ISPAD 2014

ORAL ABSTRACT SESSIONS

Oral Session I: Diabetes Acute and Chronic Complications

O1

Alpha-lipoic acid and anti-oxidant diet improves endothelial dysfunction in children and adolescents with type 1 diabetes

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Objectives: After evaluating the prevalence of early endothelial dysfunction, as measured by mean of reactive hyperemia (RHI), in adolescents with type 1 diabetes (T1D), at baseline and after 1-year follow-up, we started a 6-month, double-blind, randomized trial to test the efficacy of an anti-oxidant diet (± α-lipoic acid) in improving endothelial dysfunction.

Methods: Sixty-one children and adolescents, ages 16.0 ± 3.4 years, with T1D since 8.1 ± 5.2 years, using either MDI (n = 26, 42.6%) or CSII (n = 35, 57.4%), were randomized into 3 arms: (A) anti-oxidant diet 10.000 Oxygen Radicals Absorbance Capacity - ORAC + α-lipoic acid (n = 25); (B) anti-oxidant diet 10.000 ORAC + placebo (n = 27); (C) controls (n = 9). BMI, blood pressure, fasting lipid profile, HbA1c, insulin requirement, dietary habits and body composition were determined in each child after 3 and 6 months.

Results: After 3 months BMI, blood pressure, lipid profiles, HbA1c, and body composition did not change, while insulin requirement significantly decreased only in patients in arm A (0.74 ± 0.18 U/kg/day vs. 0.83 ± 0.26 U/kg/day, $p < 0.05$), as well as bolus insulin (22.0 ± 9.4 U/day vs. 26.3 ± 10.8 U/day, $p < 0.05$), but not basal insulin (25.9 ± 9.4 U/day vs. 25.5 ± 8.6 U/day, P NS). After 6 mo observation, RHI significantly improved only in patients in group A (1.7 ± 0.6 vs. 1.4 ± 0.7, $p < 0.05$), but not in groups B (1.6 ± 0.4 vs. 1.4 ± 0.4, $p > 0.05$) and C (1.5 ± 0.4 vs. 1.5 ± 0.6, $p > 0.05$). After 6 mo, bolus dose was still significantly lower only in group A ($p < 0.05$), while no difference has been observed regarding basal dose, BMI, blood pressure, lipid profile during the follow-up. Any change in body composition and dietary habits are still under evaluation.

Conclusions: Our data showed for the first time that an anti-oxidant diet rich in ORAC plus α-lipoic acid is effective to significantly improve the endothelial function in adolescents with T1D. Larger studies are needed to confirm these very interesting and helpful results.

O2

Association between markers of endothelial dysfunction and early signs of renal dysfunction in pediatric obesity and type 1 diabetes

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Objectives: To evaluate whether markers of endothelial dysfunction, such as intercellular adhesion molecule-1 (ICAM-1) and myeloperoxidase (MPO), are increased in youth with obesity and with type 1 diabetes (T1D) compared to normal weight healthy peers, and whether their levels are associated with markers of renal function.

Methods: 60 obese youth (M/F: 30/30, age: 12.5 ± 2.8 years; BMI-SDS: 2.26 ± 0.46), 30 with T1D (M/F: 15/15; age: 12.9 ± 2.4 years; BMI-SDS: 0.44 ± 0.77) and 30 healthy controls (M/F: 15/15, age: 12.4 ± 3.3 years, BMI-SDS: −0.25 ± 0.56) were recruited. Anthropometric measurements were assessed and blood samples were collected to measure ICAM-1, MPO and creatinine. 24-hour urine samples were collected for assessing albumin excretion rate (AER).

Results: Levels of ICAM-1 and MPO were similar between obese and T1D youth, and higher in both groups compared to controls. Similarly, levels of AER and e-GFR were not different between obese and T1D youth, but they were increased compared to healthy controls (Table 1). BMI-SDS was significantly associated with ICAM-1 ($\beta = 0.21$, $p = 0.02$) and MPO ($\beta = 0.36$, $p < 0.001$). A statistically significant association was also found between ICAM-1 and markers of renal function (AER: $\beta = 0.26$, $p = 0.004$; e-GFR: $\beta = 0.23$, $p = 0.012$), after adjusting for BMI.

Conclusions: Obese youth have increased markers of endothelial dysfunction and early signs of renal damage, similarly to their peers with T1D, confirming the role of obesity as a cardiovascular risk factor. The association between ICAM-1 with e-GFR and AER suggests a potential role of endothelial dysfunction in the pathogenesis of obesity-related renal damage.

Table 1

Markers	Obese (Ob)	T1D	Controls (Co)	P: Ob vs. T1D	P: T1D vs. Co	P: Ob vs. Co
ICAM-1 (μg/ml)	0.606 (0.460–1.033)	0.729 (0.507–0.990)	0.395 (0.277–0.596)	0.716	<0.001	0.001
MPO (μg/ml)	136.60 (69.70–220.76)	139.50 (51.00–321.28)	41.26 (39.72–106.96)	0.905	<0.001	0.001
AER (μg/min)	8.92 (6.53–10.84)	9.00 (7.75–12.40)	7.94 (5.35–8.13)	0.314	0.001	0.001
eGFR (ml/min/1.73 m^2)	142.82 (124.31–160.32)	145.50 (130.75–156.00)	134.50 (119.00–142.25)	0.485	0.007	0.002

O3

EEG based prediction of hypoglycaemia at day time in prepubertal children with type 1 diabetes

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Objectives: The fear of hypoglycaemia is a major obstacle of obtaining near-normal blood glucose levels (BGL) in children. Hypoglycaemia avoidance behaviour might adversely affect glycaemic control in T1D children thereby increasing the risk for long term diabetic complications. Here, we test an automated EEG algorithm initially developed for adults in predicting hypoglycaemia in children.

Subjects and methods: 8 pre-pubertal children (4 males), aged 9.6 ± 2.3 years, T1D duration of 3.0 ± 1.4 years, HbA1c 55 ± 3.4 mmol/mol and 7/8 on CSII treatment underwent hyperinsulinimic hypoglycaemic clamp in awake state during daytime. After a run in period of 45 min with an iv infusion of glucose (3.3–6.7 mg/kg/min) and insulin (80 mU/m^2/min) with stabile blood glucose values at 7–9 mmol/l, the hyperinsulinaemic hypoglycaemic clamp was initialized by a slow reduction in glucose infusion until BG reached nadir. The hypoglycemia was terminated at nadir either by significant hypoglycemic symptoms (evaluated by either the patient, parents or physician) or by a BGL level at 2.2 mmol/l. EEG was recorded and analyzed using an automated EEC algorithm.

Results: The automated algorithm detected the induced hypoglycaemia in all children on average at a BGL of 2,5 ± 0.5 mmol/l (range 1.7–3.0 mmol/l) and 18.4 ± 20.3 minutes (range 0–55 minutes) prior to BGL nadir on average 2.3 ± 0.5 mmol/l (range 1.6–2.9 mmol/l). No false positive alarms were recorded.

Conclusions: This automated EEG algorithm identified hypoglycaemia in 8/8 pre-pubertal children in awake state before severe hypoglycaemia developed. The potential of this new automated algorithm should be evaluated in children during sleep for predicting nocturnal hypoglycaemia.

O4

Effect of HLA-DR, DQ genotypes and family history of diabetes on the presence of diabetic ketoacidosis at diagnosis of type 1 diabetes in children

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Objectives: To explore a potential effect of the HLA DR, DQ genotypes and family history of diabetes on the presence of DKA at onset of T1D.

Methods: The study population included 2267 children diagnosed with type 1 diabetes (T1D) before 18 years of age, between 1998 and 2012. HLA-DR,DQ typing was performed using PCR SSOP. The genotypes were classified as high-risk (DRB1*03, DQB1*0201/DRB1*04, DQB1*0302); moderate-risk (DRB1*03, DQB1*0201/DRB1*03, DQB1*0201 or DRB1*04, DQB1*0302/DRB1*04, DQB1*0302 or DRB1*04, DQB1*0302/x) and neutral/low-risk. Family history of diabetes was obtained at diagnosis.

Results: The overall prevalence of DKA was 37.1%. Family history was positive for T1D in a first degree relative (FDR) or second-degree relative (SDR) in, respectively, 9.7% and 11.3% of the study participants. Presence of an FDR with T1D was associated with a lower prevalence of DKA at diagnosis (14.5–21.4%) regardless of the HLA genotype. Presence of an SDR with T1D or an FDR with T2D predicted lower rate of DKA only among children with neutral/low-risk HLA genotypes. In multivariable logistic analysis, controlling for age, race/ethnicity, and HLA genotypes, family history of diabetes was a strong independent predictor of lower rate of DKA at diagnosis ($p < 0.0001$). The odds ratios (95% CI) for DKA were 0.32 (0.22–0.46), 0.59 (0.44–0.78) and 0.69 (0.48–1.00) among children with, respectively, T1D FDR, T1D SDR and T2D FDR, compared to the Else category. The independent effect of HLA genotypes was less pronounced with odds ratios for the high-risk genotype of 1.23 (0.92–1.64) and moderate-risk genotypes 1.51 (1.03–2.21), compared to neutral/low-risk genotypes.

Conclusions: Family history of diabetes, including T1D in SDR and T2D in FDR, may protect from DKA at diagnosis of T1D in children, due to increased awareness of signs/symptoms of diabetes and access to home glucose monitoring. The highest-risk HLA-DRB1*03, DQB1*0201/DRB1*04, DQB1*0302 genotype does not appear to predispose to DKA.

O5

Achieving international society for pediatric and adolescent diabetes clinical guidelines offers cardiorenal protection for youth with type 1 diabetes?

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Objective: Most youth with type 1 diabetes (T1D) in the T1D Exchange Clinic Registry did not meet the American Diabetes Association (ADA) and International Society for Pediatric and Adolescent Diabetes (ISPAD) targets for HbA1c, SBP/DBP, LDL-C, TG and BMI. We hypothesized that ISPAD/ADA goal achievement at baseline would be associated with lower odds of elevated markers of cardiorenal health at 2 year follow-up in adolescents with T1D.

Methods: We assessed the cross-sectional and longitudinal relationships between ISPAD/ADA goal achievement at baseline and cardiorenal health at baseline and 2 year follow-up ($n = 297$; age 15.4 ± 2.1 years). Goal achievement was defined as HbA1c <7.5%, BP <90th centile for age, sex and height, LDL-C <100 mg/dl, HDL-C >35 mg/dl, TG <150 mg/dl and BMI <85th percentile for age and sex. Cardiorenal outcomes included pulse-wave velocity (PWV), brachial distensibility (BrachD) and augmentation index (AIx), estimated GFR (eGFR) by Schwartz 2009 (36.5 × height/serum creatinine) and hyperfiltration (eGFR >135 ml/min/1.73 m^2).

Results: 222 participants met more than 3 goals at baseline (53% male) and 75 did not (44% male). Participants who met more than 3 goals had significantly lower follow-up PWV (5.47 vs. 5.72 m/s, $p = 0.03$), greater change in BrachD (−0.82 vs. 0.28%/mmHg, $p = 0.02$), lower follow-up AIx (5.41 vs. 8.41%, $p = 0.049$), lower follow-up eGFR (104 vs. 116 ml/min/1.73 m^2, $p < 0.0001$) after adjusting for Tanner stage, sex and T1D duration. Moreover, achieving >3 goals at baseline was associated with 95% lower odds of follow-up hyperfiltration (1.3 vs. 17%, OR: 0.05, 0.01–0.26, $p = 0.0004$) after adjusting for age, sex and T1D duration.

Conclusions: In adolescents with T1D, ISPAD/ADA goal achievement at baseline was associated with cardiorenal protection at 2 year follow-up, emphasizing the importance of disease control.

O6

Accumulation of skin advanced glycation end-products are associated with early retinopathy in youth with type 1 diabetes

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Objectives: Non-invasive measure of skin autofluorescence (AF) correlates with accumulation of advanced glycation end-products (AGEs) in skin collagen. Skin AF is associated with vascular complications in older adults, independent of HbA1c. This study aims to determine: (1) skin AF in young people with type 1 diabetes (T1D) vs. controls, and (2) the association between skin AF and retinopathy.

Methods: Skin AF, as a mean of 6 readings at the forearm, was measured by the Diagnoptics AGE Reader in 78 youth with T1D (mean age 17.4 ± 3.8 years, duration 10.1 ± 4.0 years, HbA1c 8.8 ± 1.6%) and 70 age-matched controls (mean age 17.6 ± 6.0 years). Based on 7-field stereoscopic fundal photography, retinopathy was defined as ≥20 in any eye using the Modified Airlie House Criteria.

Results: Age-adjusted mean skin AF was higher in diabetes vs. controls (1.43 ± 0.04 AU vs. 1.22 ± 0.04 AU, $p < 0.001$). Retinopathy was seen in 22% of diabetic patients. Age-adjusted mean skin AF was higher in retinopathy-free diabetes vs. controls ($p < 0.05$) and tended to be higher in diabetes with retinopathy vs. retinopathy-free ($p = 0.08$). ROC analysis showed skin AF as a strong screening tool for presence of retinopathy (AUC 0.78, $p = 0.001$). Skin AF was associated with older age ($\beta = 0.06$, 95% CI 0.04–0.08; $p < 0.001$) and higher HbA1c (0.1, 0.04–0.15; $p = 0.001$), or longer duration of diabetes (0.04, 0.02–0.06; $p = 0.002$) and higher HbA1c (0.1, 0.04–0.16; $p = 0.002$). Highest quartile of skin AF (≥1.62 AU) was associated with retinopathy (6.3, 1.9–20.5, $p = 0.003$), which remained significant after adjusting for HbA1c (4.3, 1.2–15.3; $p = 0.03$).

Conclusions: Increased skin AF in youth with diabetes is associated with retinopathy in cross sectional analysis. Longitudinal studies will determine the utility of skin AF as a non-invasive screening tool to predict future retinopathy risk and potentially provide a measure of metabolic memory in diabetes complications, which cannot be accurately measured by serial HbA1c alone.

O7

Glycaemic control, complications and outcome following transfer of care in young adults with childhood onset type 1 diabetes mellitus

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Objectives: To establish the glycaemic control and rate of microvascular complications in young people with childhood onset type1 diabetes mellitus (T1DM). And to look specifically at a subset of patients before and after transfer from paediatric to adult care at a single centre.

Methods: Data was collected from our electronic database on patients with T1DM currently attending transition clinic and those transferred to adult services between August 2009 and 2012.

Results: Hundred and four (55 males) patients with a median age of 19.2 years were identified. Mean(±SD) age at diagnosis and duration of diabetes were 9.2(±3.8) and 9.4(±3.9) years respectively. Majorities were on multiple daily injections (66.3%) and others on Pump (27.9%) and twice daily injection regimen (5.8%). Mean HbA1c was 77 ± 18 mmol/mol. Microalbuminuria was noted in 8.6% and retinopathy in 43.2% with 41.3% having only background changes. Hypothyroidism and coeliac disease was detected in 6.7% and 3.8% respectively.

Fifty-four patients were in transition and 50 post transfer to adult care. In the latter group, mean age of transfer was 18.5(±1.2) years. Mean HbA1c one year pre and post transfer was similar (78 ± 20 mmol/mol and 78 ± 22 mmol/mol, respectively; $p = 0.22$). There was no statistically significant difference in the mean HbA1c 2 and 3 years pre and post transfer of care. Although clinic appointments became less frequent following transfer, failure to attend rate did not change. A small subset of patients ($n = 7$) who opted for e-mail support demonstrated improved mean HbA1c over one year from 68 ± 8 mmol/mol to 63 ± 10 mmol/mol, $p = 0.051$.

Conclusions: Glycaemic control and clinic attendance is stable following transfer of care of young diabetes patients. Background retinopathy is present in a large percentage of patients. Email support may represent one strategy to improve engagement and diabetes control in this population and warrants further investigation.

O8

Predictors for vascular disease hospitalisations in young adults with childhood onset T1DM; insights from 20 years of follow up

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There is evidence to suggest that improvements in the management of T1DM over the last 2 decades have been associated with a change in the epidemiology of microvascular and macrovascular complications.

The Western Australian paediatric diabetes database was established in 1987 and serves a population of 2.4 mil (>99% ascertainment for T1DM <16 years). Patient data from 3 monthly clinical visits are stored prospectively. All patients with T1DM <18 years of age by Dec 2011 were included in the study. Their paediatric clinical records were linked to all public and private inpatient hospitalisations in Western Australia for vascular disease between Jan 1992 and Jan 2012.

Of the 1,298 eligible patients (50.4% males), 915 were identified in the inpatient database. Those not identified had a lower attained age (23.6 vs. 27.5 years, $p < 0.001$), lower paediatric mean HbA1c (8.5% vs. 9.2%, $p < 0.001$) and were 30% less likely to be male ($p < 0.001$). For the 915, there were 7,657 patient years (PY) of paediatric data available for analysis against 8,652 years of follow-up data (after age 18 years); mean duration at end the end of follow-up was 17.5 years. The overall incidence rates were 3.40/1000 PY for retinopathy ($n = 26$), 0.65/1000 PY for dialysis ($n = 5$), 0.52/1000 PY for stroke ($n = 4$), 0.39/1000 PY for myocardial infarction ($n = 3$) and 1.04/1000 PY for atherosclerosis ($n = 8$).

Those with vascular disease were 3.4 times more likely to be female ($p = 0.001$), more likely to be from a lower SES, older (birth

year 1980 vs. 1984, $p < 0.001$), and have a higher mean paediatric HbA1c (11.0% vs. 9.1%, $p < 0.001$). Mean age at diagnosis was similar (9.7 vs. 9.2 years).

These data indicate reduced rates of vascular complications compared to previous reports, confirm the association between poor glycaemic control and the development of vascular complications, and identify females and those from a low socio-economic background to be at a higher future risk of vascular complications.

