.955-1.024
Total	58,584	17,080	29.1	28.8-29.5	1.009	1.003-1.015

[Table 1. Average DKA rates at type 1 diabetes onset across study populations, and ORs for annual changes between 2006-2016]

O39

Clinical profile at onset of diabetes in SEARCH and YDR youth: an international harmonization of youth diabetes registries

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Over the last several decades, diabetes in youth has increased in both India and the US, along with long-term complications, healthcare costs, and risk of diabetes in future generations. However, there are limited standardized population-based data in contemporary youth cohorts that provide the ability to compare the epidemiologic characteristics of diabetes in youth between the US and India.

To compare demographic and clinical characteristics in SEARCH (US) and YDR (Indian) youth with type 1 (T1D) and type 2 (T2D) diabetes.

We harmonized demographic, clinical, and laboratory data elements from the SEARCH for Diabetes in Youth (SEARCH) registry in the US and the Registry of People with Diabetes with Youth Age at Onset (YDR) a registry in India to the structure and terminology in the Observational Medical Outcomes Partnership (OMOP) Common Data Model (v5). Data used in these analyzes were from youth with T1D and T2D diabetes, aged < 20 years and newly diagnosed between 2006 and 2012. We compared key demographic and clinical characteristics across registries using chi-squared tests and t-tests.

There were 9,728 SEARCH (7,549 with T1D, 2,179 with T2D) and 1,579 YDR (1,416 with T1D, 163 with T2D) youth diagnosed with diabetes between 2006-2012. Demographic and clinical characteristics of youth with T1D and T2D in the two registries are shown in the table. Age at onset for T2D was younger for SEARCH vs YDR (p = 0.001). There was a higher proportion of females with T2D in SEARCH compared to YDR (p < 0.001). SEARCH with both T1D and T2D had higher BMI, higher blood pressure, and lower HbA1c compared to the YDR youth.

These data show the differences and similarities between SEARCH and YDR youth with diabetes and uses a novel method to compare data across international registries. Further research is needed to better understand why these similarities and differences exist.

Variables	Type 1 diabetes		p-value	Type 2 diabetes		p-value
	SEARCH n=7,549	YDR n=1,416		SEARCH n=2,179	YDR n=163	
Age at diagnosis (yrs), mean (SD)	10.1 (4.5)	10.7 (5.0)	0.001	14.7 (2.9)	15.8 (3.6)	<0.0001
Age at baseline visit (yrs), mean (SD)	10.6 (4.4)	11.2 (5.1)	0.002	15.2 (2.8)	16.3 (3.6)	<0.0001
Gender, n (%)			<0.001			<0.001
Female	3527 (46.7%)	675 (47.7%)		1369 (62.8%)	81 (49.7%)	
Male	4022 (53.3%)	741 (52.3%)		810 (37.2%)	82 (50.3%)	
Duration of diabetes (mos) at baseline visit, mean (SD)	10.3 (7.4)	5.4 (9.0)	<0.0001	13.3 (8.2)	6.3 (9.8)	<0.0001
Height (cm), mean (SD)	146.6 (23.0)	149.5 (22.2)	<0.0001	166.0 (11.4)	154.1 (20.6)	<0.0001
Weight (kg), mean (SD)	45.8 (21.6)	32.4 (16.7)	<0.0001	98.4 (27.1)	64.3 (23.2)	<0.0001
BMI, mean (SD)	19.6 (5.1)	16.9 (4.6)	<0.0001	35.0 (8.2)	26.8 (10.2)	<0.0001
Blood pressure, mean (SD)						
SBP	99.7 (11.8)	106.6 (15.6)	<0.0001	115.9 (12.6)	117.7 (13.8)	0.046
DBP	63.3 (9.6)	69.8 (10.1)	<0.0001	72.0 (10.0)	78.2 (9.1)	<0.0001
HbA1c, mean (SD)	7.8 (1.7)	11.1 (2.9)	<0.0001	7.2 (2.1)	10.0 (2.8)	<0.0001

[Comparison of demographic and clinical characteristics of youth with T1D and T2D in SEARCH and YDR]

O40

Clinical characteristics of pancreatic diabetes in children and adolescents documented in the German/Austrian/Swiss/Luxembourg DPV registry

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Objectives: Only few studies on diabetes following disorders of the exocrine pancreas (pancreatic diabetes (PD)) were conducted so far. The objective of our study was to examine clinical characteristics of children and adolescents < 20 years of age with PD documented in the diabetes patient follow-up registry (DPV).

Methods: We identified 622 children and adolescents <20 years of age with PD and compared them to 71,069 type 1 diabetes (T1D) patients <20 years of age. The most recent treatment year per patient was studied. Demographic and clinical characteristics of interest were: age at diabetes onset, proportion of males, type of insulin therapy (conventional (CT), intensive (ICT), insulin pump), use of continuous glucose monitoring systems (CGMS), rates of severe hypoglycaemia and number of hospitalization days.

Results: The main reason of PD in children and adolescents <20 years was cystic fibrosis (84%). Median age at diabetes onset was 14.1 years

in PD patients and 8.7 years in T1D patients. The proportion of males was higher in T1D (53%) compared to PD (41%). The proportion of patients using CT was higher in PD than in T1D patients (30.3% vs. 6.8%, $p < 0.001$), whereas the proportion of ICT was similar (57.7% vs 57.0%, $p = 0.777$). Usage of insulin pump and CGMS was more common in T1D (pump: 36.2%, CGMS 11.5%) compared to PD patients (12.0%, 4.8%, both $p < 0.001$). We observed 13.4 events of severe hypoglycaemia/100 PY in T1D and 5.4 events/100 PY in PD. Number of hospitalization days/PY were almost twice as high in PD (0.99/PY) compared to T1D patients (0.53/PY, $p < 0.001$).

Conclusions: Our results showed important clinical characteristics of PD patients that need to be considered for clinical care. Results from registries may serve as a basis for discussing guidelines on diagnosis and treatment of patients with PD. Interdisciplinary cooperation especially between diabetology and gastroenterology is important with regard to this rare diabetes type.

Oral Session VI - Newer Therapies (Insulin, OHA & Tech)

O41

Autoantigen (GAD-alum) given into lymph-nodes together with oral vitamin D to preserve beta cell function in type 1 diabetes. The DIAGNODE-1 pilot trial

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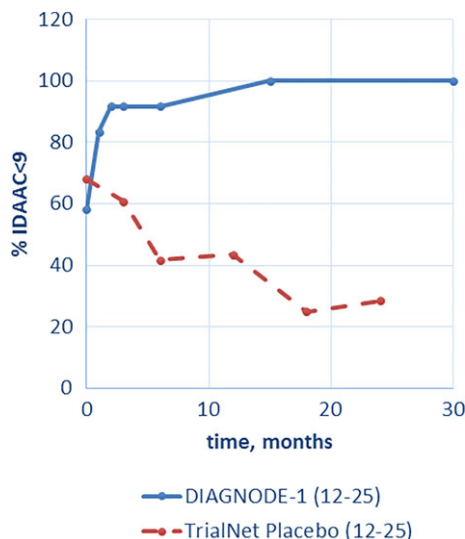
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For the first time intra-lymphatic route is tried in T1D to preserve beta cell function. Vitamin D might help to gain additional efficacy.

Objectives: To evaluate the safety, and clinical and immunological response.

Patients and methods: DIAGNODE-1 is an open-label pilot Phase I trial. 12 patients were enrolled, 8 /4 males/females, aged 12.6-23.1 years, T1D duration < 6 months, positive for GAD65- antibodies (GADA) and a fasting C-peptide ≥ 0.12 nmol/L. They got Vitamin D 2000 U/d Day 0-120 and 4 μ g GAD-alum into an inguinal lymph-node Day 30, 60 and 90. All have been followed for >6 months. GADA, including subclasses, were measured and the effect of GAD₆₅ stimulation on cytokines. Beta cell function was evaluated by MMTT.

Results: The treatment was feasible, well tolerated, and safe. So far 9 patients have been followed for 15 months. From baseline to 15 months the C-peptide AUC decreased, in mean -10.4%, while fasting C-peptide increased, in mean +15%. HbA1c decreased in 8/9 patients (mean decrease 24%) and insulin dose decreased in 5/9 (mean decrease for the whole group 19%). IDAAC remained 100% up to 30 months (n = 4). 15 months values for all patients will be available at presentation. Vitamin D concentration increased during the first 6 months from mean 60.6 (range 39.9-89.6) to 83.0 (range 54.6-138.0). GADA increased, with a subclass change: decreasing proportion of IgG1, and increased IgG2-4. The immune response was strong, suggesting a pronounced Th2-deviation.



[Figure 1]

O42

Exploring CXCL10 expression pattern in pancreatic islets in autoimmune diabetes: a new role for alpha-cells in lymphocytes recruitment?

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Background: Interferon- γ inducible protein 10 kDa (CXCL10 or IP10) is a member of the CXC chemokine family which binds to the CXCR3 receptor. CXCL10 expression is induced by a variety of inflammatory signals and it is increased in the islets of type 1 diabetic patients. In this study, we wanted to further explore the CXCL10 expression pattern in recent onset human type 1 diabetes to specify pancreatic cell subsets expressing the chemokine.

Methods: Pancreatic specimens obtained from 6 recent-onset, live T1D patients included in the DiViD study and from 3 non-diabetic, auto-antibody-negative donors included in the EUnPOD-study were investigated. Consecutive FFPE pancreatic sections were triple immunostained for CXCL10, insulin and glucagon, and then analyzed through confocal microscopy in order to evaluate co-localization rate between CXCL10-Insulin and CXCL10-Glucagon. Additionally, insulin containing islets (ICI) and insulin deficient islets (IDI) were counted and categorized based on CXCL10 expression.

Results: In the sections from the recent onset type 1 diabetic cases, analysis of the CXCL10 expression revealed 4 distinct islet subtypes: ICI with or without expression of CXCL10 and IDI with or without expression of CXCL10. Table 1 shows the distribution of the different islet categories. In ICIs, CXCL10 is expressed both in β - and in α -cells, and in IDIs, CXCL10 is exclusively expressed in α -cells. CXCL10 was not expressed in pancreatic islets from the non-diabetic donors.

Conclusions: We have identified 4 distinct islet subtypes based on CXCL10 expression. The new observation, that CXCL10 is expressed also in alpha-cells and in IDI, may lead to speculations regarding if alpha-cells contribute to lymphocyte chemokine-mediated migration. The role of the alpha-cells in the pathogenesis of T1D needs to be further explored.

	ICI CXCL10+ (%)	ICI CXCL10- (%)	IDI CXCL10+ (%)	IDI CXCL10- (%)
Case 1	5,9	0	90,2	3,9
Case 2	26,2	3,5	42,9	27,4
Case 3	40,6	0,9	5,0	53,5
Case 4	33,3	2,2	2,2	62,2
Case 5	7,6	0	67,8	24,6
Case 6	1,4	0	15,7	82,9

[Distribution of the different islet categories]

O43

Investigating the immunopathogenesis of type 1 diabetes in vitro using stem cell technologyK. Joshi^{1,2}, T. Labonne², A. Motazedian^{2,3}, S.I. Mannering⁴, A.G. Elefanty^{2,3}, F.J. Cameron^{1,2,3}, E. Stanley^{2,3}

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Objectives: Human models for studying the immune pathogenesis of type 1 diabetes mellitus (T1DM) are urgently required. We aimed to generate antigen presenting cells (macrophages) from induced pluripotent stem cells (iPSCs) derived from an individual with T1DM and to use these macrophages to study autoimmune activation of autologous T cells.

Methods: We derived iPSCs from a deceased tissue donor who had T1DM and from whom islet infiltrating T-cells had been previously isolated. iPSCs were differentiated in vitro to generate macrophages which were subsequently activated using Interferon gamma. iPSC derived macrophages were characterized using flow cytometry, confocal microscopy, phagocytosis assays and their ability to present c-peptide to autologous islet infiltrating CD4+ T-cells. Non-HLA matched macrophages were used as controls.

Results: Flow cytometry analysis indicated that iPSC derived macrophages expressed typical macrophage markers, CD14, CD11b, CD86 and HLA class II. Treatment of these cells with interferon-gamma led to up-regulation CD14 and HLA-DR, consistent with activation. Activated macrophages efficiently presented C peptide to an islet infiltrating CD4+ T-cell clone in a HLA-restricted manner. T-cell activation was evidenced by upregulation of CD69 and this activation could be blocked by anti-HLA-DQ antibodies. Non-HLA matched iPSC derived macrophages failed to activate T-cells, confirming the specificity of the HLA/TCR interaction.

Conclusions: We have generated macrophages from induced pluripotent stem cells derived from an individual who had type 1 diabetes mellitus. These macrophages expressed typical lineage markers and efficiently presented islet antigen to islet infiltrating CD4+ T cells isolated from the same individual, leading to T-cell activation. HLA matching was necessary for this interaction. This system has potential as a model for type 1 diabetes and as a platform to search for islet derived antigens that drive autoimmunity.

O44

Genistein attenuates neurological deficits induced by transient global cerebral ischemia and reperfusion in streptozotocin-induced diabetic miceS. Rajput¹, S. Sinha¹

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Genistein, an isoflavonoid phytoestrogen, has been known for its potential pharmacological properties especially for neuroprotection and treating diabetes. The present study aims to determine the neuroprotective efficacy of genistein against global cerebral ischemia-reperfusion-induced neuronal injury in streptozotocin-induced diabetic mice and explore the underlying mechanisms.

Streptozotocin-induced diabetic mice were subjected to transient cerebral ischemia by occluding both common carotid arteries for 30 min followed by 24 h reperfusion to induce neuronal injury. Effect of genistein (2.5, 5.0, and 10.0 mg/kg, i.p., o.d.) treatment on ischemia-reperfusion-induced neuronal injury in diabetic mice was evaluated in terms of cerebral infarct size, oxidative damage, mitochondrial activity in terms of neuronal apoptosis and cellular viability, dipeptidyl peptidase-4 activity and active glucagon-like peptide-1

concentration, and neurological functions measured as short-term memory and motor performance.

Genistein administration following transient cerebral ischemia significantly counteracted cognitive impairment and re-established ($p < 0.001$) motor performance in diabetic mice. Ischemia-reperfusion increased the infarct size, genistein administration prevented the increase in cerebral infarct size ($p < 0.0001$) and significantly suppressed the increase in cerebral oxidative stress in transient cerebral ischemia-reperfusion subjected diabetic mice. Genistein treatment significantly ($p < 0.001$) reduced neuronal apoptosis and increased cellular viability ($p < 0.0001$), almost completely suppressed the circulating dipeptidyl peptidase-4 activity, and enhanced glucagon-like peptide-1 concentration in diabetic mice with cerebral ischemia-reperfusion.

This study suggests that genistein has potent neuroprotective activity against global cerebral ischemia-reperfusion-induced neuronal injury and consequent neurological deficits in streptozotocin-induced diabetic mice.

O45

Sodium orthovanadate and *Trigonella foenum-graecum* ameliorates cognitive deficits in alloxan-induced diabetic ratsP. Kumar¹, N. Baquer¹

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Objectives: Diabetes is one of the leading causes of learning and memory deficits. In the present study, the effect of sodium orthovanadate (SOV) and *Trigonella foenum-graecum* seed powder (TSP) administration has been studied on blood glucose and insulin levels, oxidative stress, inflammatory cytokines, learning and memory performances in hippocampus of the alloxan induced diabetic rats and to see whether the treatment with SOV and TSP is capable of reversing these effects.