Oral Session II: Exercise & Obesity in Type 1 DM & Type 2 DM

O9

Lifestyle factors associated with glycemic control in youth with type 1 diabetes (T1D): the global TEENs Study

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Objectives: TEENs is the largest worldwide (20 countries), contemporary, observational study of T1D (n = 5960) in 8–25 years old (y/o) patients. Lifestyle factors related to glycemic control are reported.
Methods: 219 centers collected data by interview, record review and survey from 3 groups: 8–12 y/o, 13–18 y/o and 19–25 y/o. A1c was measured uniformly using A1cNow™ (Bayer); A1c targets were defined as <7.5% (58 mmol/mol) for ≤18 y/o (ISPAD) and <7% (53 mmol/mol) for 19–25 y/o (ADA). Factors associated with attaining A1c target were identified by multivariate logistic regression.
Results: Overall, 72% of participants were not well controlled: A1c target was met in 32% of 8–12 y/o, 29% of 13–18 y/o and 19% of 19–25 y/o (Table). Significant associations were found between glycemic control and exercise (p = 0.002) and smoking (p = 0.003); participants who exercised ≥30 min/week (88%) were more likely to attain A1c target (OR [95% CI]: 1.45 [1.15, 1.83]); smokers (5% in 13–18 and 16% in 19–25 y/o) were less likely to attain A1c target (0.63 [0.46, 0.85]). No significant association was found between BMI (17% of participants were overweight, 10% were obese) and glycemic control.
Conclusions: One modifiable lifestyle factor (exercise) was associated with A1c target attainment: efforts targeting exercise could promote successful health outcomes. Non-exercising and smoking may be associated with other behaviors impacting glycemic control.

Study sponsored by Sanofi.

Table: Lifestyle factors by age and A1c target attachment

	8–12 y/o		13–18 y/o		19–25 y/o	
	A1c target met n = 553 (32%)	A1c target not met n = 1,170 (68%)	A1c target met n = 833 (29%)	A1c target not met n = 2,021 (71%)	A1c target met n = 260 (19%)	A1c target not met n = 1,122 (81%)
Number of days per week spent exercising*, %						
0	4	7	8	12	13	19
1–2	28	26	26	27	26	25
3–4	35	29	34	26	27	25
5–7	33	38	30	34	32	29
BMI-for-age adjusted for sex (CDC thresholds) for 8–18 y/o, %						
<85th percentile | underweight/normal|	70	71	76	74		
85th percentile; <95th percentile |overweight|	19	15	16	15		
95th percentile |obese|	12	13	8	11		
BMI in classes for 19–25 y/o (kg/m^2), %						
<25					70	72
25; <30					25	23
30					5	6
Smokers, %	0.4	<0.1	3.7	3.1	14.0	16.5

*At least 30 min doing any physical activity or exercise.

O10

Effect of a short-term exercise training program on muscle strength and joint mobility of young subjects with type 1 diabetes mellitus

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Objectives: Diabetic patients can show limited joint mobility (LJM) and muscle weakness (MW) that are connected to other chronic complications, being also risk factors for diabetic foot. The aim of this study was to investigate the presence of LJM and MW in young subjects with T1DM and the effect of a short-term exercise training program (SETP).
Methods: We evaluated ankles range of motion (ROM) in plantar and dorsal flexion by inclinometer in: 14 young T1DM subjects (YD group), mean age 13.63 ± 1.24 years; diabetes duration 6.1 ± 4.5 years, (7/7 M/F); 14 young healthy subjects (YC group), mean age 14.43 ± 1.79 years, (6/8 M/F); and in 11 diabetic patients with history of first diabetic foot ulcer less than a year (UC group) mean age 65.09 ± 7.81 years, diabetes duration 13.91 ± 11.55 years, (10/1 M/F). Vertical jump (VJ) and standing long jump (SLJ) were used for the evaluations of muscle strength in YD and YH groups.

After SETP (a week), ankles joint mobility and muscle strength was evaluated in YD group. Each training session lasted 30′ and was structured in 3 different working areas: organic activation, stretching of muscles and tendons, and strengthening of muscles.

Results: Before the SETP period the joint mobility in YC group was significantly higher than in the others groups $p < 0.001$ while the muscle strength in the YC group (VJ 34.31 ± 4.98 cm, SLJ 14.35 ± 45.03) has not a significant difference respect to the YD group (VJ 30.71 ± 9.22 cm; SLJ 138.12 ± 23.19 cm). The ankles ROM of different groups was: YC 152.89°±13.17°, YD (before SETP) 119.46°±13.92°, YD (after SETP) 130.17°±12.14°, UC 82.33°±23.33°. After training only the ankles ROM increased significantly in YD group ($p < 0.05$) although the difference remains significant compared to the YC group ($p < 0.001$).

Conclusions: In T1DM patients there is an early reduction of ankle joint mobility instead none in muscular strength. A SETP increases significantly joint mobility even if it remains significantly limited.

O11
Association of aerobic fitness level and hypoglycaemia risk in type 1 diabetes

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Objectives: Physical activity is beneficial for type 1 diabetes (T1DM) but is usually associated with an increased risk of hypoglycaemia. We aimed to determine the impact of exercise fitness level on hypoglycaemia severity during exercise.

Methods: Thirty-four adults and 7 adolescents (14–18 yo) with T1DM and treated with pump therapy underwent an exercise session. Cardiorespiratory fitness (VO_{2max}) was measured and subjects were classified based on their fitness level. Plasma glucose (PG) were measured every 10 minutes, each patient performed physical activity at 60% VO_{2max} on either treadmill for 1 hr or 30 minutes on a bicycle. Hypoglycaemia severity was evaluated with the low BG index (LBGI), percentage of time spent in hypoglycaemia (%hypo) and PG change during exercise (Δ PG).

Results: Nineteen patients (46.3%) had optimum exercise fitness (OF) level. Hypoglycaemia events occurred in 22 patients, 9(40.9%) in the poor fitness (PF) vs. 13(68.4%) in the OF, $p = 0.07$. Severity of hypoglycaemia in the PF compared to OF was; LGBI: 3.8 ± 4.1 vs. 6.6 ± 4.4, $p = 0.04$, %hypo: 0.0 ± 0.0% vs. 18.0 ± 37.2%, $p = 0.02$, Δ PG −2.1 ± 3.0 mmol/l vs. −4.6 ± 3.5 mmol/l, $p = 0.01$. Also, we found a significant correlation between VO_{2max} and LBGI $r = 0.37$, $p = 0.01$, %hypo $r = 0.41$, $p < 0.001$ and BG $r = -0.30$, $p < 0.01$.

Conclusions: We showed for the first time that exercise hypoglycaemia occurs at any fitness level and is more severe in the optimum fitness group. This could be the result of improved glut 4 transporters function in the muscle. Further studies are needed to develop measures to decrease the risk of severe hypoglycaemia during exercise.

O12
Current practices of sports in children and adolescents with type 1 diabetes

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Objectives: To evaluate the practice of sports in children and adolescents with type 1 diabetes (T1D).

Methods: A questionnaire was jointly elaborated by two associations, involved respectively in sports with diabetes and childhood diabetes, and was filled in by 579 10–18 year old youth with T1D, during summer diabetes camps. The different parts of the questionnaire evaluated the type of sports practiced at school, in clubs, with the family and pairs, the specificities with age, the motivations and difficulties to practice sports, the management of diabetes treatment and monitoring.

Results: Ninety-six percent of youth declared that they made sports at school and 85% outside school (42% two activities, 14% three activities), mainly in clubs; more than half at least 1–2/week, more than half in competition. Their main motivations were the desire to practice sport (90%) and being with pairs (68%). Making sport meant a way to let off steam for 74%, making relationship easier for 72%, and helping to accept differences in 68%. Parents were the main supporters to make sport. Diabetes was a reason not to make sport for 2%, not to make the sport of choice for 10%, to be refused in a club for 18% of the youth. Managing diabetes was said easy by 78%, but 38% would like more support from the health care team. Adjustments of treatment and monitoring with sport were often suboptimal.

Conclusion: Diabetes may be an obstacle to practice sports in youth with T1D, but not frequently and more the fact of clubs than of youth. Information should aim at lowering persisting difficulties. Education of T1D youth should reinforce diabetes management during physical activity.

O13
DEPTOR 5′UTR polymorphisms and insulin resistance in obese children and adolescents

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Background: Mammalian Target of Rapamycin (mTOR) signalling deregulation leads to obesity and increased risk of insulin resistance (IR) and type 2 diabetes. DEP domain containing mTOR interacting protein (DEPTOR) represses mTOR signalling possibly altering insulin sensitivity by inhibition of insulin receptor intracellular signalling.

Aim: To determine gene variants in the promoter region of *DEPTOR* associated with the development of pre-diabetes in children and adolescents. This region was selected since DEPTORs actions are mainly regulated by its expression levels.

Subjects and methods: 193 obese children and adolescents (93 males/100 females, mean age 13.3 ± 3.3 years, mean BMI-SDS 2.82 ± 0.66) were studied. A standard OGTT test was performed in all. IR was estimated by HOMA-IR and WBISI according to Madsuda. Genotyping of *DEPTOR* 5′UTR region was performed by High Resolution Melting analysis and Sanger sequencing. Chi-square test was used to detect statistical significance in the frequency of analysed genotypes.

Results: Four polymorphisms (SNP) were identified: rs7840156, rs75781905, rs117543860 and rs140142743. The SNP rs7840156 (g.120885944T>C) was associated with reduced risk of IR determined by HOMA-IR (>2.6; an upper half cut-off value for the analysed population) and WBISI (<3).

The carriers of C allele had OR for IR estimated by HOMA-IR 0.63 (95% CI = 0.41–0.87; $p = 0.038$) and 0.58 (95% CI = 0.38–0.90;

p = 0.018) estimated by WBISI. Other detected SNPs were not associated with IR in the analysed population. IR and non-IR groups did not differ regarding age, gender distribution and BMI status.
Discussion: SNP rs7840156 in the promoter region of *DEPTOR* is associated with IR determined by HOMA-IR and WIBSI in obese children and adolescents. This result indirectly implicates *DEPTOR* as a new gene involved in the early phase of type 2 diabetes development.

O14
The metabolic phenotype of youth onset type 2 diabetes: the role of pregestational diabetes exposure and the hepatic nuclear factor 1α G319S polymorphism

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The prevalence of type 2 diabetes (T2D) is increasing in youth. The independent roles of (1) in utero exposure to diabetes and (2) the HNF -1 α G319S polymorphism on the metabolic phenotype at diagnosis of youth onset T2D is unknown.
Purpose: To compare the metabolic phenotype of youth with T2D at diagnosis: (a) by in utero exposure to normoglycemia, gestational diabetes or pregestational diabetes and (b) by HNF-1α G319S genotype, GG, GS or SS.
Methods: A cross-sectional retrospective chart review of youth with T2D diagnosed between 2006 and 2011 seen at a single centre in Winnipeg, Manitoba was performed. Data extracted included exposure to diabetes in utero, HNF-1α genotype and selected clinical measures at birth and diagnosis of T2D. Descriptive and regression analysis were performed.
Results: 184 youth with complete primary exposure data were included (65% female). Youth exposed in utero to pregestational T2D were younger (−1.26 years, $p < 0.001$) and had a lower waist circumference z-score (−2.77, $p < 0.001$) at diagnosis of T2D and had a shorter gestational period (−1.73 weeks, $p < 0.001$) compared to unexposed youth with T2D. Youth with SS genotype were younger (−1.77 years, $p < 0.001$), had a lower HbA1C (−1.73, $p = 0.006$), lower triglycerides (−1.02, $p = 0.04$) and higher HDL (0.23, $p = 0.001$) at diagnosis compared to youth with GG genotype. Youth with SS genotype had lower BMI and waist circumference z-scores (−0.32, $p = 0.04$ and −1.91, $p = 0.04$ respectively) and were less likely to be hypertensive (OR 0.27, $p = 0.03$) or have acanthosis nigricans (OR 0.32, $p = 0.04$) at diagnosis compared to youth with GG genotype.
Conclusion: Differences in phenotype at diagnosis of subgroups of youth with T2D suggest differing pathophysiology of diabetes. A deeper understanding of specific phenotypes is necessary in order to plan prevention and intervention strategies.

O15
Study medication adherence and outcomes in the TODAY cohort of youth with type 2 diabetes (T2D)

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Objectives: To examine relationships between study medication adherence and demographics, depressive symptoms, durability of glucose control, and insulin secretion and sensitivity in participants in the TODAY (Treatment Options for type 2 Diabetes in Adolescents and Youth) clinical trial.
Methods: 699 youth 10–17 years of age with T2D duration <2 years and on ≥8 weeks of metformin with ≥80% adherence were randomized to 1 of 3 treatments: metformin, metformin plus rosiglitazone, or metformin plus lifestyle. Study medication was taken as 2 pills twice a day. Adherence was calculated quarterly by pill count; high (HI) was defined as taking ≥80% of prescribed medication and low (LO) as <80%. Depressive symptoms were assessed with the Child Depression Inventory or Beck Depression Inventory (depending on age). Insulin sensitivity (1/fasting insulin), insulinogenic index ($\Delta I_{30}/\Delta G_{30}$), and oral disposition index (oDI) were derived from an oral glucose tolerance test. Time-to-failure methods were used to analyze the effect of medication adherence on treatment failure (defined as HbA1c >8% for >6 consecutive months). Generalized linear mixed models were used to compare medication adherence over time.
Results: Study medication adherence fell over time (72% HI at 2 months to 56% at 48 months, $p < 0.0001$) and there were no differences between treatment groups. HI and LO groups did not differ at baseline by gender, age, income, parental education, or treatment group assignment. A greater percentage of HI had clinically significant depressive symptoms at baseline (18% vs. 12%, $p = 0.04$). Level of medication adherence did not affect time to failure. Longitudinally, HI had significantly higher insulin sensitivity ($p = 0.001$) and oDI ($p = 0.02$) but no difference for insulinogenic index.
Conclusions: In youth with T2D, depressive symptoms predict lower medication adherence. Level of medication adherence did not affect treatment failure but was associated with insulin sensitivity and oDI.

O16
Improvement in lipid profile after vitamin D supplementation in indigenous Argentine school children

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Objective: To determine whether vitamin D supplementation of indigenous school children living at high altitude who are vitamin D insufficient improves lipid profile.
Methods: A prospective two-year study evaluated a group of 60 (29 males) children from Hogar school who received 100,000 units of vitamin D; and another group of 36 (16 males) children from Avelino school who received 50,000 units of vitamin D during 2 months. Anthropometric measures, Triglycerides (TG), HDL-C, TG/HDL-C, and vitamin D levels were measured in November 2011 and in 2013.
Results: 96 children were aged 8.8 ± 2 years with mean z-BMI (−0.43) and mean vitamin D (14.65 ng/ml) levels at baseline. The prevalence of overweight and obesity was 6.3%. Only two children had optimal vitamin D levels at baseline. There was not a significant difference in the prevalence of overweight/obesity and hypovitaminosis D between schools at baseline. However, HDL-C (40 vs. 44 mg/

dl), TG (128 vs. 102 mg/dl), and TG/HDL-C (3.7 vs. 2.4 mg/dl) were significantly different in Hogar compared to Avelino School at baseline. After vitamin D supplementation, mean vitamin D levels increased from 14.7 to 32.1 ($p < 0.01$) in Hogar and from 14.6 to 25.1 ($p < 0.01$) in Avelino school ($p < 0.01$). Furthermore, mean values of TG/HDL-C (3.7 to 3.1 mg/dl; $p < 0.01$) and TG (128 to 125 mg/dl; $p < 0.01$) decreased in Hogar school; whereas TG/HDL-C (2.4 to 3.1 mg/dl; $p < 0.01$) and TG (101 to 131 mg/dl; $p < 0.01$) increased in Avelino school. HDL-C levels also improved in Hogar (39 to 44 mg/dl) compared to Avelino School (44 to 45 mg/dl). Several multiple linear regression analyses showed that children from Hogar school improved TG/HDL-C by 1.3 mg/dl (R^2: 0.12), TG by 31 mg/dl (R^2: 0.10), and HDL-C by 0.34 mg/dl (R^2: 0.13), adjusted for BMI, age and gender.

Conclusions: Vitamin D was inversely associated with TG, TG/HDL-C and HDL-C values, suggesting that optimal vitamin D levels are associated with a healthier lipid profile.

Oral Session III: Diabetes Projects in Developing Countries

O17
Running a paediatric diabetes programme in a resource limited country: is it rewarding

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Introduction: Effective monitoring of biochemical and physical parameters to children with Type 1 Diabetes is important to childrens health. Failure of which will lead to premature complications and deaths; especially when children are vulnerable to socio-economic problems. Tanzania Diabetes Association launched a programme in 2005 under IDF Child Sponsorship program aiming at providing care for children with T1DM at Muhimbili National Hospital, Dar es Salaam, Tanzania. Later on CDiC, joined forces to open other clinics in the country.

Methods: Retrospective assessment was conducted at the MNH in 2011 and in 2013 other hospitals. Aims were assessing the outcomes of access to care for children with T1DM. The assessment involved data auditing, medical records, and routine reports. Various interventions for sensitization were done in the community and schools with support from Ministry of Health & Social Welfare. Other intervention like microfinance project for sustainability were initiated.

Results: Preliminary results of the project are very positive. Early diagnosis and at a younger age, increased number of enrolled children 132 in year 2011 to 1132 to date, others being shifted to adult clinic. Less incidences of acute complications, normal school atendencies, and improved metabolic control (HbA1C 9% currently). Mortality has decreased to ten deaths in the last 9 years. These programs have become a teaching model for nurses, doctors and students from within and outside Tanzania.

Conclusion: These programs have been a catalyst for initiating T1DM clinics all over the country. They have also been a centre of education for nurses, doctors and students from inside and outside the country. The Ministry of Health & Social Welfare has been a partner in this hence long term sustainability. This shows that despite being a limited resource country, great commitment from programmes and efforts to improve care can bring positive results and improve the quality of life.