Materials and Methods: Diabetes was induced by administration of alloxan monohydrate (15 mg/100gm b.wt.) and rats were treated with 2IU insulin, 0.6 mg/ml SOV, 5% TSP in the diet and a combination of 0.2 mg/ml SOV with 5% TSP separately for 21 days. The learning and memory function were assessed by Morris water maze test. The oxidative stress indicators [glutathione reductase (GRx), superoxide dismutase (SOD), neurolipofuscin and malondialdehyde (MDA)] and inflammatory cytokines (TNF- α , IL-1 β , and IL-6) were measured in hippocampus using corresponding commercial kits. The mRNA and protein levels of PPAR γ were evaluated by real time (RT)-PCR and Western blot analysis.

Results: Diabetic rats showed hyperglycemia with almost four fold high blood glucose levels. Hyperglycemia increases lipid peroxidation and neurolipofuscin, causing decreased activities of antioxidant enzymes and learning and memory performances with diabetes in hippocampus. Rats treated with combined dose of SOV and TSP had glucose levels comparable to controls, similar results were obtained with the increased antioxidant enzymes levels, improved learning and memory performances, reduced MDA levels, significantly increased PPAR γ expression, and alleviated TNF- α , IL-1 β , and IL-6 compared with the diabetic group in the hippocampus.

Conclusions: Combined therapy can indeed be considered a better alternative to be explored further as a means of diabetes-associated cognitive decline control.

O46

DAPAgli flozin add-on therapy improves glycemic control with full closed loop insulin administration in adolescents-DAPADreamT. Biester¹, T. von dem Berge¹, A. Cohen², I. Muller², R. Nimri³, E. Atlas², M. Phillip³, K. Dovc⁴, T. Battelino⁴, N. Bratina⁴, O. Kordonouri¹, M. Scheerer⁵, T. Danne¹

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Introduction: The SGLT2-Inhibitor Dapagliflozin (DAPA) comes into focus as adjunct therapy in type 1 diabetes (T1D).

The aim of the present trial was to investigate the effect of DAPA on glucose levels during the night and after unannounced meals during the day. For sufficient insulin administration, the DreaMed Substance Administration System (fuzzy logic closed loop algorithm) as a proven safe and effective closed loop system was used in a full closed loop (FCL) mode.

Method: In this monocentric, double-blind, randomized, placebo-controlled cross-over trial, eligible patients (T1D, CSII, non-severe obese) were admitted for 24 hours. On each visit, they received either 10 mg DAPA or placebo in the evening and in the following morning. Two mixed meal tests were performed, while glucose control was achieved by DreaMed FCL. The primary outcome was "Time in Range 70-180 mg/dl" (TIR).

Results: 15 adolescents aged 15.3 ± 1.5 years, HbA1c $8.3 \pm 0.9\%$, diabetes duration 9.8 ± 3.5 years were randomized. With DAPA, TIR increased significantly overall and during postprandial phase without an increase below 70 mg/dl. Time above 180 mg/dl was significantly decreased and no serious ketosis was observed.

Conclusion: The insulin-independent lowering effect of glucose by DAPA was shown both in fasting and postprandial phase without signs for hypoglycemia or ketoacidosis.

In postprandial phase a FCL with DAPA was superior by a faster metabolic normalization, nevertheless pre-prandial bolus is needed to keep the glucose in range

Variable (N = 15)	DAPA	Placebo	p
24 h Time within 70-180 mg/dl [%]	70.8 (66.6, 73.6)	52.3 (42.9, 56.8)	<0.001
Secondary			
24h Time below 70 mg/dl [%]	1.39 (0, 4.11)	0 (0, 2.53)	0.064
24h Time above 180 mg/dl [%]	29.8 (26.4, 30.2)	47.5 (41.1, 54.2)	<0.001
24 h values [mg/dl]	157 (147, 160)	188 (170, 195)	<0.001
Nocturnal values (11 pm-7 am) [mg/dl]	112 (104, 128)	129(104, 149)	0.056
Basal Insulin [U]	19,4 (18.7, 27.1)	20,8 (17.6, 22.8)	0.008
Bolus Insulin [U]	8,55 (8.2, 9.9)	15,25 (13.3, 17.4)	<0.001
Urinary glucose excretion [g/24h]	135.42 \pm 42.3	44.4 \pm 18.8	<0.001

[Glycemic Results under FCL condition]

O47

NMDA receptor antagonists for the prevention and treatment of human type 1 diabetes mellitus

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Objectives: Today, presymptomatic diagnosis of type 1 diabetes mellitus (T1DM) is possible. However, no medication exists that sustainably prevents progressive beta cell destruction to avoid disease progression. We recently demonstrated that pharmacological inhibition of pancreatic N-methyl-D-aspartate receptors (NMDARs) with Dextromethorphan (DXM) enhances islet cell survival under diabetogenic conditions, both in the type 2 diabetic mouse model db/db

in vivo and in isolated human pancreatic islets in vitro. We are now investigating the role of NMDARs in the context of human T1DM.

Methods: Islet cell viability was assessed in isolated mouse pancreatic islets following their incubation with the diabetogenic agent streptozotocin (STZ), either alone or with the NMDAR antagonist Dextromethorphan (DXM). For in vivo experiments, DXM was continuously applied for 26 weeks to female non-obese diabetic (NOD) mice, an animal model of human T1DM. NOD mice were screened weekly for diabetes incidence. After 26 weeks of treatment, non-diabetic NOD mice were sacrificed and their pancreatic sections were stained for insulin, glucagon and CD45.

Results: DXM protects mouse pancreatic islets against the diabetogenic insult induced by STZ. In NOD mice, long-term DXM treatment reduces diabetes incidence by 50%, maintains alpha- and beta-cell mass and significantly increases the number of pancreatic islets more than fourfold. DXM has no effect on the overall incidence of infiltrating immune cells as indicated by staining of leukocyte common antigen (CD45).

Conclusions: Under conditions imitating human T1DM, NMDAR antagonists promote islet cell protection, both, in vitro and in vivo. Additional experiments are required to better determine the effect of DXM on insulinitis, islet cell proliferation and neogenesis. Since NMDARs are involved in the regulation of human T-cell proliferation and polarization, we furthermore want to study whether NMDAR antagonists modulate cellular immune responses.

O48

Effects of *Lactobacillus rhamnosus* GG and *Bifidobacterium lactis* Bb12 on beta-cell function in children with newly diagnosed type 1 diabetes: a pilot study

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A significant decrease in the numbers of *Lactobacillus* and *Bifidobacterium* was observed in children with type 1 diabetes (T1D). These bacteria influence intestinal microbial homeostasis. We hypothesized that modification of the gut microbiota via the provision of probiotics may modulate the immune system for preventing islet cell destruction. The aim of the study is to examine the effects of *Lactobacillus rhamnosus* GG and *Bifidobacterium lactis* Bb12 on beta-cell function in children with newly diagnosed T1D.

Methods and analysis: 20 children with mean age 11.8 SD 2.3 years, with newly diagnosed T1D, confirmed by clinical history and the presence of at least one positive autoantibody, were included in a double-blind, randomized, trial in which they received *Lactobacillus rhamnosus* GG and *Bifidobacterium lactis* Bb12 or a placebo, for 6 months. The primary outcome measures were the area under the curve of the C-peptide level (AUC_{C-peptide}) during 2-h responses to a mixed meal. This is a primary analysis of an ongoing study registered at ClinicalTrials.gov. NCT03032354

Results: There was no difference between both groups in AUC_{C-peptide} at baseline (p = 0.665) and after 6 month (p = 0.605). In both groups the mean value of AUC_{C-peptide} decreased after 6 month, without statistical difference (p = 0.921). We noted a slight positive correlation between GADA and AUC_{C-peptide} at baseline r = 0.486, p = 0.029. After 6 month of follow up in both groups children were in partial remission phase, the mean HbA1c was < 6.5% and the mean insulin daily dose was 0.3unit/kg. Probiotic tolerance was good, one child reported bloating. The adherence was good, 96% of capsules were taken.