O18
A potential herb-drug interaction of Gymnema sylvestre with metformin

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Gymnema sylvestre is a medicinal plant, with reported use as a remedy for diabetes mellitus. The leaf extract of *G. sylvestre* (GSE) is known for its property to increase the serum insulin through regeneration of pancreatic β-cells. Considering its wide use and consumption as an anti-diabetic herb, the present study investigates the ability of *G. sylvestre* to interact with pharmacokinetics and pharmacodynamics of metformin through cytochrome P450 enzymes. The standardized GSE was tested for its potential to inhibit the CYP2C9, CYP2D6, and CYP3A4 isozymes of human liver microsomes. Later, the pharmacokinetic and pharmacodynamic interactions were assessed in normal and streptozocin (STZ) induced diabetic rats, respectively. GSE showed differential effect of cytochrome P450 activites with an order of inhibitory potential as CYP3A4 > CYP2D6 > CYP2C9 having IC50 of 69.5, 81.4, 214.5 μg/ml. It also produced a twofold increase in the $AUC_{(0\text{-}24)}$, $AUC_{(0\text{-}\infty)}$, $t_{½}$ of single dose of metformin (200 mg/kg, p.o.) after a 1 week treatment with GSE (40 mg/kg, p.o.). Even though the STZ rats gained a significant ($p < 0.05$) weight, they showed severe ($p < 0.01$) hypoglycemia (35 ± 5 mg/dl) on concomitant treatment for 2 weeks. The serum insulin was peaked at 25.56 ± 3.03 μU/ml in combination treated group, demonstrating a 1.5-fold increase in the insulin secretory activity when compared to metformin alone treated group (16.80 ± 1.73 μU/ml). Despite the fact that metformin is mainly metabolized by CYP3A4 in the intestinal microglia, the cytochrome P450 inhibition lead to decreased intestinal degradation and prolonged elevation of portal drug concentrations resulting in a pharmacokinetic and pharmacodynamic synergism of metformins anti-diabetic activity on supplementation with GSE. The results revealed a potential herb-drug interaction of GSE with metformin suggesting that GSE should be further examined for its interaction potential with controlled clinical trials in humans.

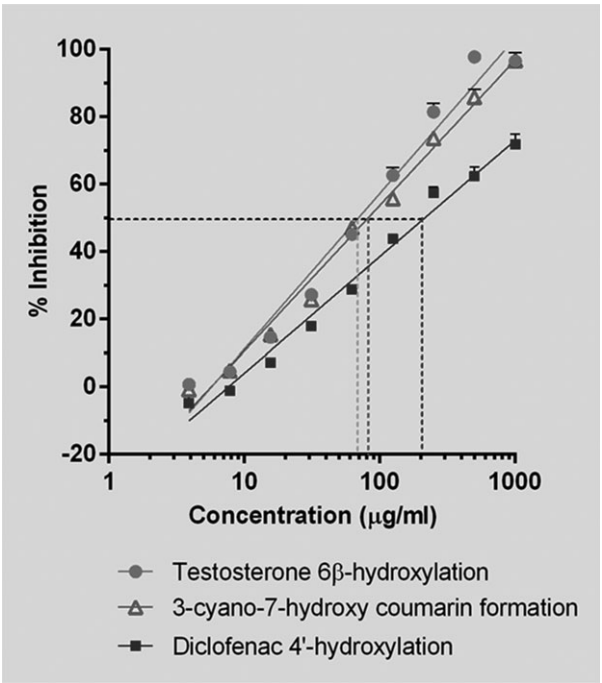

Figure Concentration-dependent CYP450 inhibition of poole.

Table Pharmacokinetics of metformin before and after tre

Parameters	Metformin	GSE + Metformin
Cmax (μg/ml)	16.64 ± 2.06	12.19 ± 1.42*
AUC(0–24) (h μg/ml)	67.41 ± 6.56	116.81 ± 11.48*
AUC(0–∞) (h μg/ml)	68.24 ± 6.60	126.50 ± 12.50*
CL/F (ml/h/kg)	22,168.50 ± 2,336.92	11,949.13 ± 1,117.92*
Kel (1/h)	0.19 ± 0.01	0.10 ± 0.01*
Vz/F (ml/kg)	114,411.59 ± 13,936.75	120,563.32 ± 16,163.96
Terminal T1/2 (h)	3.57 ± 0.15	7.00 ± 0.78*
MRT (h)	4.27 ± 0.07	7.62 ± 0.08*

O19

Translation and validation of the diabetes self-management profile (DSMP) in Brazilian Portuguese language: first instrument to access type 1 diabetes self-management in a Brazilian pediatric population

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Objective: To translate and validate the instrument DSMP - Conventional and Flexible Regimens - into Brazilian Portuguese language, for a population of children and adolescents with type 1 diabetes mellitus (T1DM) and their caregivers, in order to evaluate the quality of self-management in our population, besides comparing it to American self-management data.

Method: DSMP is a semi-structured interview, composed of 25 questions, divided into 5 items (exercise, hypoglycemia, eating, glucose monitoring, insulin). DSMP was administered to T1DM youths between 6 and 18 years (n = 102) and their families. Children under 11 years old were interviewed with their caregivers, and children over 11 years old did it apart. Patients were interviewed two times in a 3-month period by the same researcher. This interview was audiotapped and register by another researcher. Statistical analysis assessed the reliability and validity of the DSMP, including its associations with HbA1c and physician perception. The results were compared to American DSMP data.

Results: The DSMP total scores demonstrated adequate internal consistency (Cronbachs 0.79), 3-month test-retest reliability (Pearson correlation, r = 0.43), inter-interviewer agreement (r = 0.37). DSMP total scores and all subscales were significantly correlated to HbA1c (r = −0.53, p < 0.001). Physician perception of adherence was also significantly related to DSMP (r = 0.67, p < 0.001). When compared to American data, our group had low total DSMP score (58.5 versus 48.9), specially due to diet and insulin scores, and high exercise, glucose monitoring and hypoglycemia scores (p < 0.001).

Conclusion: Translation of DSMP into Brazilian Portuguese language was successful and it was demonstrated to be a reliable and valid tool to assess diabetes self-management. DSMP was strongly correlated with HbA1c in our Brazilian population and it is now the first self-management instrument validated in our language to evaluate our patients.

O20

Longitudinal observations of a large, collaborative insulin pump therapy program for children in Kazakhstan

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Objectives: Kazakhstans Ministry of Health (MoH) partnered with Medtronic to develop an insulin pump (CSII) therapy program for children with type 1 diabetes (T1DM). The MoH provided funding for pumps; Medtronic provided training for patients, their parents, and healthcare providers (HCPs). Data from the first year of the program are presented.

Methods: Children ages 5–15 with T1DM were eligible. Visits with local HCPs were to occur at 3-month intervals and were to include A1C and blood glucose measurements, insulin usage pattern, and quality of life assessments. Initial A1C values were obtained using various methods; follow-up A1C measurements were with the In2it analyzer (Bio-Rad). Pump and blood glucose data were uploaded to CareLink (Medtronic) for retrospective analysis.

Results: Currently, 731 children are enrolled, 603 of whom have used CSII for ≥12 months and 417 of whom have baseline and 1-year A1C measurements. Of these 417 children, 71% had baseline A1C values >7.5%. In this group, the mean baseline A1C was 10.43 ± 2.25% and decreased to 9.33 ± 2.15% at 12 months, a difference of 1.11 ± 2.52 percentage points. Data from Asian (68.4%) and non-Asian children were analyzed separately. Among Asians, 74% had baseline A1C values >7.5%, whereas among non-Asians, 65% had A1C values >7.5%; Asians in this group had higher mean A1C values than non-Asians (10.74 ± 2.24% vs. 9.69 ± 2.11%, respectively, p < 0.001). The decrease in A1C at 12 months was larger for Asians than for non-Asians (1.2 ± 2.67 vs. 0.87 ± 2.1 percentage points, respectively, p = 0.025). Based on the program results, the MoH decided to expand program eligibility to children age 1–18.

Conclusions: Introduction of CSII therapy to Kazakh children and adolescents with T1DM resulted in meaningful decreases in A1C, especially among those with baseline A1C >7.5%, regardless of ethnicity. As the program expands and continues it will serve as a model for rapid large-scale deployment of advanced diabetes technologies.

O21

Evaluation of differing type 1 diabetes treatment regimens in youth in Rwanda

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Objectives: A challenge to delivering diabetes care to youth in the developing world is food insecurity leading to inadequate insulin dosage from fear of hypoglycemia. To determine the feasibility of conducting a randomized controlled trial (RCT) assessing the value of using basal insulin alone (with introduction of meal time coverage when the youth become skilled with self-management) a pilot study was conducted.

Methods: This was funded by NIH without pharmaceutical involvement and based on 50 youth (mean age = 20.1 years, duration = 5.72 years; 52% female) with Type 1 diabetes aged

<26 years. It comprised an open label RCT with two arms; basal glargine insulin (G) followed by prandial regular insulin versus NPH/regular (N/R) insulin twice daily. There were 5 visits (V), 6 months apart starting in May 2011 with three staggered groups of participants; final V5s due in May 2014. The primary endpoint was HbA1c at V4 after 12 months (V2-4) treatment following randomization (V2).

Results: Complete follow up was obtained for 47 participants, 2 participants died (one hypoglycemia, the other malnutrition; both on G) while 1 was not seen within V4 window. No significant differences were seen at baseline by treatment group for HbA1c (mean G = 9.28%, N/R = 9.44%) though the glargine group was a little younger (19.1 vs. 21.2 years, p = 0.11) and comprised more females (61.5 vs. 38.5, p = 0.16). Intention to treat analysis, with last observation carried forward for noncompleters, revealed no treatment difference in V4 A1c (G 9.68% vs. N/R 9.10%, p = 0.39); change in A1c from V2 to V4 (p = 0.10); proportion with severe hypoglycemia requiring external assistance (G 9.1% vs. N/R 22.7%) or hyperglycemia requiring hospitalization (0% vs. 4.6%).

Conclusions: This pilot study demonstrates the feasibility of conducting a RCT of diabetic youth in Rwanda. The suggestion of a lower rate of acute complications with glargine accompanied by a worsening of glycemic control, needs evaluation in a fully powered RCT.

O22
"Insulin, love and care": "Poor response" subset in a "have-not" FREE type 1 diabetes clinic [DISHA] in India

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Objectives: To identify the spectrum of glycemic control and overall clinical responses associated with recent provision of significant material boost in a 3 decade long *philanthropic* type 1 diabetes care program.

Methods: Project DISHA - Insulin Lifeline: Beginning 1987, nearly 3,000 children [600+ active] provided free insulin and syringes, health education counseling, 24 hour helplines; since 2006, BG meters and 5–10 strips/month added; Basal bolus insulin [meal time regular plus bedtime NPH] 100%.

DISHA + CDiC/ LFAC: 2011 - ongoing: [Changing Diabetes in Children and Life for a Child with Diabetes: Since 2011, 250 children are receiving 100 BG strips per month, limited biochemical evaluations [TSH, quarterly HbA1c testing, annual urine albumin: creatinine ratio], with partial manpower support [part time Diabetes Educator, Physician and Ophthalmologist].

Table "CDiC / LFAC enhanced support": 2 year follow up

Group	HbA1c baseline and trend	Baseline %	Latest %
Prior discipline	Baseline A1c <8 and stable	7.3	7.0
Responder High	Baseline A1c >8 and >3 decline	14.8	9.1
Responder	Baseline A1c >8 and 0.6–3 decline	10.9	9.2
Non-responder	Baseline A1c >8 and <0.6 decline	10.4	11.5

Results: Percent of children achieving HbA1c target <8 [29%], <7 [12%]. Nephropathy % [mean UAC μg/mg of Creatinine]: Nil 58% [10], Incipient 29% [88], Overt 13% [1073]. Primary hypothyroidism: Newly detected 13%.

Conclusions: Despite enhanced material support, a subset of poverty associated type 1 diabetes children, do not demonstrate improved glycemic control and overall health. Varying combination of detrimental psychological, social and economic factors contribute to this poor-response. Identification of these negative therapeutic factors and other coexisting life challenges, and efforts to mitigate the same [*molecular sociology; psychosocial therapy; High risk type 1 diabetes clinics*], are crucial to health and survival of these children. The long term sustenance of such programs, and support to newly arriving children remains a big challenge.

O23
Type 1 diabetes (T1D) among underserved youth in the Dominican Republic (DR)

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Objectives: We investigated the level of T1D control among underserved youth in the DR to help in development of strategies for delivering and facilitating optimal diabetes management to vulnerable youth in a middle-income country in Latin America.

Methods: Youth with T1D in the DR were ascertained upon enrollment into a diabetes educational program organized by Aprendiendo A Vivir (AAV). Criteria for inclusion were age 0.5–21 years old, duration of T1D >3 months, and first-time participation in AAV. Criteria for exclusion were presence of renal failure and attendance at another AAV education program. Informed consent was obtained. HbA1c values were determined using Siemens DCA Vantage (upper limit of 14%).

Results: 28 subjects (15 female) were enrolled. Mean and median age of subjects was 11.3 and 11.7 years old, respectively. Mean and median duration of T1D was 3.5 and 1.8 years, respectively. At enrollment, subjects were receiving Lantus alone (n = 4), NPH alone (n = 5), and NPH+R (n = 19). No subject used an insulin correction factor. No subject carb counted. The vast majority of subjects (89.3%) had HbA1cvalue >8.5%. Among all subjects, HbA1c level was <7.5% in 1; 7.5–8.5% in 2; 8.6–9.9% in 3; 10.0–11.9% in 10; 12.0–13.9% in 4, and >14% in 8. There was no correlation between duration of T1D and HbA1c level.

Conclusions: Nearly all of the subjects in this study of underserved youth had a HbA1c level above the target (<7.5%) recommended by ISPAD. This shortcoming in diabetes care exists despite access to insulin in government-supported facilities. This observation indicates the need and also highlights the potential value of supplemental ongoing diabetes education to ensure optimal use of supplies. The data we present come from an analysis of youth at entry into a program that provides comprehensive education and social support services. Future studies will investigate the effectiveness of this program in the improvement of their diabetes management.

O24

Growth attainments of Indian children with type 1 diabetes: a mixed longitudinal study

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Objectives: To study the pattern of distance and velocity growth of different body parameters of male and female patients diagnosed as a case of Type 1 Diabetes mellitus by following a mixed longitudinal growth study.

Setting: Pediatric Diabetic Clinic and Pediatric Growth Lab of Advanced Pediatrics Centre, Post Graduate Institute of Medical Education and research (PGIMER), Chandigarh (A tertiary health care hospital).

Patients: Diabetic children between 5 and 10 years of age and without coexisting disorder that could affect growth, attending to the Pediatric Diabetic Clinic of Advanced Pediatrics Centre, PGIMER, Chandigarh, were included and were followed for 1 year.

Materials and methods: Every child included in the study was measured for anthropometric parameters (Body weight, height, BMI, skin fold thickness) at the start of study period. Thereafter each child was subsequently measured for the above mentioned body parameters at half yearly interval.

Statistical analysis: Tanners 1951 method was used to compute mean (±SD) distance and velocity growth statistics, for each auxological parameter. The magnitude of differences for gender, was calculated by applying Students unpaired *t*-test.

Conclusions: Boys with Type 1 Diabetes mellitus in general weighed heavier than girls at most of the age levels. Boys with Type 1 Diabetes mellitus measured taller than girls throughout the study period and their gender differences became statistically significant at 7.0 and 10.0 years. Girls with Type 1 Diabetes mellitus in general possessed higher BMI than the diabetic boys except for some ages, but the gender differences never became statistically significant. All the three skinfold thicknesses demonstrated inconsistent pattern of growth.

Oral Session IV: Diabetes Genetics and Immunology

O25

An effective treatment approach of T-cell induced autoimmune diabetes through sitagliptin-anti CD4 immuno-nano conjugates in BALB/c mice

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Objective: Immune modulators can arrest autoimmunity in type 1 diabetes (T1D), but they have not caused permanent disease remission or restored normal insulin secretion. Dipeptidyl peptidase IV (DPP-IV) inhibitors increases insulin secretion and β-cell proliferation, and decreases β-cell apoptosis. It could be a better approach of treatment i.e., combination of immune modulators (anti-CD4 monoclonal antibody, CD4 mAb) and DPP-IV inhibitors (sitagliptin, SP). The objective of the work was to prepare sitagliptin-anti-CD4 immuno nanoparticles (immuno-NPs) and study their effect on cellular and metabolic responses of β-cells in BALB/c mice.
Methods: The pharmacokinetics and bioavailability studies were conducted for SP solution, SP-NPs and mAb-SP-NPs. Diabetic BALB/c mice were treated with Immuno-NPs and CD4 mAb or SP alone. The efficiency of Immuno-NPs and CD4 mAb or SP-NPs alone on insulin content, GLP-1 content, glucose tolerance, and the rate of diabetes (glucose >200 mg/dl) were compared with diabetic mice. Histology of pancreas was taken at the end of the study to determine the treatment related effects.
Results: mAb-SP-NPs significantly distributed in pancreas compared to SP solution and SP-NPs (Table 1). Diabetic mice treated with immuno-NPs have a higher rate of remission than mice treated with CD4 mAb or SP-NPs alone. The effect of immuno-NPs on reversal of diabetes was greatest in mice with a glucose level of <350 mg/dl at diagnosis (Fig. 1). Reversal of T1D with immuno-NPs was associated with recovery of insulin in islet cells that were identified at diagnosis. Increased insulin content, glucose tolerance, and insulin release from b-cells improved in mice treated with immuno-NPs. Immnohistochemistry of the pancreas reveals the effect, which supports the data favoring in the treatment of T1D with immuno-NPs.
Conclusion: We conclude that treatment with Immuno-NPs enhances remission of T1D and recovery of residual pancreatic islets in mice.