Conclusions: Probiotics were well tolerated and do not cause side effects. Families were satisfied with their participation in the research, which is confirmed by good adherence. It is necessary to continue the study to determine the therapeutic effect of probiotics on a larger number of patients.

Oral Session VII - Technology in Diabetes

O49

Real-world glycaemic outcomes of youth with T1D using the MiniMed™ 670G system compared to participants in the pediatric MiniMed™ 670G system pivotal trial

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Objectives: To compare glycaemic data of young patients in the Commercial Launch of the MiniMed™ 670G system with SmartGuard™ technology with those reported during the system pivotal trial in children aged 7-13 yrs.

Methods: System data from patients (n = 105, 7-13yrs, mean ± SD 10.4 ± 1.2 yrs) in the Commercial Launch with >10,292 days of sensor wear were voluntarily uploaded to CareLink™ Personal software from Mar 2017-Dec 2017, de-identified, and retrospectively analyzed. System data from participants (n = 105, 10.8 ± 0.8 yrs) completing the MiniMed™ 670G system pediatric pivotal trial are also presented.

Results: Data from the trial (2-week baseline Manual Mode run-in and 12-week Auto Mode-enabled study phase) and the Commercial Launch (~2-week initial Manual Mode and 12-week Auto Mode-enabled period) are shown (Table). For Commercial Launch, the median Auto Mode and sensor usage were 79.9% and 94.4%, respectively; the mean percentage of time in target glucose range (70 mg/dL-180 mg/dL, 3.9 mmol/L-10 mmol/L) during Manual Mode was 56.4 ± 16.3% and during Auto Mode was 67.1 ± 9.1%

Conclusions: Real-world CareLink™ data and pivotal trial outcomes data of children with T1D using the MiniMed™ 670G automated insulin delivery system display similar trends in improved glycaemic metrics suggesting correlation between these datasets.

Pediatric pivotal trial data and real-world pediatric Commercial Launch data of the MiniMed™ 670G system with SmartGuard™ technology.

	MiniMed™ 670G System Pediatric Pivotal Trial		MiniMed™ 670G System Commercial Launch	
	Manual Mode (2 weeks)	Auto Mode (12 weeks)	Manual Mode (~2 weeks)	Auto Mode (12 weeks)
Patients, N	105	105	105	105
Sensor use, days	1730	9402	1224	9173
Time in Auto Mode, days	NA	78.5	NA	81.9
Median Auto Mode use per patient, %	NA	80.6	NA	79.9
SG, mg/dL (mmol/L)	169 ± 22 (9.4 ± 1.2)	162 ± 12 (9.0 ± 0.7)	178 ± 26 (9.9 ± 1.4)	161 ± 16 (8.9 ± 0.9)
Percentage of sensor glucose values across ranges, mg/dL (mmol/L)				
<50 (<2.8)	0.8	0.5	0.2	0.2
<54 (<3.0)	1.2	0.7	0.3	0.4
<70 (<3.8)	4.4	2.8	1.4	1.9
70-180 (3.9-10.0)	56.5	65.2	56.4	67.1
>180 (>10.0)	39.1	32.0	42.2	31.1
>250 (>13.8)	13.3	10.3	14.6	9.2
>300 (>16.6)	4.7	3.1	5.4	3.3

All values are shown as averages or mean ± SD, unless indicated otherwise.

N=Number

[MiniMed™ 670G system pediatric trial data and real-world MiniMed™ 670G system pediatric data]

O50

Avoidance of overnight glucose excursions with predictive alerts in the Guardian™ Connect CGM system: real-world data of pediatric patients with T1D

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Introduction: The Guardian™ Connect system allows users to view sensor glucose (SG) data on a smartphone, has SG threshold alerts that notify users about low and high SG excursions, and predictive SG threshold alerts that notify users 10-60min before a low or high SG excursion.

Objectives: To compare real-world rates of overnight alerts and outcomes of pediatric Guardian™ Connect system users to a control dataset in which alerts were disabled.

Methods: De-identified CareLink™ SG data from 1,183 youth ≤15 yrs old with >5 days of overnight (10PM-7AM) sensor data, from 1/2/2017-3/13/2018, were analyzed. For control, low and high thresholds, which were the median of low and high thresholds of all users, were marked during periods when alerts were not enabled and when SG hit 4.0 mmol/L (73 mg/dL) and 12.9 mmol/L (233 mg/dL), respectively; low and high predictive alerts were marked when SG would have hit low and high thresholds 17.5min and 15min before median settings, respectively. The excursion start time window was 60min after an alert and excursions were segmented into avoided, ≤20 min, 20-60 min, and >60 min.

Results: Low and high excursion data results, stratified by "avoided" and duration, are shown (Table).

Conclusion: Guardian™ Connect system predictive alerts allowed pediatric users to avoid 58% and 38% of predicted low and high excursions, respectively. Predictive alerts help maintain target SG range and are useful for young T1D patients looking to optimize glycaemic control.

	Cohort	Low SG Excursion		High SG Excursion		
		Predictive Alerts Enabled	Alerts Not Enabled	Predictive Alerts Enabled	Alerts Not Enabled	
Time to Excursion Resolution	Total Alert Count	103165	4554	45115	50763	
	Avoided	Excursion Count	60025	1076	17235	5461
		% of Total Alerts	58%	24%	38%	11%
	≤20 min	Excursion Count	16151	991	5022	5608
		% of Total Alerts	16%	22%	11%	11%
	20-60 min	Excursion Count	16785	1043	6648	7970
		% of Total Alerts	16%	23%	15%	16%
	>60 min	Excursion Count	10204	1444	16210	31724
		% of Total Alerts	10%	31%	36%	62%

[Predictive Alert Results Table]

O51

Artificial Pancreas (AP) Ski Camp 2018: successful use of the Tandem Control-IQ AP system in adolescents and children during winter sports and at home

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Objective: Artificial Pancreas (AP) systems improve glycaemic control during both the day and night. However, glycaemic control during high intensity and prolonged exercise remains challenging. We tested the Tandem Control-IQ AP system in adolescents and children during a winter/ski camp study, where high altitude, low temperature, intense prolonged activity, and stress challenged different components of the system (pump, continuous glucose monitor, and control algorithm).

Methods: In a randomized controlled trial, 24 adolescents (ages 13-18 years) and 24 school-aged children (6-12 years) with Type 1 Diabetes (T1D) participated in a 3-day ski camp (~5 h skiing/day) at three sites: Wintergreen, VA; Kirkwood, CA and Breckenridge, CO. The school-aged children's camps were followed by an additional 72 hour at-home phase under parental supervision. Study participants were randomized 1:1 into two groups at each site. Control group used sensor-augmented pump (SAP), and experimental group used the t:

slim X2 with Control-IQ Technology AP system. All subjects were remotely monitored 24 h per day by study staff.

Results: The AP system improved mean glucose 156.8 mg/dL (AP) vs 173.8 mg/dL (SAP), with similar hypoglycemia exposure. Adolescents had a significant improvement in mean glucose, while the mean glucose was unchanged for school-aged subjects, however they had a marked improvement in mean glucose when they were at home: 153.7 (AP) vs 180.2 mg/dL (SAP). There were no adverse events.

Conclusions: AP use in adolescents with T1D improved glycemic control and reduced exposure to hyperglycemia during prolonged intensive winter sport activities. The home use of AP by school-aged children improved time-in-range without increasing hypoglycemia.

Mean CGM (mg/dL) (mmol/L)	All			13-18 y/o			6-12 y/o					
	All			Camp			Camp			Home		
	SAP	AP	p	SAP	AP	p	SAP	AP	p	SAP	AP	p
173.8	155.6	<0.001	168.0	139.7	p=0.005	170.1	173.1	ns	180.2	153.7	p<0.001	
	9.7	8.6		9.3	7.8		9.5	9.6		10.0	8.5	
% <50 mg/dL (2.8 mmol/L)	0.3%	0.2%	0.09	0.6%	0.5%	ns	0.2%	0.2%	ns	0.3%	0.1%	p=0.16
% <60 mg/dL (3.3 mmol/L)	0.9%	0.9%	ns	1.3%	1.8%	ns	0.6%	0.5%	ns	0.8%	0.6%	ns
% <70 mg/dL (3.9 mmol/L)	2.5%	2.8%	ns	3.6%	5.8%	ns	1.9%	1.7%	ns	2.1%	1.7%	ns
% 70-180 mg/dL (3.9-10 mmol/L)	56.2%	68.9%	<0.001	55.9%	73.3%	p=0.006	61.2%	61.2%	ns	53.0%	71.4%	<0.001
% >180 mg/dL (10 mmol/L)	41.3%	28.3%	<0.001	40.5%	20.9%	p=0.003	36.9%	37.1%	ns	44.9%	26.9%	<0.001
% >250 mg/dL (13.9 mmol/L)	14.8%	9.2%	<0.001	14.5%	5.5%	p=0.013	12.9%	15.4%	ns	16.3%	7.3%	p=0.002
% >300 mg/dL (16.7 mmol/L)	5.6%	3.6%	0.017	5.6%	0.9%	p=0.044	5.9%	7.2%	ns	5.4%	2.9%	p=0.109
CHO gr for hypo	26.26	24.25	ns	29.5	37.4	ns	45.2	35.2	ns	11.5	9.0	ns
# hypo events	1.81	1.69	ns	2.0	2.2	ns	3.3	2.6	ns	0.7	0.8	ns

[Table 1. Glycemic Control During Ski camp and at Home]

O52

Closed-loop insulin delivery in suboptimally controlled type 1 diabetes: a multicentre 12-week randomized trial

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Objectives: We assessed the safety and effectiveness of day-and-night hybrid closed-loop insulin delivery (CL) compared with sensor-augmented pump therapy (SAP) in youths and adults with suboptimally controlled type 1 diabetes (T1D).

Methods: In an open-label, multi-centre, multi-national (UK and USA), single-period, parallel study, we randomly assigned subjects with T1D aged 6 years and older treated with insulin pump and HbA1c between 7.5% and 10% to receive either CL with Cambridge control algorithm (n = 46) or SAP (n = 40; control) over 12 weeks of unrestricted living. Training on study pump and continuous glucose monitor took place over a 4-week run-in period.

Results: In an intention to treat analysis and relative to run-in period, CL increased time that glucose was in target range by 13 ± 8 percentage points compared with a 2 ± 6 percentage point increase in control group (primary endpoint; p < 0.001; closed-loop vs control). In CL group, HbA1c was reduced from screening value of 8.3 ± 0.6% to 8.0 ± 0.6% post run-in and 7.4 ± 0.6% post intervention. In control group these values were 8.2 ± 0.5%, 7.8 ± 0.6%

and 7.7 ± 0.5%; reductions in A1c levels were significantly greater in CL group compared to control (mean difference in change 0.4%; 95% CI, 0.2% to 0.6%; p < 0.001). Mean sensor glucose was lower in CL group (p < 0.001) as was the time spent with sensor glucose levels below 3.9 mmol/L (p = 0.008) and above 10.0 mmol/L (p < 0.001) (table). Time spent with glucose levels below 2.8 mmol/L was not different between interventions (p = 0.11). Similarly, total daily insulin dose was not different (p = 0.09). No severe hypoglycaemia occurred. One diabetic ketoacidosis presented in CL group due to infusion set failure.

Conclusion: Hybrid CL is safe and improves glucose control and HbA1c while reducing the risk of hypoglycaemia across a wide age range in suboptimally controlled T1D supporting adoption of CL in clinical practice.

	Closed-loop (N = 46)	Control (N = 40)	p-value
Time spent at glucose level (%) 3.9-10.0 mmol/L*	65 ± 8	54 ± 9	<0.001
<3.9 mmol/L	2.6 (1.9-3.6)	3.9 (1.7-5.3)	0.008
<2.8 mmol/L	0.3 (0.2-0.6)	0.5 (0.2-0.9)	0.11
>10.0 mmol/L	32 ± 8	42 ± 10	<0.001
>16.7 mmol/L	3.5 (1.9-4.6)	4.4 (2.9-6.5)	<0.001
Mean glucose (mmol/L)	8.9 ± 0.7	9.7 ± 1.0	<0.001
Glucose SD (mmol/L)	3.5 ± 0.5	3.8 ± 0.5	<0.001
Glucose CV (%)	40 ± 4	40 ± 4	0.50
Total daily dose (U/kg/day)	0.81 ± 0.25	0.71 ± 0.19	0.09

[Study endpoints by treatment group. Randomized population:23 children, 19 adolescents/young adults, 44 adults. Mean ± SD or median IQR; *prim. endpoint]

O53

Home use of day-and-night hybrid closed-loop contrasting U20 and U100 insulin in very young children with type 1 diabetes: a 3-week, randomized cross-over trial

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Objectives: To evaluate the feasibility, safety and efficacy of day-and-night hybrid closed-loop insulin delivery (CL) in very young

children with type 1 diabetes under free-living conditions, contrasting diluted (U20) versus standard strength (U100) insulin in a population with low insulin requirements.

Methods: In an open-label, multi-centre, multinational, randomized crossover study, 24 young children aged 1 to 7 years on insulin pump therapy (age 5 (3 to 6) years, median (IQR); HbA1c $7.4 \pm 0.7\%$, mean \pm SD; duration of diabetes 3.1 ± 1.7 years) underwent two 21-day periods of unrestricted living comparing CL with diluted insulin aspart (U20) and CL with standard strength insulin aspart (U100) in random order. During both interventions Cambridge model predictive control algorithm was used.

Results: The proportion of time that sensor glucose was in the target range between 3.9 and 10 mmol/l (primary endpoint) was similar between interventions ($72 \pm 8\%$ vs. $70 \pm 7\%$; CL with diluted U20 insulin vs. CL with standard strength U100 insulin; $p = 0.14$). There was no difference between interventions either in mean sensor glucose (8.0 ± 0.8 mmol/l vs. 8.2 ± 0.6 mmol/l; $p = 0.12$) or sensor glucose variability (SD 3.1 ± 0.5 mmol/l vs. 3.3 ± 0.4 mmol/l; $p = 0.14$). The proportion of time when sensor glucose was below 3.9 mmol/l ($4.5 \pm 1.7\%$ vs. $4.7 \pm 1.5\%$; $p = 0.46$) or below 2.8 mmol/l ($0.6 \pm 0.5\%$ vs. $0.6 \pm 0.4\%$; $p = 0.98$) was comparable. Total daily insulin dose did not differ between interventions (17.3 ± 5.6 U/day vs. 18.4 ± 6.6 U/day; $p = 0.09$). No CL-related severe hypoglycaemia or ketoacidosis occurred.

Conclusions: Day-and-night CL in very young children with type 1 diabetes under free-living home conditions is feasible, safe, and effective. Use of diluted insulin during CL does not provide additional benefits compared to standard strength insulin.