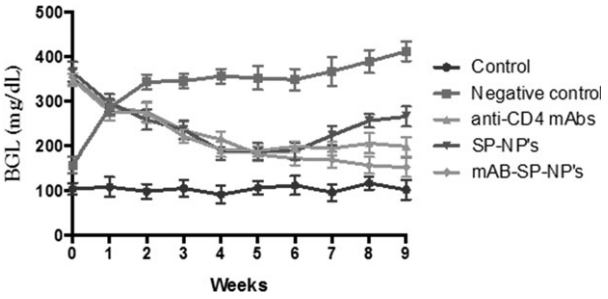

Figure Blood Glucose Levels followed by the treatment

Table Bioavailability studies in Pancreas

PK Parameters	SP Solution	SP-NPs	mAb-SP-NPs
Cmax (ng/ml)	197.59 ± 12.34	278.98 ± 22.08	369.87 ± 21.87
Tmax (h)	3	4	4
T1/2 (h)	5.08 ± 0.98	6.42 ± 0.76	7.98 ± 0.25
Keli (h^{-1})	0.14 ± 0.02	0.11 ± 0.06	0.09 ± 0.01
AUC0-24 h (ng.h/ml)	1,284.99 ± 45.76	2,286.07 ± 154.92	3,354.36 ± 228.52
AUC0-inf (ng.h/ml)	1,365.15 ± 36.21	2,562.91 ± 187.28	4,014.02 ± 212.62

O26

Circulating microRNA profiling in monogenic diabetes reveals differential regulation of expression by HNF1B and HNF1A genes

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Objective: Mutations of transcription factors *HNF1A* and *HNF1B* result in different phenotypes of monogenic diabetes (MODY) due to varying transcriptional regulation of genes. We investigated whether microRNA (miRNA) profiles is altered in this two types of MODY.
Methods: The study group covered 11 patients with *HNF1B*-MODY and 17 with *HNF1A*-MODY. Three control groups were used: 10 healthy individuals, 13 patients with *GCK*-MODY and 9 HbA1c-matched patients with type 1 diabetes (T1DM). Exiqon realtime-PCR arrays were used to profile 762 human miRNAs circulating in the patients sera. ANOVA with adjustment for multiple comparisons was used to establish differentially-expressed miRNAs.
Results: The groups did not differ significantly in terms of age, sex, BMI or HbA1c ($p > 0.1$). Significance criterion was met by eleven distinct miRNAs: miR-223, miR-24, miR-99b, miR-423, miR-92a, miR-27b, miR-23a, miR-199a, miR-101, miR-145 and miR-32. Among those, six differed significantly between the *HNF1A*- and *HNF1B*-MODY groups (Figure 1). Differences between the other groups were less pronounced.
Conclusions: Circulating miRNA levels exhibit altered expression profiles depending on the patients etiology of diabetes, particularly when the causative gene was a transcription factor, suggesting targeted regulation of specific miRNAs by *HNF1A* or *HNF1B*.

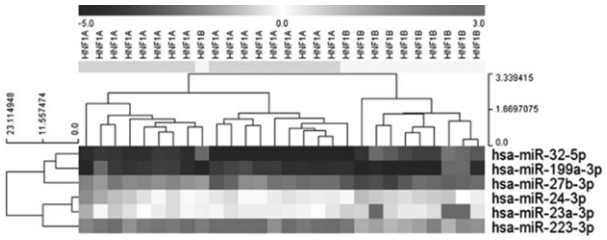

Figure 1. Differential expression of miRNAs between *HNF1A*- and *HNF1B*-MODY. Heatmap colors represent standardized expression scores.

O27

Low-grade enterovirus infection in the pancreatic islets of Langerhans in newly diagnosed type 1 diabetic patients

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Objectives: Despite intensive research, the causes of type 1 diabetes (T1D) are still unknown. One suggested environmental factor is enterovirus. The lack of availability of well-preserved pancreatic tissue limits our knowledge. In the Diabetes Virus Detection-study (DiViD) pancreatic tissue was collected from living subjects very soon after the time of diagnosis of T1D.

Methods: Six type 1 diabetic patients (three women, three men), age 24–35 years, were recruited to the study. Pancreatic tail resection was processed under sterile conditions median 5 week after diagnosis. Human enterovirus (HEV) detection was performed by different methods: Tissue sections were analyzed by immunohistochemistry (IHC) for viral capsid protein VP1 and hyperexpression of MHC class I, while fresh, hand-picked isolated islets were analyzed for viral genome by RT-PCR. Nine healthy, non-diabetic age-matched organ-donors collected by the network for pancreatic organ donors (nPOD) served as controls for IHC analyses, while six older organ-donors from Uppsala served as methodological controls for the PCR-analyses.

Results: Six of six cases compared to two of nine controls were positive for VP1 and showed hyperexpression of MHC class I ($p < 0.01$). Four of six patients were positive for enterovirus RNA by RT-PCR in the medium harvested from islet cultures on day one and/or three, while none of the islet cultures from the six methodological controls were virus positive.

Conclusions: This is the first study of living newly diagnosed type 1 diabetic patients showing the presence of enterovirus proteins and genome in the pancreatic islets using sensitive viral detection techniques. Hyperexpression of class I MHC indicates an anti-viral response in the tissue. Even though our results do not prove causality between enterovirus and T1D, the results are consistent with a low grade enteroviral infection in the pancreatic islets of Langerhans at diagnosis of T1D.

O28

Cord blood IA-2 autoantibodies increase the risk of type 1 diabetes in the population based DiPiS study cohort

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Objective: Early prediction of who will develop type 1 diabetes is crucial in the attempts at stalling or preventing the disease. We wanted to examine the effect of autoantibodies present in cord blood, in the population based DiPiS cohort in southern Sweden, on the risk for the child to develop type 1 diabetes.

Methods: The DiPiS screened newborns in the general population for risk factors for type 1 diabetes between September 2000 and August 2004. A total of 35,853 samples were collected at birth and incubated with antigen to GAD, Insulin and IA-2. Samples and birth data were compared between children developing type 1 diabetes ($n = 151$) and controls. Chi-2 analysis was used to assess differences between groups. A multivariate Cox proportional hazards model was used to assess hazard ratios (HR) with corresponding 95% confidence interval and adjusting for parental type 1 diabetes, sex, and HLA genotype.

Results: A total of 151 (0.04%) children in the total cohort had developed type 1 diabetes by the end of 2013. At least one diabetes-related autoantibody was found in 756 samples (GAD65A $n = 295$; IA-2A $n = 78$; IAA = 509). GAD and IA-2 autoantibodies were more frequently present in patients than controls but no difference could be seen for IAA (GAD $p = 0.015$; IA-2 $p < 0.001$; IAA $p = 0.129$). Presence of IA-2 in cord blood increased the risk for the child to develop T1D (HR 6.9 ($p = 0.001$; 95% CI 2.2–21.8)) while no increased risk was seen in children positive to GAD or IAA in cord blood (GAD $p = 0.88$; IAA $p = 0.58$).

Conclusions: Our study indicates that the presence of cord blood autoantibodies to IA-2 increases the risk of developing type 1 diabetes compared to the general population. This finding is contrary to earlier published studies. No increased risk could be seen for GAD and insulin autoantibodies in cord blood. Our findings in the large, population-based, DiPiS-study may be of significance for future screening and study protocols on type 1 diabetes prediction.

O29

Mass sequencing of the faecal virome: a study in children with early onset of islet autoimmunity

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Objectives: The search for an association between viruses and islet autoimmunity has been limited mostly to candidate viruses, whereas

information has been very scarce about the whole virome (i.e. the complete virus flora). We therefore used next generation sequencing to contrast the stool virome between children who developed very early islet autoimmunity with subsequent type 1 diabetes, and their matched peers in the Finnish prospective Diabetes Prediction and Prevention (DIPP) birth cohort.

Methods: Nineteen cases were selected among children with the earliest onset of islet autoimmunity (mean age 15 months at first islet autoantibodies). Control children without islet autoimmunity were matched 1:1 for gender, time and place of birth and for the HLA risk. The virome was sequenced in 96 available stool samples that preceded the onset of autoimunity by 3, 6 and 9 months. After mechanical enrichment of the virus fraction, random libraries were prepared and sequenced on an Illumina MiSeq instrument. The resulting sequence reads were analysed for human viruses, and the association assessed using conditional logistic regression.

Results: At least one human virus was identified in 40/96 samples (42%), with 9.4% samples being simultaneously positive for more than one human virus. We observed parechoviruses (31/96 samples, 32%), bocaviruses (9.4%) and sapoviruses (8.3%), whereas enteroviruses and rhinoviruses were rare. We noted a clustering of virus findings within the matching groups, indicating adequate matching strategies. No globally significant virus association with the development of islet autoimmunity was observed at the genus level (all $p > 0.4$).

Conclusions: This study shows a richness of human viruses previously not appreciated in the stools of otherwise healthy Finnish children, and underlines the utility of massive parallel sequencing of the virome. Further extension of this pilot dataset will allow studies of individual virus subtypes and strains.

O30
β-Cell differentiation of human pancreatic duct-derived cells using synthetic modified mRNA

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Background/Objective: Type 1 diabetes results from a selective destruction of insulin-producing β cells and there is a need of alternative cell sources for replacement therapy. We designed a protocol for expansion of human pancreatic duct-derived cells (HDDCs) and showed their β-cell engineering potential. In this study, we reprogrammed HDDCs into the β cell-like lineage by overexpressing mRNAs of key pancreatic transcription factors (TFs).

Methods: We isolated and cultured human pancreatic duct cells ($n = 11$) in endothelial growth-promoting media. During the proliferation, HDDCs achieved up to 22 population doublings over 9 passages. Synthetic modified (sm) RNAs were manufactured by unidirectional subcloning of *PDX1*, *NGN3* and *MAFA* into a plasmid containing 5′ and 3′ UTR regions. The UTR-flanked inserts were excised by restriction enzyme digestion and poly(A)-tailed. The final smRNAs were synthesized through in vitro transcription followed by phosphatase and DNase treatments, before being daily transfected in HDDCs. Gene and protein expression assays were performed to screen for β cell-specific markers and activation of innate immune response (insulin, synaptophysin, *PDX1*, *NGN3*, *MAFA*, interferon alpha, *RIG-1*).

Results: In all donors ($n = 5$), transfection of *PDX1*, *NGN3* and *MAFA* upregulated endogenous target genes (ex: *NGN3*) and β-cell markers (insulin, synaptophysin) expression (from 1.6- to 15-fold). Amongst TFs, *MAFA* led to highest levels of insulin gene and protein expression (28.5-fold). However, co-transfection protocols failed to show significant upregulation of β-cell markers. After transfection of a control RNA, cell viability was unaltered and expression of immune markers was no significantly elevated.

Conclusion: We showed that transfection of *PDX1*, *NGN3* and *MAFA* reprograms HDDCs toward a β-cell phenotype. We thus believe that this technique, might be useful to generate significant amounts of insulin-producing cells in a timely manner.

O31
Characterization of rapid progression to type 1 diabetes in children with genetic disease susceptibility

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Objective: To assess the characteristics of rapid progression to type 1 diabetes (T1D) in children with genetic disease susceptibility, recruited from general population.

Methods: We followed from birth 7,410 children (52.6% males) with HLA-conferred disease risk for development of islet autoimmunity and progression to T1D over a median follow-up time of 13.2 years (range 0.9–18.2). Islet cell autoantibodies (ICA), autoantibodies to insulin (IAA), to glutamic-acid decarboxylase (GADA), and islet antigen-2 (IA-2A) were analyzed for screening for β-cell autoimmunity. Rapid progression was defined as progression to T1D within one year after prediabetic seroconversion.

Results: Among the 7,410 children, 1,563 (21.1%) tested positive for islet autoantibodies, and 221 (14.1%) of the seroconverted children progressed to T1D by the end of 2012. The median delay from seroconversion to diagnosis was 0.27 years (range 0.02–0.96) in rapid progressors ($n = 36$, 2.3%), while it was 4.04 years (1.02–15.81) in children with slower disease development. Compared to unaffected autoantibody positive children, children with rapid progression were younger at seroconversion (median 1.8 vs. 5.5 years, $p < 0.001$), carried more often the high-risk genotype HLA-DQB1*02:0302 (44 vs. 26%, $p = 0.03$), and had higher frequency of multipositive seroconversions (81 vs. 6%, $p < 0.001$). Also their levels of ICA (median 13.5 vs. 4.0 JDFU, $p < 0.001$), IAA (4.4 vs. 0.0 RU, $p < 0.001$), GADA (5.8 vs. 0.1 RU, $p < 0.001$), and IA-2A (0.11 vs. 0.08 RU, $p < 0.001$) were higher at seroconversion. Compared to rapid progressors, children with slower disease progression had lower levels of ICA (5 JDFU, $p = 0.004$) and were less often ICA positive (54%, $p = 0.04$) or multipositive (55%, $p = 0.004$) at seroconversion.

Conclusions: At seroconversion, young age, high-risk HLA genotype, higher levels of ICA, IAA, GADA and IA-2A, and multipositivity are characteristic of individuals with rapid progression to T1D.

O32

Diabetic fetopathy due to transplacental transfer of high doses of sulfonylurea in a woman with neonatal diabetes due to a KCNJ11 mutation

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Half of patients with permanent neonatal diabetes (PNDM) have mutations in the *KCNJ11* and *ABCC8* genes. It is important to identify patients with these mutations as the majority can be switched from insulin to sulfonylurea (SU) compounds while maintaining stable glycemic control. In PNDM, the high SU doses used are of concern.

We report the case of a woman with PNDM who continued high doses of Glibenclamide (85 mg/day) during her pregnancy. She refused prenatal genetic testing. The baby was born preterm and presented with macrosomia and severe hypoglycaemia. Insulin levels were markedly increased (129.5 mU/l on day 2). Postnatal genetic testing excluded a *KCNJ11* mutation in the baby. Glibenclamide levels in serum and mothermilk were measured with a very sensitive and reproducible liquid chromatography-tandem mass spectrometry assay. Glibenclamide was detected in both the babys blood and the maternal milk.

We hypothesize that the high glibenclamide doses lead to transplacental passage, resulting in overstimulation of fetal beta-cells, macrosomia and severe hypoglycaemia in babies not carrying the mutation. We suggest that in the specific setting of maternal PNDM, glibenclamide should be avoided if the baby does not carry the mutation, while glibenclamide may be beneficial when the fetus is a PNDM carrier. Such a tailored treatment can only be done if prenatal screening is available.

Oral Session V: Diabetes Education

O33

Education needs and management of food intake in children, adolescents and young adults with type 1 diabetes (T1D): the global TEENs Study

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[a]*Hosted by West Midlands Strategic Clinical Network, Birmingham, UK;* [b]*Joslin Diabetes Center, Pediatric, Adolescent and Young Adult Section, Boston, USA;* [c]*Sanofi, Paris, France;* [d]*Sanofi, Chilly Mazarin, France;* [e]*Kinder und Jugendkrankenhaus "Auf der Bult", Hannover, Germany;* [f]*Institute for Endocrinology and Diabetes, National Center for Childhood Diabetes, Schneider Children's Medical Center of Israel, Petah Tikva, Israel;* [g]*Hospital de Pediatría J P Garrahan, Nutrition Department, Buenos Aires, Argentina;* [h]*Baylor College of Medicine, Department of Pediatrics, Section of Psychology, Houston, USA;* [i]*Gothenburg University, Department of Pediatrics, NU Hospital Group, Uddevalla and Sahlgrenska Academy, Gothenburg, Sweden;* [j]*Jaeb Center for Health Research, Tampa, USA;* [k]*University Hospitals UZ, Leuven, Belgium*

Objectives: TEENs is the largest worldwide (20 countries), contemporary, observational study of T1D (N = 5960) in 8–25 year old (y/o) patients. Data on education needs and diet management are presented.

Methods: 219 centers collected data by interview, record review and survey from three groups: 8–12 y/o, 13–18 y/o and 19–25 y/o. A1c was measured uniformly using A1cNow™ (Bayer); target A1c was defined as <7.5% (58 mmol/mol) for ≤18 y/o (ISPAD) and <7% (53 mmol/mol) for 19–25 y/o (ADA).

Results: Patients of all ages commonly requested education on insulin usage, illness, exercise, diet and carbohydrate counting (Table). Patients at A1c target were more likely to request education on psychosocial factors (e.g. alcohol, smoking) (odds ratio [95% CI]: 1.24 [1.06, 1.45]) and continuous glucose monitoring (1.25 [1.06, 1.48]).

Patients measured food intake mostly by carbohydrate counting (40%) or by experience (35%). Association was observed between glycemic control and the method used to measure food intake (p = 0.005); patients who only avoid sugars were less likely to attain A1c target than those who used carbohydrate counting (0.61 [0.45, 0.84]).

Table: Diabetes management and educational needs by age and A1c target attainment

	8–12 y/o		13–18 y/o		19–25 y/o	
	A1c target <mmol/mol n=553 [32%]	A1c target not <mmol/mol n=1170 [68%]	A1c target <mmol/mol n=833 [29%]	A1c target not <mmol/mol n=2021 [71%]	A1c target <mmol/mol n=260 [19%]	A1c target not <mmol/mol n=1122 [81%]
Educational needs, n (%)						
Insulin:						
Administration	144 [28]	369 [33]	195 [24]	542 [28]	58 [23]	248 [23]
Adjusting dose	161 [31]	388 [35]	193 [25]	582 [30]	56 [22]	283 [26]
Managing:						
T1D during illness	216 [42]	461 [41]	241 [31]	700 [36]	74 [30]	389 [36]
BG with exercise	221 [43]	451 [40]	319 [41]	777 [40]	84 [34]	389 [36]
Nutrition and dietary issues	164 [32]	425 [38]	280 [36]	731 [38]	76 [30]	368 [34]
Carbohydrate counting	134 [26]	304 [27]	171 [22]	457 [23]	70 [28]	327 [30]
Method used to measure food intake, n (%)*						
Carbohydrate counting	267 [48]	466 [40]	361 [43]	740 [37]	112 [43]	428 [38]
Carbohydrate exchanges	31 [6]	106 [9]	73 [9]	134 [10]	12 [5]	48 [4]
Weighing/measuring	41 [7]	74 [6]	47 [6]	94 [5]	7 [3]	36 [3]
Based on experience	172 [31]	347 [30]	203 [24]	706 [35]	106 [41]	443 [40]
Avoiding sugars	33 [6]	144 [12]	44 [5]	226 [11]	14 [5]	113 [10]

*Columns may not add up to 100% due to missing responses, only one response per participant was allowed

Conclusions: Demand for education on fundamental disease management and dietary issues was high across all ages, highlighting a need for ongoing education of young T1D patients and their parents. 40% of patients monitored food intake by carbohydrate counting, which was associated with attaining A1c target.