O54

Translating glycated hemoglobin A1c into time spent in glucose target range: a multicenter study

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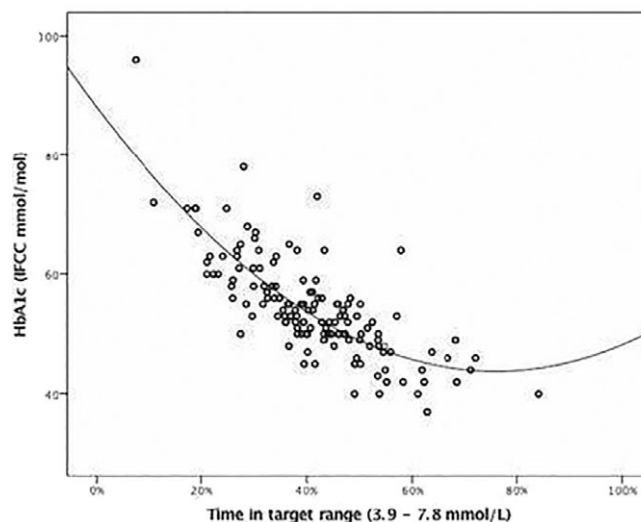
Objectives: Approximately 90.3% of Sweden's children and adolescents with type 1 diabetes (T1D) use continuous glucose monitoring (CGM), either as rtCGM or iCGM to monitor their glucose levels. CGM gives people with diabetes and their health care providers access to new glucose variables, such as "time within target range" for a given time period. Time spent in target range (TIT) is an easy understandable variable to assess glycemic control. However, the relationship between TIT and HbA1c is currently unknown. The objective of this study was to examine the relation between TIT and HbA1c.

Methods: Subjects were recruited from 3 different diabetes care centers in Sweden. Glucose data were collected for 150 children and adolescents with T1D for different time periods through CGM using Diasend[®]. Subjects were included in the analysis if registration time was $>80\%$. HbA1c was collected from SWEDIABKIDS, the Swedish pediatric diabetes quality registry. TIT was defined as 3.9 - 7.8 mmol/L (70 - 140 mg/dL) and time in range (TIR) as 3.9 - 10 mmol/L (70 - 180 mg/dL). Data were analyzed using regression analysis in SPSS.

Results: 138 subjects provided complete data for analyzes during a time period of 30 days. Mean age was $11.7 (\pm 3.5)$ years, mean HbA1c $54.3 (\pm 8.5)$ mmol/mol (7.1%) (compared to Sweden's mean HbA1c of 56.6 mmol/mol (7.3%)). CGM data showed mean glucose $8.5 (\pm 1.4)$ mmol/L (153 mg/dL), mean CV $42.4\% (7.2)$, mean TIT $41.2\% (\pm 12.8\% \text{-units})$ and mean TIR was $60.8\% (\pm 14.2)$. There was a non-linear correlation between TIT and HbA1c, $R^2 = 63.2\%$ and TIR, $R^2 =$

46.2% . This implies that 63.2 % of HbA1c's variation could be explained by time spent within glucose target range.

Conclusion: This study suggests a non-linear correlation between time spent in glucose target range and HbA1c. The finding implies that time spent in glucose target range could be a useful variable in addition to HbA1c to assess glycemic control.



[Relationship between HbA1c and time spent in glucose target range.]

O55

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.

Objective: We evaluated a commercially available device that already exist (Minimed 640G system, Medtronic, CA, USA) for the comparable management of children with diabetes.

Methods: We prospectively analyzed data of all patients who started 640G system at Cremona Hospital after its introduction in Italian market after May 2015.

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, HbA1c at baseline $8.2 \pm 0.7\%$, HbA1c at end of observation $7.3 \pm 1.8\%$, $p = 0.001$) used PLGM system. All patients have been instructed about the use of the system according to our recommendations (Pediatr Diabetes 2017). The patients who used the system over 70% of the time (90% of them for 100% of the time) showed more than 75% of time spent in target range (Table). From the download of the last 3 month data each, patients were within the target range (71-160 mg/dl) 79.5% of the time, which increased to 82.2% when 180 mg/dl was considered as the upper limit. Patients were hypoglycemic (<70 mg/dl) 2.9% of the time and hyperglycemic (>161 mg/dl) 17.6% of the time. No severe hypoglycemia or diabetic ketoacidosis events were recorded during the observation period.

	All patients (n = 62)	Compliant patients (n = 39)	Non-compliant patients (n = 23)	Significance (P)
Age (years)	11.42 ± 3.35	11.22 ± 3.29	11.856 ± 3.37	0.93
Diabetes duration (years)	6.01 ± 3.36	6.67 ± 3.34	5.89 ± 4.14	0.64
HbA1c at baseline (%)	8.2 ± 1.7	7.4 ± 0.7	8.8 ± 1.9	0.04
HbA1c at last follow-up visit (%)	7.3 ± 1.8	6.9 ± 0.8	7.6 ± 1.2	0.03
%time in target (71-160 mg/dl)	59.7	79.5	38.9	0.02
%time in hypo (<70 mg/dl)	3.2	2.9	3.3	0.76
%time in hyper (>161 mg/dl)	37.1	17.6	57.8	0.01

[Clinical characteristics of children using 640G system according to their compliance or not to education pathway.]

Conclusions: It is noteworthy that PLGM system, if used most of the time after a systematic educational pathway, attains results that are close, or better, to those obtained using hybrid closed-loop or fully AP. It is solacing to know that we already have useful tools for the best possible care of our patients with type 1 diabetes while we wait for the commercial availability of an AP or a more performant hybrid CL system.

O56

Do small inaccuracies affect the bigger picture? Reliability of flash glucose monitoring system in children and adolescents with type 1 diabetes in light of glycemic variability

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Objectives: Flash glucose monitoring (FGM) allows for continuous, minimally invasive monitoring of glycemia. Longer intervals between measurements than in continuous glucose monitoring (CGM) systems beg the question of whether FGM is interchangeable with CGM. In this study, we reported the difference of glycemic variability (GV) indices between FGM and CGM according to the International Consensus on The Use of Continuous Glucose Monitoring.

Methods: Children with T1DM aged 12-18 years with disease duration of ≥2 years were recruited into the study. We equipped them with FGM and blinded CGM sensors worn on each arm for a maximum of 7 days. Raw data was downloaded, aligned along measurement timeframes between systems and analyzed with in-house software Glyculator 2.0 to calculate 22 GV indices listed in the Consensus.

Results: Eighteen patients (15.5 ± 1.6 years old, duration of diabetes 6.4 ± 3.5 years) agreed to the experiment and completed measurements. Both CGM and FGM duration equaled 5.82 ± 0.13 days. GV indices differed between CGM and FGM in: time spent in the range 70-180 mg/dl (3.9-10 mmol/l) 8.0% 95%CI 3.9-12.1;p = 0.0003, low blood glucose index by -1.6 95%CI-2.5- -0.7; p < 0.0001, coefficient of variance -5.3 95%CI-7.3- -3.3; p < 0.0001, MODD -8.2 95%CI-13.5- -2.9;p = 0.0049, CONGA_{1h} -4.9 95%CI-7.8 to -1.9;p = 0.0030, GRADE -1.5 95%CI-2.4 to -0.6;p = 0.0032, completeness of measurements by 13.9%95%CI10.0-18.0;p = 0.0095. CGM and FGM did not differ significantly in mean glycemia (p=0.6851), estimated HbA1c (p = 0.6851), high blood glucose index (p = 0.6739) and J-index (p = 0.4819).

Conclusions: Calculations of GV based on FGM differ substantially from those done using CGM, which may lead to a potential underestimation of times spent in hypoglycemic ranges and an overestimation of high amplitude fluctuations of glucose levels resulting in unfounded attempts to optimize insulin and meal regimens.