Study sponsored by Sanofi.

O34

KiDS project: children and diabetes in schools

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Objectives: The number of children with both Type 1 (T1DM) and Type 2 (T2DM) diabetes is increasing worldwide. There is a need to educate children early in order to prevent the development of T2DM in the future. The KiDS project was develop to: -improve the lives of children with diabetes at school and fight discrimination by informing school staff, parents and children about the needs of children with T1DM at school; - provide information about how T2DM can be prevented.

Methods: A technical advisory committee (TAC) of diabetes experts from around the world was established to develop a global diabetes information pack for schools. Meetings of the TAC together with IDF staff, parent representatives and in- country Working Groups from India and Brazil were held face to face and virtually to agree content and structure of the diabetes information pack.

Results: A *Global Diabetes Information Pack (GDIP)* was developed and then tailored for use in both India and Brazil to meet cultural and local needs. The GDIP will be available on the IDF website free of charge. The GDIP is divided in two sections; the first section focuses on T1DM and the needs of children at school offering guidelines for the management of children with diabetes at school and a sample diabetes management plan. The second section focuses on a healthy lifestyle to prevent T2DM. The pack is further subdivided into discrete units tailored for use by school staff, parents, parents of children with diabetes and children.

Conclusions: The poor management of children with diabetes at school has been well documented internationally. The KiDS GDIP offers the opportunity to improve the lives of children with T1DM at school and to educate others in the prevention of T2DM. The *Pack* will be also be supported by an app which will be available in June 2014, recognising the need to utilise new technologies to establish better engagement and dissemination.

O35

Delivering Early Care In Diabetes Evaluation (the DECIDE study): the effect of hospital versus home management at diagnosis in childhood diabetes on psychological, social, physical and economic outcomes

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Objectives: There is debate in the UK about the best way to manage type 1 diabetes (T1D) in clinically well children at diagnosis. This

study, using the largest sample of children with T1D recruited to a study at diagnosis in the UK, investigated the impact of home or hospital management on biopsychosocial and economic outcomes.
Methods: Multi-centred randomised controlled trial. Newly diagnosed children aged 0–17 years were randomised for treatment initiation at home or in hospital. Primary outcome: difference in glycosylated haemoglobin (HbA1c) at 2 year follow-up. Secondary outcomes: coping, anxiety, quality of life, diabetes knowledge, social activities, satisfaction and total costs. Qualitative interviews were undertaken with health professionals, parents and children.
Results: 203 children from 8 centres randomised to home (n = 101) or hospital (n = 102). There was no difference in mean HbA1c between home (72.1 mmol/mol) and hospital (72.6 mmol/mol) at 2 years (difference adjusted for baseline = 1.01% (95% CI 0.93–1.09%); p = 0.86), nor for most secondary outcomes. Diabetes specific resource use was similar between groups during initiation (Days 0–3) but total initiation costs were significantly higher in the hospital arm due to indirect hospital-related (hotel) costs of children being in-patients. Post initiation NHS costs were similar between arms during 2 year follow up. Many children/parents initially desired the home arm but in retrospect preferred whichever arm they had been randomised to. Most nurses preferred home management despite logistical challenges. Consultants had less contact with home-managed children and reported difficulties building rapport with these families. No children in the home arm were re-admitted to hospital in the first 4 days.
Conclusions: Hospital management of T1D in clinically-well children at diagnosis increases NHS costs, with no difference in glycaemic control or quality of life over the first 2 years compared to home management.

O36
Effectiveness of an online type 1 diabetes educational module for school teachers

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Objective: Type 1 diabetes demands attention at school and teachers have reported feeling unprepared when managing diabetes in the classroom. Diabetes education for school teachers is limited due to economic, geographic and temporal reasons. In 2009, diabetes nurses at the Izaak Killam Walton (IWK) Health Centre, in Halifax, Nova Scotia (NS), Canada, launched an online educational module, aimed at educating school teachers about diabetes. The aim of this study was to evaluate the effectiveness of this online educational module in improving diabetes knowledge.
Methods: In this quasi-experimental study, 61 Bachelor of Education (B.Ed.) students from Mount Saint Vincent University (MSVU) in Halifax completed a pre-module diabetes knowledge questionnaire prior to watching the online module. Following the module, participants then completed a post- (short term) and 6-week post-(long term) module diabetes knowledge questionnaire. Differences in mean questionnaire scores were compared.
Results: The mean difference between pre- and post- (short term) diabetes knowledge questionnaire scores was 6.5 ($p < 0.01$; CI (5.523, 7.657). The mean difference between pre- and 6 week post-(long term) diabetes knowledge questionnaire scores was 5.7 ($p < 0.01$; CI (4.682, 6.728). 45 out of 61 students chose in-service/workshop as the most effective way to learn about diabetes. All students indicated that there is a need for more education about Type 1 diabetes in the classroom.
Conclusion: Online education is effective in improving diabetes knowledge and maintaining knowledge retention in future school teachers. Although not a preferred method of education, online educational modules have the ability to disseminate knowledge to a large number of people at once. Developing additional online modules for other childhood health problems encountered in the classroom should be considered.

O37
What we say really matters. Impact of health care providers attitudes towards diabetes on newly-diagnosed patients

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Objectives: The moment of being diagnosed with Type 1 Diabetes (T1D) can be emotionally difficult for many people, often because the majority of the patients are at a young age. Usually newly diagnosed patients lose their grip on everyday reality and experience a lot of uncertainty. Their attitude towards the illness is not yet formed at that period and is very susceptible to the influence of other people. Patients easily adopt the beliefs of others, especially those of health care providers. The aim of this study was to investigate possible impact of several approaches to providing information on T1D on newly diagnosed patients.
Methods: Biographical and narrative approaches were used to interview 22 people that have been diagnosed with T1D later than the age of 15 and living with the illness for more than a year.
Results: The results consider the relationship between the health care procedures (or lack of) utilised by medical staff and the attitudes of the patients towards the illness at the early stage following diagnosis, as well as at later stages of the illness. It has been found that there is no standard procedure to follow concerning informing patients about diabetes related complications and everyday management of the illness.
Conclusions: The ways patients perceive diabetes therapy burden can be highly influenced by the attitudes of health care providers towards the illness. This influence has both positive and negative consequences and can be observed in both short and long term.

O38
A 10-year evaluation of the impact on participants of the international science school for health care professionals (ISPAD-SSHP): 2004-2013

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Background: Since 2004 the international ISPAD-Science School for Health Care professionals (SSHP) has been conducted annually for 15 multidisciplinary participants including nurses, dieticians, psychologists and social workers. The 3-day course is aimed at increasing research skills and productivity in non-physician diabetes health professionals. The effectiveness of the SSHP and the impact on personal career development has been analysed after 10 years of courses.
Method: All 149 alumni participants (9 males) from 41 countries were invited to complete an evaluation questionnaire. Information

collected included outcome measures for course content and structure as well as data on their self assessment of their knowledge to scientific work before and after participation, previous research activities and professional development after the course.

Results: A total of 68 (46%) questionnaires were completed (Europe: 27, North America: 17 and Australia: 14) primarily from diabetes nurses/educators (28) and dieticians (18). 98% of the responders are still working in diabetes care and 92% rated the course as valuable and useful for their workplace. Approximately 60% reported improved knowledge and understanding, 69% had more confidence in their research and 63% have undertaken a research project since completing the SSHP. Half (51%) have submitted a peer reviewed scientific abstract, 39% gave an oral and 43% a poster presentation. 30% have written publications. Furthermore, 16 of 59 responders (27%) had achieved a higher academic degree of which 7 theses were based on their Science School project.

Conclusion: The 10 year evaluation of the innovative SSHP course demonstrates it is beneficial in enhancing research skills and increasing research activities within pediatric diabetes services. It also leads to benefits for personal academic career development. The feedback justified the course continuation and further support from leadership is essential.

O39

Facilitators and barriers to adhering to clinical practice guidelines for the management of children and youth with type 1 diabetes - the health care provider's perspective

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Objective: To identify factors perceived as facilitators and barriers to adhering to the Canadian Diabetes Association Clinical Practice Guidelines (CDA CPGs) for the treatment of childhood type 1 diabetes (T1D) among pediatric health care providers (HCPs).

Methods: An online survey was administered to 260 HCPs who care for children with TID in British Columbia from July to November 2013. Descriptive statistics were used.

Results: Survey response rate was 37%. Ninety-two percent (81/88) of HCPs were aware of the CDA CPGs and 76.6% (62/81) were familiar or very familiar with the guidelines (mean Likert score 3.94 ± 0.91 on a five-point scale). Only 2.4% (2/85), 1.2% (1/85), and 11.6% (10/86) disagreed with the recommended glycemic targets for children <6, 6–12, and 13–18 years of age, respectively. Lack of time, lack of resources (i.e. access to a mental health professional or social worker), and patient preferences were identified by HCPs as common barriers to adhering to CDA CPGs. In a multiple response question (92 responses, 65 respondents), inadequate support for families was identified by HCPs as the most common barrier to achieving recommended glycemic targets (28.3%). Only 13.6% (11/81) of HCPs felt it was feasible or very feasible for children and families to be seen by a mental health care professional. In a multiple response question (204 responses, 79 respondents) HCPs identified the following resources that might facilitate adherence to CDA CPGs: reminders embedded in a diabetes clinic visit template (28.9%), web-based information (23%) and patient-specific questionnaires to facilitate discussion during the clinic visit (22.5%).

Conclusion: Knowledge of, agreement and familiarity with the CDA CPGs are not perceived as barriers to guideline adherence among HCPs and improved access to mental health services is needed. Future research identifying facilitators and barriers to guidelines adherence among patients and families is necessary.

O40

Improved results in paediatric diabetes care using the Swedish paediatric diabetes quality registry, SWEDIABKIDS

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Background: There are differences between the 43 paediatric diabetes centres in mean haemoglobin HbA1c, year 2012 range 13.5 mmol/mol (IFCC)/1.2% (NGSP/DCCT). Twelve paediatric diabetes teams (IQ1) participated in an improvement collaborative during 18 months aiming to improve the paediatric diabetes care. SWEDIABKIDS was used as a tool for outcome measures. A second program including 14 teams (IQ2) was also performed.

Methods: The teams, who together had 70% of the children and adolescents with diabetes in Sweden, participated in the two programs including definition of treatment targets, areas needing improvement and action plans. Data from the previous six months (period 1), the last six months of the program (period 2), and the long-term follow up of IQ1, 12–18 months after completing the program (period 3) was studied.

Results: The proportion of patients with HbA1c ≥72 mmol/mol (IFCC)/8.7% (NGSP/DCCT) decreased significantly in all clinics, for IQ 1 from 24.2% (period 1) to 14.3% (period 3), IQ2 21.3% (period 1) to 16.9% (period 2) and for non-participating teams, corresponding figures to IQ1, from 24% to 16.1%. also in those not attending the program, $p < 0.001$. The proportion of patients with HbA1c <57 mmol/mol (IFCC)/7.4% (NGSP/DCCT) increased significantly periods as above for IQ 1 from 25.6% to 45.7%, IQ2 34.5% to 46.7% and for non-participating teams, corresponding figures to IQ1 from 30.0% to 44.3%. Those changes were found for both genders, and all ages, except for patients above 16 years of age.

Conclusions: By involving paediatric diabetes teams in a quality improvement collaborative and access to a quality registry, paediatric diabetes care can improve and thereby contribute to reducing the risk of late complications. Many of non-participating teams started on their own to improve their results. This kind of substantial spill over effect is known from other studies and thereby the programs also have beneficial secondary effects.

Oral Session VI: Diabetes and Adolescence

O41

Ketoacidosis at diagnosis of type 1 diabetes in children and adolescents: role of the general practitioners

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Objectives: To evaluate the frequency and severity of DKA at diagnosis of type 1 diabetes (T1D) in children and adolescents, the effect of a prevention campaign and the role of general practitioners.

Methods: Since November 2009, 146 French pediatric centers participated in a survey to evaluate the frequency and severity of DKA at diagnosis of T1D and the effect of a campaign of prevention. Age, sex, duration of symptoms, patients pathway to diagnosis, clinical and biological signs, family history of T1D, were collected for each new patient (<15 years). As general practitioners made the diagnosis in more than half the cases, a questionnaire was elaborated to evaluate their practices at diagnosis and it was filled in by physicians in three different regions.

Results: The frequency of DKA decreased from 43.9% (year before the campaign) to 40.5% (year 1) and 35.1% (year 2), severe DKA from 14.8% to 11.4% and 10.6%; severe DKA decreased from 24% to 13% in Franche-Comté and from 20% to 3% in Midi-Pyrénées, two regions involved in more intensive information campaigns. The main causes of delay to diagnosis were diagnostic errors (50% of patients who consulted emergency units at the familys initiative had a medical consultation before) and blood samples prescribed in laboratories. Answers to the questionnaire from 200 general practitioners showed that: 50% never diagnosed T1D in youth; T1D did not exist before 2 years according to 36%; DKA could not be lethal at diagnosis for 13%; enuresis might evoke T1D for 40%; fasting venous blood measurements were needed for 88%; urine analysis could not make the diagnosis for 39%; 30% would start the treatment by themselves, 47% with diet alone.

Conclusion: General practitioners are an important target for a campaign of information to prevent DKA at diagnosis of T1D in children and adolescents.

O42

Holding the horses of insulin pump infusion: usage and effectiveness of the low glucose suspend feature during fasting in Ramadan among adolescents with type 1 diabetes mellitus to prevent hypoglycemia

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Background and aim: Severe hypoglycemic episodes during the daytime of Ramadan fasting is the most feared complication. Sensor-augmented pump therapy with insulin in combination with automatic insulin shutoff (low glucose suspend [LGS]) can be used to reduce or prevent hypoglycemia. In a prospective observational study we investigated the effect of the LGS algorithm on the frequency of hypoglycemic episodes in adolescents with type 1 diabetes who wished to fast Ramadan 2013.

Subjects and methods: Thirty-seven patients (23 males and 14 females, 15.6 ± 3.3 years, duration of diabetes 4.9 ± 4.2 years, pump therapy for 1.8 ± 1.1 years, used the Paradigm(®) Veo(™) system (Medtronic) and were divided into two groups: First (n = 21): those who wished to wear the sensor and use LGS feature. Second (n = 16): those who did not want to wear sensor and measured their BG level regularly.

Results: A total of 2,314 LGS alerts occurred, and 70% began in the afternoon between 2 pm and 5 pm. The mean duration of LGS events was 26.55 min, 38% lasted for <5 min, and 7% lasted for 120 min. Among these episodes, the mean sensor glucose was 61.3 ± 9.4 mg/dl at LGS activation, rose to 110.7 ± 34.6 mg/dl by the end of the LGS episode (when insulin delivery was automatically resumed), and was 163.33 ± 42.1 mg/dl at 240 min. Compared to the second group, LGS usage significantly reduced the number of BG readings <70 mg/dl (p = 0.001) and >250 mg/dl (p = 0.03). Non of the LGS group broke their fast vs. eight in the second group (p = 0.02). No episodes of severe hyperglycemia, DKA or emergency hospital visits were observed in both groups. HbA1c levels did not change after Ramadan (7.6 ± 1.3 vs. 7.8 ± 0.8, p = 0.3).

Conclusions: This confirms the advantages provided by insulin pump with LGS feature used in diabetic patients who wishes to fast Ramadan. Use of the LGS significantly reduced exposure to hypoglycemia without compromising safety.

O43

Improvements in vascular function and renal inflammatory marker profile associated with vitamin D supplementation in adolescents with diabetes

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Objectives: Vitamin D (VitD) deficiency early in Type 1 Diabetes (T1D) is associated with future development of macro- and microvascular complications. The aim of this study was to assess the role of VitD supplementation on endothelial function (EF) and renal inflammation in adolescents with T1D.

Methods: Subjects were recruited from the diabetes clinic at the Hospital for Sick Children (Toronto, Canada) as part of a non-randomized, open-label clinical trial (clinicaltrials.gov, NCT01103817). Patients with suboptimal levels of active VitD [25 (OH)D] (<75 nmol/l) were supplemented for 12–24 weeks with VitD analog ($VitD_3$) at 1,000 IU/day and patients with 25(OH)D <20 nmol/l were supplemented at 2,000 IU/day. Anthropometric measurements, blood pressure (BP), EF testing and biochemistry (lipid profile, HbA1c, 25(OH)D, Ca^{2+}, parathyroid hormone [PTH] and albumin creatinine ratio [ACR]) were completed at baseline and following treatment. Urine cytokine/chemokines inflammatory profile was assessed in a subset of subjects pre- and post treatment.

Results: 31 T1D subjects with a mean age of 15.7 ± 1.4 years completed the study. Mean 25(OH)D levels significantly increased post-treatment (33.0 ± 12.8 vs. 67.0 ± 23.2 nmol/l, p < 0.01). None of the subjects developed hypercalcemia and PTH levels decreased (37.1 ± 13.9 vs. 24.1 ± 24.1, p < 0.01). $VitD_3$ supplementation did

not significantly impact HbA1c, BMI, BP, lipid profile and ACR. We observed a significant improvement in EF following supplementation (lnRH-PAT 0.58 ± 0.20 vs. 0.68 ± 0.21, p = 0.03). Several key cytokines/chemokines; EGF, Fractalkine, Il-5, Il-9, IL-15, TNFα, and MCP-3 were also significantly decreased post-treatment ($p < 0.05$).

Conclusions: Treatment with $VitD_3$ at doses of 1,000 IU & 2,000 IU/day was associated with an improvement in EF and reduced expression of urinary inflammatory markers in a cohort of uncomplicated T1D adolescents. Our data is suggestive of an additional benefit of VitD supplementation in T1D patients.

O44

Abstract withdrawn

O45

Determinants of diabetes distress in adolescents with type 1 diabetes

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Objectives: When children with diabetes become adolescents, many experience difficulties in controlling diabetes. The objective of the TODS (Teenagers with Diabetes Sweden) study was to conduct a national survey to gain a better understanding of the main drivers of and barriers to optimal treatment among adolescents with type 1 diabetes.

Methods: In 2013 all adolescents born in 1995, 1996 and 1997 (ages 15–17) with type 1 diabetes ($N = 2,112$) were invited to complete an online questionnaire.

The questionnaire was developed and validated in collaboration with pediatric diabetologists and survey experts. A two-item diabetes distress scale (DDS2) was included in the survey. Determinants are identified in a regression analysis.

Results: The survey was answered by $N = 453$ (21.4%). Adolescents who trust that their parents can handle their diabetes (p = 0.047) and those who use a CGM (p = 0.002) are significantly less distressed than others.

Patients who do not communicate with a friend about their diabetes ($p < 0.001$) or who wish their parents were more involved ($p < 0.001$) are significantly more distressed than others. Diabetes distress is also significantly higher for patients showing a higher level of Hba1c (p = 0.002) and for those who do not know their Hba1c-value ($p < 0.001$). Similar results are seen among those who are smokers ($p < 0.001$), have unhealthy eating habits (p = 0.007), weigh more (p = 0.025), and express fear of hypoglycemia (p = 0.008). Female patients express more diabetes distress in comparison to male patients ($p < 0.001$). Data also show that distressed female patients tend to have a higher Hba1c-value than distressed male patients (p = 0.050).

Conclusions: This national survey shows that modern technology such as CGM and actively involved family and friends may reduce diabetes distress. However, female adolescents in particular are more vulnerable, as are adolescents with unhealthy lifestyle choices. Extra focus and support must be put on these groups of patients.

O46

Into the blue yonder?: Capturing diabetes transition in a regional metropolitan center, Auckland, New Zealand, 2006-2013

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Objectives: To examine the capture rates of young people referred from the Starship Paediatric Adolescent Service within the Auckland region.

To examine metabolic control (HbA1c) between those who engaged in the transition programme, to examine ethnicity and social deprivation within the transitioning population

Methods: 322 young people under the care of the Starship Paediatric Diabetes Service during the period 01 September 2006 to 01 January 2013.

Results: Attendance at Adolescent Transition clinics was 81% followed by a 96% rate of capture of all the young people into at least one Young Adult Clinic. 88% of the young people were captured and retained in clinics from the whole period of transition to age 21. Of the 308 captured into adult services, 38% of first follow up appointments occurred within the aimed timeline of 3 months, and 80% were within 6 months. Of 44 young people who actively opted out, capture and retention into adult clinics was 77%. There was no difference in capture rate related to dep score (p = 0.9). The capture rate in European young people was marginally higher than non-Europeans (90% vs. 84%, p = 0.20).

Young people engaged in the transition programme were more likely to have lower HbA1c than those who did not engage with the programme (p = 0.007). Young people living in areas of high social deprivation were more likely to have a higher HbA1c (p = 0.0001). Maori and Pacific Island populations were more likely to have a higher HbA1c than European populations (p = 0.0001).

Conclusions: The Starship transitional programme, in partnership with Auckland region adult services, is helping achieve a high rate of attendance in young adult clinics. Identifying key times and influential factors influencing attendance at clinics could provide information essential to modifying existing models of transition to improve outcomes throughout the transition period.

O47

How do young people with type 1 diabetes experience transition from pediatric to adult health care?

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Objectives: To identify the experiences of young people with Type 1 diabetes (T1D) on transition from pediatric to adult health services by use of focus group interviews. Qualitative data from the interviews will be used as supplement in the ongoing development of a national, population-based survey. This is part of a quality improvement project on transition.

Methods: 80 young adults with T1D who had been transferred to adult health services 1.5–4 years earlier, were invited to take part in a focus group interview. The patients were chosen based on data from

their last annual control registered in the Norwegian Childhood Diabetes Registry (NCDR). Gender, duration of diabetes, HbA1C were comparable to the diabetic population in NCDR. 8 patients from 4 different hospitals participated, 4 male. Mean age 20.7 years, mean diabetes duration 10.3 years. Interviews were done in 3 groups.
Results: Preliminary results indicate that continuity and a feeling of being met as an Individual was important in the pediatric health care. Threshold for contact was low.

None of them had any impression of being formally prepared for transfer. They did not meet health personal at the adult clinic before transfer, nor did they have any written information. The gap between the last visit at the pediatric clinic and the first visit at the adult clinic was 6–18 months and was difficult for several of them. At the adult clinic they unanimously experienced a lack of continuity, often meeting different nurses and doctors, having to tell their story again on every visit. The young participants pointed at the need for continuity and communication between health personal prior to transfer so that individual challenges with diabetes was known and could be taken care of adequately, especially for those with special needs and problems concerning diabetes regulation.
Conclusions: It is a need for identifying the quality of transition on a national basis in Norway to initiate quality improvement in this field.

O48
Relationship between age at menarche and cardiovascular risk factors in women with type 1 diabetes

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Objective: To determine the relationship between age at menarche with glycemic control and cardiovascular risk factors in patients with type 1 diabetes.
Methods: This was a multicenter cross-sectional study conducted between 2008 and 2010 in 28 public clinics in 20 cities from the four Brazilian regions. Data were obtained from 1,527 female patients, 59.3% Caucasian, aged 25.1 $\pm$ 10.6 years. Diabetes duration was 11.4 $\pm$ 8.1 years. Patient information was obtained through questionnaire and chart review. Age at menarche was stratified in four groups: 8 to 11 (group 1, early menarche), 12 (group 2), 13 (group 3) and 14–18 years (group 4, late menarche).
Results: The mean age at menarche was 12.7 $\pm$ 1.7 years without difference among regions, economic status, level of care or ethnicity. Patients from group 1 had greater BMI than patients from the other groups ($p < 0.001$), and were also more likely to be overweight or obese, [169 (31.5%) vs. 152 (28.3%), vs. 117 (21.8%) vs. 99 (18.4%), $p < 0.001$], respectively. BMI had an inverse correlation with age at menarche ($r = -0.14$, $p < 0.001$). No significant difference was observed among the four groups of age at menarche for blood pressure, lipid profile and diabetes-related chronic complications. Logistic regression analysis showed that early age at menarche, [(8–11 years, (odds ratio (ORs) 1.77 [1.30–2.41, $p < 0.001$)] and duration of diabetes [ORs 1.01 (1.00–1.03), $p = 0.02$], were related to greater risk of patients overweight or obesity; adherence to diet [ORs 0.78 (0.60–0.93), $p = 0.01$], physical activity [ORs 0.75 (0.94–0.94), $p = 0.01$, and lower insulin dose (U/kg) (ORs 0.54 [0.59–0.90, $p = 0.001$]) were related to lower risk for overweight or obesity.
Conclusions: Early menarche occurred in 23.4% of women with type 1 diabetes and was strongly associated with overweight or obesity in pubertal/adult life. This association could be minimized with lifestyle changes, such as better adherence to diet and physical activity.

Oral Session VII: Diabetes Epidemiology

O49

The TEENs study: glycemic control, family status and emotional burden of type 1 diabetes (T1D) in a global sample of children, adolescents and young adults

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Objectives: TEENs is the largest global (20 countries), contemporary, observational study of T1D care and psychosocial parameters in 8–25 year old (y/o) T1D patients. Glycemic control, family status, emotional burden are reported.

Methods: 219 centers collected data (interview, record review, survey) from 8–12 y/o, 13–18 y/o, 19–25 y/o. A1c was measured uniformly (A1cNow™, Bayer). A1c targets were defined as <7.5% (ISPAD) for ≤18 y/o, <7% (ADA) for >18 y/o. Emotional burden was assessed with validated surveys: PAID for ≥13 y/o, PAID-PR for parents of 8–18 y/o (scored 1–100; higher score=greater burden). Factors associated with glycemic control were assessed by multivariate logistic regression.

Results: Overall mean A1c was 8.5 ± 1.8%, 28% of youth attained A1c target. Diabetes management and burden varied between groups (Table). A1c target non-attainment was associated with: family conflict around checking glucose levels ($p < 0.001$) - youth who almost always argued were 0.59 (0.49, 0.72) times less likely to attain target; family status ($p = 0.019$) - youth not living with both parents were 0.81 (0.68, 0.97) times less likely to attain target.

Conclusions: In the TEENs study, most youth did not attain A1c target. Family conflict around diabetes management was associated with target non-attainment. Parents reported higher emotional burden than youth. Opportunities exist to improve glycemic control and reduce the emotional burden of T1D youth and their families.

Study sponsored by Sanofi.

Table: Responsibility for blood glucose monitoring and insulin administration, and emotional burden by age and A1c target attainment

Age group	8–12 y/o (N=1723)		13–18 y/o (N=2854)		19–25 y/o (N=1382)	
	A1c at target n=553 (32%)	A1c > target n=1170 (68%)	A1c at target n=833 (29%)	A1c > target n=2021 (71%)	A1c at target n=260 (19%)	A1c > target n=1122 (81%)
Responsible for checking and interpreting blood glucose levels in the previous month, n (%)*						
Mostly parents/adults	178 (32)	402 (34)	79 (9)	195 (10)	17 (7)	97 (9)
Mostly child/teen	117 (21)	253 (22)	484 (58)	1141 (56)	213 (82)	878 (78)
Both	256 (46)	510 (44)	268 (32)	679 (34)	18 (7)	106 (9)
Responsible for selecting and giving insulin doses in the previous month, n (%)*						
Mostly parents/adults	226 (41)	463 (40)	73 (9)	205 (10)	17 (7)	98 (9)
Mostly child/teen	93 (17)	205 (18)	510 (61)	1185 (59)	217 (83)	891 (80)
Both	231 (42)	496 (42)	249 (30)	627 (31)	13 (5)	91 (8)
PAID survey†						
N Mean score (SD)			804 22 (18)	1971 28 (20)	252 24 (19)	1097 32 (20)
PAID-PR survey‡						
N Mean score (SD)	537 48 (21)	1107 52 (20)	731 47 (22)	1842 52 (21)		

*Data for response "other" have not been included here;
†PAID: Problem Areas in Diabetes (20 items), completed by participants aged 13–25 y/o;
‡PAID-PR: Problem Areas in Diabetes, Parent-Revised version (18 items), completed by parents/guardians of participants aged 8–18 y/o

O50

Mortality in a nationwide, population-based cohort of childhood-onset type 1 diabetes in Norway

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Objectives: Norway has one of the highest incidences of childhood-onset type 1 diabetes (T1D) in the world. Despite advances in diabetes care, T1D is still associated with increased mortality. The aim of this study was to evaluate the long-term mortality of childhood-onset T1D.

Methods: The study is based on data from the Norwegian Childhood Diabetes Registry (NCDR), a nationwide population-based registry including all new-onset cases with T1D age 0–14 years, in 1973–82 and 1989–2012. We identified 7,884 individuals. The follow-up period for each patient was calculated from diabetes onset to the date of death, emigration or 30. September 2013, whichever occurred first, by matching the personal ID number assigned to each resident of Norway to the National Population Registry. This represented 132,420 person-years. The mean age at diagnosis was 8.8 years (SD 3.7). Mean diabetes duration was 16.8 years (range 2 days–40.7 years).

Results: During follow-up 249 (3.2%) individuals died, 174 males and 75 females. Mean diabetes duration was 20.0 years (range 2 days–40.4 years). Mean age at death was 29.9 years (range 0.8–51.8). The overall mortality rate was 1.88 per 1,000 person-years (95% CI 1.66–2.13). The mortality rate was significantly higher in males than females (2.44/1,000 vs. 1.22/1,000, RR 2.0, 95% CI 1.52–2.61, $p < 0.001$) and in individuals with pubertal-onset of diabetes (10–14 years) compared to prepubertal-onset (<10 years), (2.57/1,000 vs. 1.36/1,000, RR 1.90, 95% CI 1.47–2.43, $p < 0.001$). The estimated cumulative survival according to diabetes duration was 90.9% at 35 years. There was a significant improvement of 30% in the survival rate between the cohort diagnosed during 1973–82 and 1989–2012 (HR = 0.70 95% CI 0.50–0.99, $p = 0.041$).

Conclusions: This study indicates that mortality in a nationwide cohort of childhood-onset T1D seems to vary by gender, age at onset and time period of diagnosis. Improved survival was observed in the cohort of most recently diagnosed diabetes (1989–2012).

O51

Utility of pancreatic autoantibodies for classification of new onset diabetes in children

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Objectives: To test the hypothesis that measuring pancreatic autoantibodies (PAA) in children with new onset diabetes (NODM) can be restricted to patients with equivocal diabetes type.
Methods: Retrospective analysis of all NODM patients presenting to Boston Childrens Hospital from 1/1/09 to 7/1/13. Data collection included clinical assessment of diabetes type at discharge. We used logistic regression to predict antibody positivity and assign a clinical score to classify diabetes type.
Results: Of 987 patients with NODM (47% female, 76% white, mean age 10.6 ± 4.7 years), clinical diagnosis was 926 (94%) type 1 (T1D), 38 (4%) type 2 diabetes (T2D), and 23 (2%) other. 812 patients with clinical T1D or T2D had PAA (glutamic acid decarboxylase, insulin, IA-2) measured within 5 days of diagnosis. Six of 31 (19%) with clinical T2D had positive PAA, and 89 of 781 (11%) with clinical T1D had negative PAA. Among 623 patients with available BMI, a scoring system using BMI z-score, age and race was generated to predict diabetes type. Sensitivity and specificity to detect patients with T1D were 94% and 77%, respectively (positive predictive value 98%).
Conclusion: Application of a simple scoring system to NODM patients may reduce to ~10% the number of PAA measurements needed to classify diabetes type, resulting in significant cost savings. Clinical judgment should guide the decision to measure PAA. Further validation of such a scoring system in diverse clinical populations is warranted.

Table 1 Type 1 Diabetes Score

Category	Points assigned
BMI z-score	
<1	0
1–2	1
>2	3
Age	
<10 years	0
10–15 years	1
>15 years	2
Race	
White	0
Other	2

Total score = sum of points in each category.
If total score ≤3 assume T1D; If total score >3 obtain PAA.

O52

Bacillus Calmette-Guérin (BCG) vaccination and childhood diabetes in the Québec birth cohort on immunity and health (QBCIH)

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Type 1 diabetes is one of the most serious chronic childhood disorders. BCG vaccination can prevent and treat diabetes in animal models, but epidemiological evidence is sparse and inconsistent.
Objective: To investigate the association between BCG vaccination and childhood diabetes.
Methods: The QBCIH is a population-based birth cohort assembled through linkage of provincial administrative databases, comprising 81,496 subjects born in the province of Québec (Canada) in 1974 at ≥32 weeks of gestation. Information was extracted from the birth and death registries (1974–1994), as well as from the BCG Vaccination Registry. Health services relating to a diabetes diagnosis (ICD-9: 250) were obtained from physician billing claims (1983–1994) and hospitalization data (1987–1994). Subjects were classified as diabetic according to the validated National Diabetes Surveillance System definition: ≥2 physician claims in 2 years or ≥1 hospitalization. Age at 1st occurrence of diabetes was defined as age at 1st physician billing claim or hospitalization. Cox proportional hazards regression was used to estimate hazard ratios (HR) and 95% confidence intervals (CI) adjusted for sex, perinatal and socioeconomic characteristics, and history of allergic diseases.
Results: BCG vaccination status could not be determined for 89 subjects. Among the remaining 81,407 subjects, 46.4% were BCG vaccinated; 42.8% in the 1st year of life. A total of 310 (0.38%) subjects were classified as diabetic. No association was found between BCG vaccination and diabetes; the adjusted HR was 0.98 (95% CI: 0.78–1.24), and did not differ by sex. Similar results were found for children vaccinated in their 1st year of life (HR 0.94, 95% CI: 0.74–1.19) and those vaccinated later (HR 1.50, 95% CI: 0.91–2.49), as compared to those non-vaccinated.
Conclusions: In the largest study ever to address this hypothesis, we did not observe a protective effect of BCG vaccination on occurrence of childhood diabetes.

O53

A comparison of characteristics of youth with type 1 diabetes (T1D) with and without a family history of T1D in the T1D exchange clinic registry

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Objective: Compare characteristics of T1D children and adolescents with a first-degree relative with T1D to those without a positive family history in the T1D Exchange clinic registry.
Methods: Analysis included 14,104 who were <18 years old at time of enrollment (mean age 11.9 years, 48% female, 78% white); 1,859 (13%) reported a first-degree relative with T1D (+FH group) and 12,245 (87%) did not (−FH group). Analysis variables were demographics, socioeconomic factors, age and DKA at diagnosis, HbA1c level, and diabetes management parameters. Comparisons used chi-squared/Fisher exact and logistic regression methodology for categorical variables and *t*-test/non-parametric and regression methods for continuous variables.
Results: In the +FH group, 285 (15%) had a mother with T1D, 575 (31%) father, 25 (1%) both parents, 803 (43%) a sibling, and 171 (9%) both a parent and sibling. The table compares the two groups. Compared with those with −FH, those with +FH were more likely non-Hispanic white, diagnosed six months earlier, less likely to have had DKA at diagnosis, and more likely to be using an insulin pump. HbA1c levels were similar between groups.
Conclusions: Notable differences in some demographic and management parameters are observed between members with vs. without a first-degree relative with T1D. Further studies are needed to

explain these differences and their implications. Even with a +FH, 20% of youngsters still presented with DKA at diagnosis of T1D.