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Oral Session VIII - Diabetes Education

O57

Validation of a diabetes knowledge test for Indian children, adolescents and young adults with type 1 diabetes mellitus

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Introduction: Diabetes knowledge has a large impact on glycemic control. There is a pressing need for creation of validated tests of knowledge for different ethnic groups.

Objective: To create and validate a diabetes knowledge test (DKT) for young Indians with type 1 diabetes mellitus (T1DM).

Methods: We created a 34 item Hindi language DKT, with basic (19-questions) and advanced (15-questions) components. It was administered to 77 consecutive patients who had previously received in-hospital diabetes education. We hypothesized that the test scores would be higher for patients residing in urban regions, for patients with higher maternal education, and those with lower HbA1c. Cronbach's coefficient α was used to calculate the test reliability.

Results: Our study population (n = 77) belonged to age 3 to 25 years (median 14 years). Forty two patients (54.5%) were male and 60 (77.9%) resided in an urban area. The mean HbA1C was 8.2 % (66 mmol/mol) [5.6-12.8 % (38-116 mmol/mol)]. In DKT, they received 63.7 \pm 16.2 marks out of 100 in the entire test while 69.2 \pm 15.8% marks in the basic and 64.5 \pm 17.3% marks in the advanced diabetes knowledge test respectively. The DKT score was significantly higher in families with higher (>class 12th) maternal formal education compared with lower [70.0 (48.5-94.0) vs 54.3 (21.0-78.0), p < 0.001] and urban residence compared with rural [68.5 (25.0-94.0) vs 54.5 (21.0-82.0), p < 0.001]. It had negative correlation with HbA1c (r = -0.268, p = 0.019). The Cronbach's coefficient α was 0.87 for the entire test, and for the basic and advanced components was 0.78 and 0.74 respectively.

Conclusion: The DKT India is a valid and reliable instrument to evaluate diabetes knowledge in Hindi speaking Indian children, adolescents and young adults with T1DM.

O58

Young children with type 1 diabetes spend majority of time outside of target glucose range

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Objectives: There are limited data on sensor glucose profiles among youth less than 8 yrs of age with type 1 diabetes (T1D). We analyzed blinded continuous glucose monitoring (CGM) data collected at baseline in a randomized trial assessing the effect of CGM on glycemic control.

Methods: Data from 135 children enrolled in the Strategies to Enhance New CGM use in Early Childhood (SENCE) study at 14 sites in the United States were analyzed. Major eligibility criteria for the trial included age 2-< 8 yrs, T1D duration \geq 3 months, no use of real-time CGM in the 30 days prior to enrollment and an A1c between 53-<86 mmol/mol. All participants wore a blinded Dexcom G4 CGM at baseline for up to 14 days to collect at least 200 hours of CGM data. Associations of demographic and clinical characteristics with

CGM-measured glucose indices and A1c were assessed using linear regression models.

Results: Participants had a median age 5.9 (IQR 4.2, 7.3) yrs and median T1D duration 1.9 (IQR 0.7, 4.0) yrs; 65% were non-Hispanic white and 36% used insulin pumps. Mean A1c was 70 \pm 8.7 mmol/mol. Children spent a median 41% (9.8 hrs/day) of time in target glucose range (21-63 mmol/mol) and a majority of time in hyperglycemic range, with median 55% of time >63 mmol/mol (13.2 hrs/day) and 27% of time >89 mmol/mol (6.6 hrs/day). We observed a median 4% of time <21mmol/mol (60 min/day) and 1% of time <15 mmol/mol (20 min/day). Factors associated with more time in target range included minority race (p = 0.04) and higher parent education level (p < 0.01). Lower A1c was associated with higher parent education (p = 0.02).

Conclusions: On review of blinded CGM data, young children <8 yrs of age with T1D spent a minority of time in target range, with over half of their time spent in hyperglycemia, and a substantial amount spent in hypoglycemia. Given that both hypo and hyperglycemia may negatively impact young children's cognitive development, strategies to increase time in target glucose range are needed.

O59

Influence of intensive education coupled with counseling on glycosylated hemoglobin levels and other parameters of diabetes control in pediatric patients with type 1 diabetes mellitus in India

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Introduction: Intensive education in diabetes self-management coupled with psychosocial counseling is an integral part of management of Type 1 diabetes (T1D). For this purpose, we conduct residential camps, where patients, their parents & the medical team live together for three days in an out of hospital setting.

Objective: To determine whether residential camps for T1D lead to improved glycemic control.

Methods: This was a prospective, cohort, interventional study. Patients with T1DM, on treatment for over 1 year, who attended at least one camp (December 2014 & /or 2015), were included. Besides diabetes education patients were counseled on overcoming barriers to compliance.

Result: Of 58 patients included in the study, 20(34.5%) attended both camps and 38(65.5%) attended any 1 camp. There were 31 males & 27 females. Ages ranged from 4-18 years (mean12.52 years). All patients had height, weight & BMI between 3rd-90th centile. 72.4% patients were on basal-bolus insulin regime, 22.4% were on 2 injections a day regime and 5.2% were on insulin pump. Mean HbA1c at 1st camp was 9.1%. 3 months later it was 8.7%. [p = 0.001]. 9 months later it rose marginally to 8.852%. At the 2nd camp mean HbA1c was 8.718%. 3 months later it was 8.421%. In those attending both camps, mean HbA1c reduced further 3 months after 2ndcamp (7.795% vs.7.865%). Number of patients performing SMBG > 3 times a day increased significantly after the camps (82.7% vs. 39.7%). Incidence of severe hypoglycemia decreased after the camps, though this was not statistically significant. Hospitalization for ketoacidosis during acute illnesses in 6 months before camp was 15.5%, post camp this reduced to 1.7%.

Conclusion: Residential camps for education and counseling in T1DM can lead to significant improvement in HbA1c, better compliance with SMBG, reduction in risk of hypoglycemia and of ketoacidosis. Reinforcement is needed for these benefits to be sustained.

Month & Year	Mean HbA1c	No. of patients with HbA1c <7.5	No. of patients with HbA1c <8.5
Sept. 2014	8.395	3	6
Camp/Dec. 2014	8.378	2	6
Mar. 2015	7.865	4	10
Sept. 2015	8.104	6	5
Camp/Dec. 2015	8.305	6	6
Mar. 2016	7.795	9	5

[HbA1c of 20 patients who attended 2 consecutive camps]

O60

Impact on glycemc profile, glycemc variability and unexplained hypoglycemia among people with T1DM having lipohypertrophy, after correction of insulin injection technique

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Objectives: Lipohypertrophy (LH) is a frequent complication of insulin injection therapy in Type 1 Diabetes Mellitus (T1DM). People with LH are more likely to have glycemc variability (GV) and unexplained hypoglycemia (UH). Our study evaluated whether the correction of insulin injection technique has any impact on glycemc control and other LH related complications in T1DM.

Method: Study done at tertiary diabetes care center from Central India. 36 subjects of age 20.2 ± 10.67 yrs. having LH of grade 1 and grade 2 were selected from June 2017 to December 2017. They were counseled in one to one interactive sessions, for proper insulin injection techniques and rotation of injection sites. Grades of LH, Glycemc control, GV, UH were compared in pre and post education session after minimum three months. Continuous parameters were compared using paired t-test. The before and after effect of intervention for grades was evaluated using marginal homogeneity test, while the dichotomous response variables were evaluated using McNemar test. The statistical significance was tested at 5% level.