Table Participant characteristics

	+FH	−FH	p-value
Mean Current Age (years)	12.0	11.9	0.31
Gender (female)	50%	48%	0.27
White Non-Hispanic	82%	78%	0.0002
Mean Age at Diagnosis (years)	6.4	6.9	<0.0001
DKA at Diagnosis	20%	34%	<0.0001
Pump Use	52%	46%	<0.0001
Mean SMBG (times per day)	5.8	6.0	0.004
Mean HbA1c	8.6%	8.5%	0.08

O54

Diabetes care in young adults with type 1 diabetes after transition to adult care

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Transition from pediatric to adult diabetes care is a period of vulnerability with increased risk for interruption in care and adverse health outcomes. A population-based cohort study was conducted from 2002 to 2012 using local electronic medical records (Web DR). The goal was to determine the impact of transition on glycemic control and diabetes-related complications. Data from 148 subjects (47.3% male), age 16–20 years with type 1 diabetes was collected. The majority (n = 89, 60.1%) of subjects were on insulin pump therapy or multiple daily injections (n = 58, 39.2%). Mean A1C values during the 2 years prior to and post transition were 8.7 ± 1.7% and 8.9 ± 1.8% (p = 0.33). Mean diastolic blood pressure increased from 67.3 ± 6.3 to 72.6 ± 7.9 mmHg (p < 0.001) following transition but there was no change in systolic blood pressure. Mean LDL cholesterol values did not change during transition. Screening for microalbuminuria and dyslipidemia 2 years following transition were completed in 47 (31.8%) and 36 (24.3%) participants. Prior to transition there were 4 (2.7%) participants with nephropathy and 1 (0.7%) with dyslipidemia. Following transition, there were 8 (5.4%) patients with nephropathy, 7 (4.7%) with dyslipidemia, 4 (2.7%) with retinopathy, 4 (2.7%) with neuropathy, and 3 (2.0%) with hypertension.

We documented a trend toward deteriorating glycemic control and increasing diabetes-related complications following transition from pediatric to adult diabetes care. Interpretation of these results is limited by the low uptake of complication screening. Strategies to optimize complications screening in those at risk should be explored.

O55

Comparing type 1 diabetes in East African immigrant and nonimmigrant black youth

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Objectives: The aims of this study were to (a) describe and compare demographic and clinical characteristics of East African immigrant and nonimmigrant Black youth with type 1 diabetes (T1D) at time of diagnosis and (b) estimate the prevalence of T1D among these two populations in King County, Washington, USA.

Methods: This retrospective study identified all East African immigrant (n = 60) and nonimmigrant (n = 53) Black youth with T1D and treated at Seattle Childrens Hospital from 2000 to 2011. Descriptive analyses were conducted for all demographic and clinical characteristics. T1D prevalence was estimated using study data and U. S. Census Bureau estimates.

Results: Estimated T1D prevalence rates for East African immigrant youth in King County are nearly 4 times that of nonimmigrant Black youth (6.76/1,000 vs. 1.74/1,000). East African immigrant youth were on average younger at the time of T1D diagnosis, more likely to have government-sponsored insurance, and more likely to have a family history of diabetes. East African Immigrant youth had lower mean hemoglobin A1c and C-peptide levels, and were overall less likely to present in diabetic ketoacidosis (DKA) at diagnosis, but more likely to have severe DKA when present, and tested positive for diabetes-related autoantibodies less frequently than did nonimmigrant Black youth.

Conclusions: We found a substantial difference in estimated T1D prevalence rates as well as differences in disease trends at diagnosis between East African immigrant and nonimmigrant Black youth. These observations are lost within the Black/African American race classification and additional work is needed to confirm and further explore these findings.

O56

Establishment of diabetes registers in four under-resourced countries

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Objectives: Accurate diabetes registers are valuable in organising care, improving follow-up, determining incidence/prevalence, and advocacy. Whole-country registers have been established in four nations supported by the IDF Life for a Child Program - Fiji, Maldives, Mauritania and Mali.

Methods: The Fiji register was first compiled in 2008 from annual data from 2001 onwards; Maldives in 2013, data from 2010; Mali 2014, data from 2007; and Mauritania prospectively from 2013. Accuracy was improved by further detail on dates of birth and diagnosis. Data collection was cleaner and more complete when the register was simple, consisting of ID number, name, age, gender, region, date of birth and diagnosis, type of diabetes, and status (alive, deceased, lost to follow-up).

Results: In Fiji, type 1 incidence per 100,000 children <15 years per year (y) was 0.97 (average, 2001–13), with rates higher in Indo-Fijian children (2.3) compared to native Fijians (0.2, p < 0.001). Cases of type 2 were also noted in Fiji. In Maldives (predominately Indian population) average incidence 2010–13 was 3.2. Malian data is being finalised, and for Mauritania prospective observation time is insufficient. Insulin-requiring children are diagnosed as type 1 by default in most of the countries, it is possible that some have other forms of diabetes.

Peak age of onset in Fiji (0–15 y only) was 11–12 y, Maldives (0–23 y) 17–20 y, Mali (0–23 y) 15–18 y, Mauritania (0–23 y) 11–14 y. It is possible that some children (especially younger ones) are dying undiagnosed, particularly in Africa. Mortality over the respective periods has been very low in Fiji and Maldives, but higher in Mali.

Conclusions: Registers can be successfully established in low-income countries, and lead to useful information. Field numbers should be kept to a minimum, at least at first. Further country registers are being developed, and epidemiological studies indicated to determine the proportion of classic type 1 versus other types.

Oral Session VIII: Psychosocial Issues in Diabetes

O57

A lack of confidence and management of diabetes self care in youth with behavioral problems is associated with increased HbA1c

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Objective: The cohort study DINO (Diabetes IN Development) examines biological and psychosocial development in youth with type 1 diabetes. Previous studies indicated a relation between behavior problems and glycemic control. Here we examine if the association is mediated by confidence and mismanagement in diabetes self care.

Methods: We used baseline data of the DINO study (N = 88, 11–15 years). Problem behavior was assessed by Strengths and Difficulties Questionnaire: Externalizing, Internalizing and Total difficulties scores. Mediating variables were assed by Confidence In Diabetes Self Care-Youth and Diabetes Mismanagement Questionnaire. HbA1c was derived from charts. Multiple mediation analyzes was utilized, correcting for age and gender.

Results: The relation between Total problem behavior and HbA1c was mediated through *confidence in diabetes self care* and *mismanagement* (a_1b_1+a_2b_2*path* Point estimate = 0.50 BCa CI 95% 0.25–0.85, see Fig). Both Externalizing and Internalizing problem behavior showed this indirect effect (externalizing: a_1b_1+a_2b_2*path* Point estimate = 0.73 BCa CI 95% 0.36–1.25; internalizing: a_1b_1+a_2b_2*path* Point estimate = 0.50 BCa CI 95% 0.14–0.96), however, in Internalizing problems *mismanagement* is no independent mediator.

Conclusions: Problem behavior is associated with increased HbA1c, mediated by less confidence in diabetes self care and more diabetes mismanagement. Detecting problem behaviors and building confidence in diabetes self care at an early stage might reduce Hb1ac.

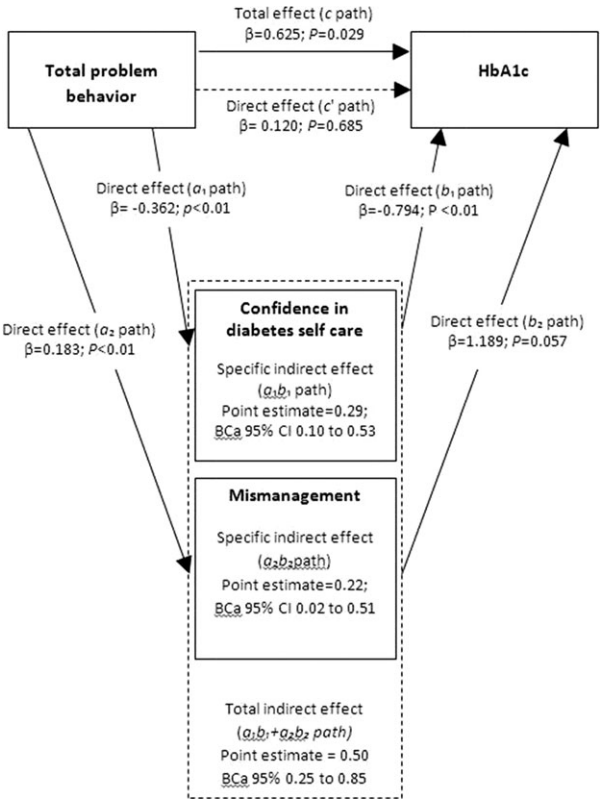

Figure Representation of multiple mediation model.

O58

Burdens related to diabetes management in Italian children, adolescents and young adults with type 1 diabetes (T1D) in the TEENs study

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Objectives: TEENs is an international, cross-sectional, observational study aiming to assess T1D management and psychosocial parameters in children, adolescents and young adults in order to identify approaches to optimize glycemic control and outcomes.

Methods: Twenty-three centers collected data by interview, medical record review and participant/parent survey from 1,009 Italian youths (mean ± SD T1D duration: 7.5 ± 4.6) in three groups: 8–12 years old (y/o), 13–18 y/o, 19–25 y/o. HbA_{1c} was measured centrally. Target HbA_{1c} was <7.5% (≤18 y/o) and <7% (>18 y/o).

Participants aged 13–25 y/o completed the validated PAID (Problem Areas in Diabetes) survey and parents/guardians of youths 8–18 y/o completed the validated PAID-PR (Parent/guardian-Revised version) survey. Scores range from 0 to 100 (higher score indicates greater perceived diabetes burden).

Results: Mean HbA_{1c}±SD varied by age group: 7.8 ± 1.0% in 8–12 y/o, 7.9 ± 1.3% in 13–18 y/o and 7.6 ± 1.2% in 19–25 y/o. Overall, 40% of patients achieved HbA_{1c} targets. Occurrence of acute complications varied by HbA_{1c}. In the last 3 months, 2.8% of those not at HbA_{1c} target and 1.2% of those at target had ≥1 diabetic ketoacidosis episode, while 1.6% and 1.0%, respectively, had ≥1 severe hypoglycemic event (seizure/loss of consciousness).

Parents/guardians perceived greater diabetes burden than adolescents/young adults based on the mean ± SD scores for the PAID (24 ± 18; 95% CI: 22–25) and PAID-PR (45 ± 21; 95% CI: 43–46). No difference was observed when data were evaluated according to age.

Conclusions: Parents/guardians reported higher perceived burden than youth with T1D. Overall, in this sample of Italian youths, frequent self-monitoring and intensive management leads to a satisfactory mean HbA_{1c}, even if supplementary education and support are needed to further increase the number of patients reaching target HbA_{1c}, and in order to reduce burdens associated with T1D.

Study sponsored by Sanofi.

O59
Perceptions of health risk in youth with type 1 diabetes

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Objectives: This study examined perceptions of health risks in relation to intellectual ability and executive functioning, as well as regimen adherence and glycemic control in a sample of youth with type 1 diabetes.

Methods: Seventy youth with mean age of 13.2 years (range 11–16.8 years) were recruited for the study during outpatient visits. Mean A1c was 9.31% (range 5.7–19.7%) and mean diabetes duration was 4.43 years. The assessment consisted of standardized measures of intelligence (WISC) and executive functioning (Trails B, Childrens Category Test), parent and youth-rated regimen adherence (Self Care Inventory), and ratings (1–5 Likert scale) of risk of short- and long-term diabetes-related health problems for self and others (Diabetes-related Health Problems Scale) as well as seriousness of diabetes and susceptibility to health problems (Diabetes Health Belief Questionnaire).

Results: Mean ratings of risks were less for self vs. others with diabetes (ps < 0.05). Mean short- and long-term risks for self were 2.6 and 1.9, respectively; mean short- and long-term risks for others were 3.2 and 2.7, respectively. Higher regimen adherence was associated with decreased long-term health risk for both self ($r = -0.26$, $p < 0.04$) and others ($r = -0.22$, $p < 0.07$). Higher A1c was associated with higher short-term health risks to self ($r = 0.24$, $p < 0.05$), long-term risks for others ($r = 0.23$, $p < 0.06$), and lower regimen adherence ($r = -0.29$, $p < 0.02$). Higher non-verbal reasoning was related with less perceived short-term health risks to self ($r = -0.27$, $p < 0.03$) and less susceptibility to health problems ($r = -0.25$, $p < 0.04$). Executive functioning was unrelated with health risk perceptions, regimen adherence, and glycemic control.

Conclusions: These findings indicate youth perceive low to moderate levels of diabetes-related health risks, and attribute greater risk to others than to themselves. Youth related greater risk to higher A1c and lower adherence, but risk was not related to executive functioning.

O60
Coping in adolescents with T1D: different in boys and girls

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Objectives: Coping is a heterogeneous concept and several cognitive, emotional and behavioural strategies of coping are differentiated. The relationship between coping strategies and blood glucose regulation (HbA1c) is examined in teenage boys and girls with T1D.

Methods: 65 boys (mean 14.8 ± 1.7 years) and 86 girls (mean 14.9 ± 1.7 years) with T1D reported their coping strategies (CODI coping questionnaire for children and adolescents). The questionnaire consists of 29 items, answered on 5-point scale, varying from 1 (never) to 5 (always), clustered in six domains: acceptance, (emotional) avoidance, cognitive-palliative, distance, emotional reaction, and wishful thinking. A separate last item Satisfaction: how well do you think you cope with your illness? measures the participants own assessment and satisfaction of the way (s)he copes with the disease, also answered on 5-point scale, varying from 1 (not at all) to 5 (very successful). HbA1c was recorded from medical charts.

Results: In girls an accepting coping style was significantly related to lower HbA1c values, after adjusting for age ($B = -0.49$, $p = <0.00$). In boys none of the different coping styles was significantly related to HbA1c values. A higher level of satisfaction with their coping ability was significantly related to lower HbA1c levels only in girls ($B = -0.35$, $p = 0.00$), not in boys ($B = -0.11$, $p = 0.41$).

Conclusions: Teenage boys and girls differ in their coping with diabetes, with a different relation to their bloodglucose regulation. In girls an accepting coping style and a higher level of satisfaction with their coping ability was related to better bloodglucose regulation, whereas in boys none of the coping styles was related to HbA1c. For clinical practice it seems necessary to evaluate the kind of coping strategies used by adolescent patients, and to differentiate between boys and girls, in counselling and treatment.

O61
How many times do I have to ask you to test your sugar? A qualitative study of parent-adolescent interactions in poorly controlled diabetes

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Introduction: Diabetes-specific family conflict is a strong predictor of quality of life and associated with increased depressive symptoms in teens and higher levels of depression and anxiety in parents. Associations between conflict and regimen adherence are bi-directional, and often evolve, resulting in a negatively reinforcing cycle of interaction. Our work describes these interactions from a systemic relational perspective.

Methods: Adolescents age 13–18 years with type 1 diabetes >1 year and HgbA1C values >9.0%, were invited to participate in a semi-structured family interview. Utilizing a qualitative approach, with Grounded Theory as methodological framework and data analysis saturation to measure trustworthiness; we asked descriptive circular questions to capture a comprehensive overview of family interactions around diabetes management.

Results: 27 adolescents and their parents participated, 9 males and 18 females age 15 years (SD-1.5), diabetes duration 10.3 years (SD-3.8) and HgbA1C 10.8% (SD-1.6). Predominant themes, expressed by both teens and parents, included persistent feelings of sadness and loss related to the diagnosis of diabetes and anger and frustration related to a persistent inability to perform diabetes tasks. A chronic repetitive parent/adolescent transactional process, often exacerbated by external factors, resulted in 3 distinct negative cycles of interaction we describe as dyadic, triadic and disengagement.

Discussion: From a systemic, relational perspective, we observed that poor diabetes adherence is associated with conflict, with patterns and progression varying by family. This conflict, often a byproduct of futile and desperate efforts to increase responsibility and improve metabolic control, may result in family disengagement from diabetes care. Deeper understanding of parent/teen interactions surrounding sub-optimal diabetes care may provide an opportunity for more effective intervention.

O62

Mental disorder and type 1 diabetes: initiation and discontinuation of CSII in pediatric and young adult patients with ADHD, depression, eating disorder, needle phobia, anxiety or obsessive compulsive disorder or psychosis. A German/Austrian DPV analysis

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Objectives: The risk of suicide or manipulation, but also coping with complex electronic devices, may deter treatment teams from using insulin pumps (CSII) in patients with mental disorder (MD). Therefore, we analyzed the use and discontinuation of CSII in type 1 diabetes (T1D) patients with and without clinically recognized MD.
Methods: The multicenter, prospective German/Austrian diabetes patient registry (www.d-p-v.eu) was searched for the diagnosis and/or specific treatment of MD in T1D. Between 2005–2013, 48,716 T1D patients aged 5 to <30 years (median [Q_1; Q_3]: 15.6 [12.0; 17.7]) with documented insulin dose were registered. A diagnosis of attention deficit hyperactivity disorder (ADHD) was documented in 1,405 patients (2.9%, males only: 4.6%). Further comorbid MDs included depression (n = 447, 0.9%), eating disorders (ED; n = 397, 0.8%, females only: 1.4%), needle phobia (n = 326, 0.7%), anxiety/obsessive compulsive disorders (OCD; n = 260, 0.5%) and psychosis/neuroleptic medication (n = 206, 0.4%). Multivariable regression models adjusted for age, sex, diabetes duration and migration background were created; adjusted estimates were calculated. Statistical package: SAS 9.4.
Results: An MD was recognized in 6.2% of T1D patients. Compared to non-MD patients (34.6%), the use of CSII was more common in patients with depression (42.8%), anxiety/OCD (41.9%), or needle phobia (76.5%) and less common in patients with psychosis (26.7%) (each $p < 0.05$). Patients with ADHD (35.9%) or ED (33.8%) revealed a similar use. Except for psychosis (3.6%, $p > 0.05$), the discontinuation rate of CSII was higher in MD patients (no MD vs. ADHD, depression, ED, anxiety/OCD, and needle phobia: 5.1 vs. 10.0, 8.8, 10.0, 5.8, and 5.8%). For ADHD, depression and ED the differences were significant ($p < 0.05$).
Conclusions: Low rates of MDs probably point to difficulties in recognizing MDs in T1D. However, early recognition is important as most comorbid MDs seem to contribute to discontinuation of CSII.