Results: LH size showed statistically significant reduction after the intervention p-value 0.0001. There was statistically significant change in the post-intervention grades of LH ($p = 0.0001$), as obtained using marginal homogeneity test. Referring to a cut-off value of 9 for HbA1c, a significantly higher proportion of patients with pre intervention values > 9 got reduced to < 9 post intervention (60%) with a p-value 0.0388. The proportion of cases with unexplained hypoglycaemia reduced significantly post-intervention as indicated by p-value of 0.022. Glycemc variability reduced in significantly higher proportion of cases (38.89%) with a p-value of 0.0001 after intervention.

Conclusion: Implementation of insulin injection techniques through proper education can reduce the risk of LH, improve glycemc control, will reduce the risk of GV, UH and in turn improve the quality of life among T1DM.

O61

Care triad for diabetes in children & adolescents - diabetes education, counseling & support

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Objectives: To understand the role and requirement of education, counseling, and holistic support in the management of children with type 1 diabetes (T1D) along with medical treatment.

Methodology: Review of medical literature including guidelines and other scientific literature

A qualitative observation during patient interactions & reviewing outcomes at the Changing Diabetes in Children centers across India.

Results

1. Education is the keystone of diabetes care and is the key to a successful outcome. It begins with teaching of survival skills and continues with higher learning to fit diabetes into lives of people.
2. The diagnosis of diabetes in children usually has a major psychological impact. There is a need for training the diabetes team not only in the principles of structured education but also in behavioral change management including counseling techniques for better outcomes.
3. Peer support is a concept that has generated interest recently. Sharing experiences with others undergoing the same medical or behavioral- life style tasks is an effective means of gaining mastery of tasks and improving disease outcomes.

Conclusions: Evidence suggests that children with T1D do better when they receive effective treatment within an integrated system with self-management support and regular follow up. Best of diabetes education fails when it is not coupled by appropriate counseling and support. Only counseling does not work until a person gets an appropriate support and diabetes education. Best of support fails when it does not work on principles of diabetes education. Changing Diabetes in Children program provides all these elements, in a resource limited settings, as all three are essential for comprehensive care for every child with type 1 diabetes.

O62

A novel and successful e-learning solution to school personnel training in complex type 1 diabetes management

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Objectives: To evaluate novel Type 1 Diabetes (T1D) e-learning courses for school based upon ISPAD guidelines using Moodle platform.

Methods: Australia has not provided adequate school staff training to manage complex T1D care. Teachers and families feel unsupported. Students experience discrimination, substandard management options and inappropriate care. Only 27% reach target HbA1c $< 7.5\%$. To address this deficiency, novel on-line courses were created for school staff based upon ISPAD guidelines. A suite of 3 courses, pitching to different levels of school staff responsibility utilized Moodle, a Learning Management System not previously described in T1D school training. The no-cost courses provide an adjunct to on-site school training in complex T1D care including insulin administration.

A voluntary exit survey examined participants' perception of course usefulness, understanding the need for complex medical care at school, logistics and technology and the effect on confidence in managing T1D.

Results: In 6 months, 9222 users accessed the website with 2097 courses completed. Feedback was overwhelmingly positive. 1071 completed Course 1 (generic education). The survey sample clearly understood reasons for insulin administration at school (97%), basic T1D logistic / technical issues (97%) and confidence managing T1D (91%). 659 completed Course 2 (advanced training) with increased understanding of T1D medical (100%), emotional (90%), exercise (88%), nutrition (98%), technical (93%) issues, role delineation (100%) and instillation of confidence in management (100%). 367 completed Course 3 (insulin administration) with understanding of medical (93%), logistical (93%), legal (95%) and confidence (71%).

Conclusions: Our Moodle-based T1D e-learning courses for school significantly increased understanding of T1D, instilled confidence and

were received with overwhelming enthusiasm. This innovative, free on-line resource is an effective adjunctive T1D training tool.

O63

Empowering D-Moms [mothers of children with type1diabetes] to become diabetes coaches in rural India to reach the unreached

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Objective: We designed a module to train D-Moms as diabetes coaches in rural India and observed how effectively these coaches act as a bridge between the doctor/educator and a T1D child.

Methods: Our center currently provides free support to 536 children from resource restrained, low literacy and rural backgrounds. With non-availability of diabetes educators within 100 kilometer radius, we needed to create innovative options.

D-Moms were selected based on defined criteria to enroll into a structured training program of three months duration. The academic qualifying requirement was kept at minimum to broaden the reach in community. These women were trained and received a specialized toolkit in their local language. They underwent practical training sessions under supervision before becoming diabetes coaches. The job of diabetes coaches was specified and restricted to teach predefined basics to T1D families and motivating them with personal experiences. The diabetes coaches kept a log of their interaction with each child and passed on the details to the educator/doctor.

The diabetes coaches also provided 24x7 helplines to children. 15 such D-Moms were trained to become coaches in the first phase.

Results: Two years of experience with 15 diabetes coaches who are D -Moms, assisting the team of doctor and qualified educators yielded some interesting outputs.

1. Individualized education resulted in better self-care.
2. Stronger bonding as the coach herself was a mother to a T1D child.
3. Local myths and social issues were effectively handled.
4. Dropout rate minimized with increased followup.
5. 24 × 7 help lines helped in preventing and managing acute complications at home, thereby reducing hospitalization drastically.

Conclusion: In resource restrained and rural areas, diabetes coaches can act as a bridge between healthcare providers and the T1D child. We believe that empowering D-Moms to becoming diabetes coaches is a reproducible model of community care.

O64

"Reaching the unreached??" in childhood diabetes patient - family health education and counseling: three decades challenges, failures and successes from India [DISHA - CDIC - LFAC]

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Objectives: To reflect on our diabetes health education and self-care counseling efforts and examine possibilities for further improvement.

Methods: DISHA Free Diabetes Clinic for the Poor [1987 - Ongoing]: Since 2011, 386 children are receiving enhanced support - free insulin [Basal bolus insulin (meal time regular + bedtime NPH) 100%], syringes, health counseling, 24 h help lines, BG meters, 30 BG strips/month and limited biochemical evaluations [TSH, quarterly HbA1c, annual urine albumin: creatinine ratio] [Changing Diabetes in Children and Life for a Child with Diabetes].

Results:

Strategies	Perceived Effectiveness Score [0-10]	Successful Implementation Score [0-10]
Individual Counseling: Initial, Continued, Reinforcement	10	8
Group Counseling: Classes, Seminars, Workshops	8	6
24 hour helplines: Short term problem solving, Emergencies	10	10
Peer counseling: Motivation by achievers - Role models	8	4
Learning resource materials: Age, Literacy, Language tailored	6	4
Residential camps: Learning + Fun + Confidence building	6	2
"Giving Tree": Friends of DISHA Stars - Support a Child	6	2
Scholarship grant for school and college education	6	2
Mental Health Clinic: Psychology and Psychiatry services	8	4

[HE]

Successes: QID insulin = in 100%, **SMBG Quantity Score** (number of tests performed per month) = 28/30; **SMBG Quality Score** = 9/10; and **SMBG Accuracy Score**: 9.8/10; **Self-insulin adjustment score** = 6/10; **HbA1c trend (%)** Improvement: 39%; Stable: 50%; Worsening: 11%; **HbA1c < 8%** = Enrolment: 11%, Latest: 23%

Failures: Self-urine ketone testing <10%; Glucagon injection at home/school = 0% [unaffordable]

Strengths: Led by pioneers in diabetes health education in India, dedicated staff/ volunteers/ peers [Motto: Service with Devotion], long experience

Limitations: Need for more structured programs, meager finances, volunteer manpower time shortage

Conclusions: In a resource limited setting, philanthropy based health education, counseling and psychosocial support has improved health and welfare in children with diabetes in our community. However, more systematic, committed and culture sensitive [including "Out of Box"] programs are necessary to bridge the health education / care gap between **haves** and **have nots**.