O63

Impact of sleep disturbance on daytime function for parents and children with type 1 diabetes

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Objectives: To explore the extent and impact of sleep disturbance on parents of, and children with Type 1 diabetes (T1DM).
Methods: Systematic literature review, in-depth interviews (n = 67 parents and n = 56 children) and data analyses were conducted to explore the experiences of parents and children with type 1 diabetes across three independent research studies in two countries; these experiences were also compared.
Results: Parents reported fear of nocturnal hypoglycaemia and generalized anxiety associated with caring for a child with T1DM. Parents of young children described setting alarms or waking spontaneously, often several times each night, to seek reassurance that their child was still breathing and monitor their blood glucose. Parenting a child with T1DM is associated with increased risk of psychological stress and poor physical health in the primary caregiver, usually the mother. Maternal sleep quality is a potential mediator of these effects and has hitherto received little consideration. Poor sleep in the children impacted on daily functioning and school performance. New technologies, e.g. continuous glucose monitoring and the artificial pancreas helped reduce sleep disturbance for some children and parents with subsequent improved daily functioning.
Conclusions: Parental anxiety is common, with specific fear of nocturnal hypoglycaemia leading to chronic sleep disturbance. Research is required to determine the prevalence of sleep disturbance in parents and children, the impact on glycaemic control, quality of life and psychosocial functioning; as well as exploring better ways to support parents who suffer sleep disturbance.

O64

Parental influence on glycemic control at baseline and one year post diagnosis in children and adolescents with type 1 diabetes mellitus

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Aim: The aim of this study was to examine the change in the childs glycemic control from the onset of the T1DM to 1-year post diagnosis examining mothers and fathers data separately by using the following repeated measurements; the childs age and gender, parent and family functioning (PedsQL™ Family Impact Module, FIM) and parent level of education.
Methods: Participants were 101 children, aged 3–15 years, recently diagnosed with Type 1 Diabetes and their parents. Data was collected at baseline and at 12 months after diagnosis. A Linear mixed model was used for longitudinal analysis of the variables parent and family functioning, parent educational level, and age and gender of the child explanatory of the continuous variable HbA1c.
Results: Parent and family functioning (PedsQL™ FIM), parent educational level, and age of the child were all explanatory variables of glycemic control 1-year post-diagnosis. The father model had at least as high explanatory value as the mother model.
Conclusion: This study highlights the importance of involving both parents in the childs diabetes treatment, both at onset and henceforth in the ongoing care.

Oral Session IX: Regimen-Based Innovations

O65

In Vitro derivation of insulin-producing cells from 3D spheroids of human amniotic epithelial cells

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Objective: Regenerative medicine and stem cell therapy represent a promising tool for the treatment of non-curable human diseases such as type 1 diabetes. Human amniotic epithelial cells (hAECs) from term placenta have attracted growing interest for their immunological properties, plasticity and availability which make them a promising tool for stem cell-based therapeutic applications. The aim of our study was to culture hAECs in serum-free condition preserving their phenotypic and genetic traits, evaluating their pancreatic differentiative potential in a 3D fashion.

Methods: hAECs were isolated and cultured in standard serum-rich medium and serum-free optimized media. Flow Cytometry analysis was performed to evaluate stemness and specific epithelial cells markers. qPCR assessed stem cell and proliferation markers. We established a 3D culture procedure on basement membrane extracts to obtain spheroids mimicking the *in vivo* morphology and spatial organization of pancreatic islets.

Results: The serum free protocol we developed proved to maintain hAECs stemness characteristics and confirmed their immunomodulatory activity on PHA stimulated PBMCs as revealed by proliferation assays. Immunofluorescence revealed the presence of pancreatic endocrine hormones and transmission electron microscopy (TEM) analysis showed a clear membrane-associated organization of secretory granules, consistent with beta cell ultrastructure *in vivo*.

Conclusion: We accordingly propose the outcomes of this study as a novel contribution to the development of a future cell replacement therapy for type 1 diabetes.

O66

Long-term efficacy and safety of insulin degludec (IDeg) in combination with bolus insulin aspart (IAsp) in children and adolescents with type 1 diabetes (T1D)

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Objectives: This 1:1 randomized controlled, open label, treat-to-target trial investigated efficacy and safety of IDeg OD + IAsp vs. insulin detemir (IDet) OD or BID + IAsp in children and adolescents with T1D for 26 weeks (n = 350) followed by a 26-week extension (n = 280).

Methods: 85 subjects aged 1–5 years (IDeg: 43), 138 6–11 years (IDeg: 70) and 127 12–17 years (IDeg: 61) were included, with baseline mean (SD) diabetes duration 4.0 (3.5) years, HbA_{1c} 8.1 (1.1)% and FPG 8.7 (5.1) mmol/l.

Results: Non-inferiority of IDeg vs. IDet at 26 weeks was confirmed for HbA_{1c} (primary endpoint); estimated treatment difference (ETD) 0.15% [−0.03; 0.32]$_{95\%CI}$ ($p < 0.05$). At 52 weeks, HbA_{1c} was 7.9% (IDeg) vs. 7.8% (IDet), NS, change in mean FPG was −1.29 mmol/l (IDeg) vs. +1.10 mmol/l (IDet) (ETD −1.62 mmol/l [−2.84; −0.41], $p < 0.05$) and mean basal insulin dose was 0.38 U/kg (IDeg) vs. 0.55 U/kg (IDet). Rates of confirmed hypoglycemia (i.e. severe [altered mental status, cannot assist in own care, semiconscious/unconscious, or in coma±convulsions] and/or PG <3.1 mmol/l) were similar with IDeg vs. IDet at 52 weeks (57.7 vs. 54.1 events/exposure year, NS), as were rates of nocturnal (11 pm–7 am) hypoglycemia (6.0 vs. 7.6, NS). Incidence and rates of severe hypoglycemia tended to be higher with IDeg vs. IDet (17.8% vs. 13.7%; 0.51 vs. 0.33, NS). Rates of severe hypoglycemia, including only episodes of semiconscious/unconscious and coma±convulsions, were 0.09 vs. 0.14 (NS, *post-hoc* analysis). Rates of hyperglycemia with ketosis (SMBG >14.0 mmol/l with blood ketones >1.5 mmol/l) were significantly lower for IDeg vs. IDet (0.7 vs. 0.11, treatment ratio 0.41 [0.22; 0.78], $p < 0.05$). Adverse event profiles were similar for IDeg and IDet.

Conclusion: IDeg improved long-term glycemic control at lower dose, achieving greater reduction in FPG vs. IDet. Severe hypoglycemia tended to be higher with IDeg than IDet, with similar rates of overall and nocturnal hypoglycemia and significantly lower rates of hyperglycemia with ketosis.

O67

Sulfonylurea therapy corrects hypotonia, attention deficits, improves complex neuropsychological functions and motricity in patients with neonatal diabetes secondary to mutation in potassium channel subunits, through a central nervous system effect

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Introduction: Sulfonylurea therapy (SU) allows a better metabolic control than insulin in patients with neonatal diabetes secondary to mutation in potassium channel subunits (ND-K). Most of these patients have neurological and neuromotor developmental impairments whose changes under SU has not been studied in a systematic and prospective way in a large cohort.

Objective: To demonstrate the beneficial effect of SU on neuropsychological functioning in ND-K patients.

Patients and methods: 18 patients (15 boys – 0.1 to 18.5 years). Neurological (MRI, electroencephalogram, electromyography (EMG) and quantitative neuropsychological and neuropsychomotor evaluations were performed before and 12 months after the switch from insulin to SU.

Results: SU improved HbA1C (Mean: −1.55%, range −3.8 to 0.1% $p < 0.01$). 17 patients presented neuro-motor developmental delay or defect (hypotonia, developmental coordination or attention disorders). One showed pyramidal signs and epilepsy. MRI was abnormal in 12 patients (periventricular white matter abnormalities, multiple punctate white matter or brainstem hyper intensities).

At M12, Hypotonia was corrected in 12 out 15 affected patients and visual attention deficits in 10 out 13. In all patients younger than 4 years ($n = 8$), global motricity impairments were corrected and fine motricity in 3. In older patients ($n = 10$), gesture conception and realization were also improved (two hands praxia improved in 4 out 8 affected patients, imitation of gesture and body spatial integration in 6). Motor and sensitive nerve conduction and membrane excitability studies with EMG were normal at baseline and at M12. SU didnt significantly improved intelligence scores.

Conclusion: SU therapy in ND-K allows a measurable improvement of neuropsychomotor impairments greater in younger patients. EMG shows that it is not a peripheral but rather a central effect. All efforts should be made for an early genetic diagnosis allowing a rapid switch to SU in ND-K.

O68

Comparative study between the use of insulin glargine and intermediate acting insulin (NPH) in type 1 diabetic children less than eight years old

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Background: Insulin glargine is a long- acting insulin analogue increasingly used instead of neutral protamine Hagedorn (NPH) insulin in children below eight years old with type 1 diabetes.

Objectives: To compare the efficacy and safety of insulin glargine with NPH insulin in children with type 1 diabetes mellitus (T1DM) below years old regarding glycemic control, frequency of hypoglycemia, quality of life and serum level of hsC-reactive protein (C-RP) as an inflammatory marker.

Methods: One hundred children from 3 to 8 years old with T1DM had been randomly enrolled in this study. They had been randomized into two groups, every group comprised 50 children. Group A received basal-bolus regimen using insulin glargine once daily and group B received NPH insulin twice daily as basal insulin for 6 months. Both groups received rapid acting insulin analogue at meal time. Quality of life were evaluated, self monitoring of blood glucose 4–6 times per day, HbA1C at baseline and 3, 6 months after as well as serum level of hsC-RP.

Results: Quality of life improved in all children receiving glargine but not in NPH group. Frequency of nocturnal hypoglycemia and severe hypoglycemia/month was significantly lower in group A compared with group B. ($p < 0.05$). At the end of the study, there was highly significant decrease in fasting blood glucose (FBG) in group A than in group B ($p < 0.001$) and 2 hours post prandial BG was significantly lower in group A compared to group B ($p < 0.05$).Mean value of HbA1c at the end of the study was $6.6 \pm 0.5\%$ for group A versus $7.4 \pm 0.7\%$ for group B with highly significant difference between both groups ($p < 0.001$).A significant reduction of hsC-RP was detected in both groups, with no significant difference between them.

Conclusions: Insulin glargine administered once daily,as a basal insulin is safe and more effective than NPH insulin in children with T1DM below eight years old, regarding glycemic control, overall hypoglycemia and quality of life.

O69

Evaluation of the uptake of a novel tool to adjust insulin boluses based on CGM trend arrows and insulin sensitivity (CGM TIME Trial Trend Arrow Adjustment Tool©)

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Background: Effective strategies for adjusting insulin boluses for CGM trend arrows are lacking. The JDRF CGM Study Group recommended adjusting boluses for trend arrows with a 10–20% increase/decrease of the bolus dose (10% for one arrow; 20% for two arrows). However, the original bolus dose is dependent on the amount of carbohydrate to be consumed and current blood glucose, which could potentially lead to overcorrection with elevated preprandial glucose and/or large meals. The formula also requires the pump user to perform mathematical calculations with each trend arrow, which has limited the tools uptake in pediatrics. We developed an alternative tool for adjusting boluses for CGM trend arrows, based on insulin sensitivity factor, with the goal of increasing its uptake and control of postprandial glucose.

Objective: To examine use of the Trend Arrow Adjustment Tool amongst participants in the CGM TIME Trial (Timing of Initiation of Continuous Glucose Monitoring in Established Pediatric Diabetes).

Methods: A retrospective audit of CGM data was conducted using CareLink Professional to examine uptake of the Trend Arrow Adjustment Tool in the 6 months after CGM initiation in 38 children and adolescents who had completed the main study in the TIME Trials lead site.

Results: Overall uptake of the Trend Arrow Adjustment Tool (TAAT) was 87% (i.e. TAAT was used by 33/38 study subjects). 73% of participants using CGM at 6 months were still using the TAAT. Mean use of the tool was 0.9 times per week (range 0–10 times per week), and this was sustained throughout the 6 months.

Conclusions: Uptake of the Trend Arrow Adjustment Tool (TAAT) was high and sustained amongst these CGM TIME Trial participants over the first 6 months after CGM initiation. A more detailed evaluation of TAAT including comparison with the JDRF trend arrow adjustment method is underway to assess effect on postprandial glycemic control and patient satisfaction in the clinical research unit and home settings.

O70

Insulin pump use in pediatric type 1 diabetes: multinational comparison with 54,768 pediatric patients from the T1D exchange (US), national paediatric diabetes audit (England and Wales), and the DPV initiative (Germany and Austria)

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Objectives: Advances in diabetes technology have improved care of children and adolescents with type 1 diabetes (T1D). While continuous subcutaneous insulin infusion (CSII) pump use has expanded in the past decade, there remains considerable variability between countries in the support for and use of pump technology. In this study, investigators in 3 large multicenter registries of T1D patients pooled their pediatric data to compare the frequency of use of CSII in children in the US, England/Wales and Germany/Austria.

Methods: Data for 2011 and 2012 from the T1D Exchange (US), the UK National Paediatric Diabetes Audit (England/Wales) and the DPV initiative (Austria/Germany) were compared. Data were analysed using multivariable logistic regression models (SAS9.4).

Results: The overall use of CSII was much lower in children in England/Wales than in the US or Germany/Austria. CSII use was higher in patients with longer T1D duration in all countries. Odds (95% CI) of CSII use was higher in females in the US (OR = 1.09, 1.02–1.17), Germany (OR = 1.29, 1.22–1.36) and Austria (OR = 1.50, 1.23–1.84). Additionally, patterns of CSII use by age exist by country as does cross sectional HbA1c (Table). Mean HbA1c values were lower in CSII versus injection patients ($p < 0.001$).

Conclusions: In Europe young children are more likely to be on CSII in contrast to older children being more likely in the US. The optimal age and time after T1D diagnosis to begin CSII therapy requires further study.

Table Rates of CSII by Country and Age and Mean HbA1c

	<6 years old (%)	6 to <10 years old (%)	10 to <14 years old (%)	14 to <18 years old (%)	CSII overall (%)	HbA1c CSII (%)	HbA1c injections (%)
US, *n* = 13,966	33	44	50	49	47	8.2	8.6
England, *n* = 13,666	22	16	14	11	14	8.5	9.0
Wales, *n* = 873	21	17	18	14	16	8.2	9.0
Germany, *n* = 24,483	69	42	37	34	41	7.9	8.1
Austria, *n* = 1,779	70	39	38	32	41	7.9	8.1

O71

Does frequent, extended use of an automated bolus advisor reduce hypoglycemia in pediatric patients treated with insulin pump therapy? First results of the BABE study

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Objective: The Bolus Advisor Benefit Evaluation (BABE) study, a single-center, retrospective cohort study, showed that frequent use of an automated bolus advisor (BA) over 6 months was associated with significant improvements in glycemic control, more therapy changes and no increase in hypoglycemia in 104 pediatric type 1 diabetes patients on insulin pumps therapy. We further assessed the impact of long-term BA use in a consistent cohort of study patients.

Methods: HbA1c values and blood glucose (bG) data at 12 and 24 months were available for 40 study patients: 28 high frequency (HF) users (≥50%); 12 low frequency (LF) users (<50%). Mean (SD) baseline characteristics were: HbA1c 7.6(1.0)%, age 13.4(4.3) years, diabetes duration 47.2(40.4) months, and 57.5% female. ANCOVA controlled for baseline differences in HbA1c, diabetes duration and age.

Results: Clinically significant between-group differences in HbA1c persisted to 24 months, but without statistical significance in this small study group. Percentage of blood glucose values <60 mg/dl in both HF and LF users increased at month 3 but decreased over time and was significantly lower in HF users at 24 months: 7.1(1.0) vs. 12.5(1.8), $p < 0.0253$ (Figure). A higher percentage of HF than LF users received therapy parameter changes, 57.1% ($n = 16$) vs. 16.7% ($n = 2$), at 24 months, $p = 0.0354$.

Figure. HbA1c and % bG values <60 mg/dL over 24 months

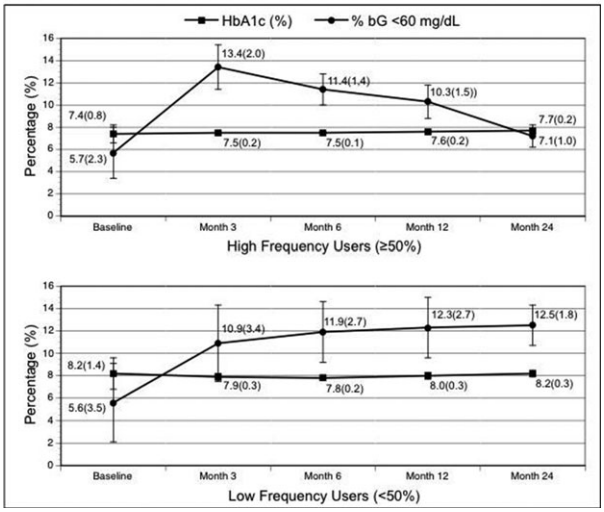

Figure HbA1c and % bG values <60 mg/ml over 24 months.

Conclusions: Frequent, persistent BA use is associated with improved glycemic control over time in pediatric type 1 diabetes patients.

O72

Effects of automatic insulin pump interruption on the timing and rate of nocturnal hypoglycemic events in the ASPIRE in-home study

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Objectives: The ASPIRE In-Home Study was designed to evaluate the Threshold Suspend (TS) feature of sensor-augmented pump therapy, which automatically suspends insulin delivery at a pre-set sensor glucose (SG) value. Because nocturnal hypoglycemia (NH) occurring in the latter half of the night is characterized by a diminished counter-regulatory response and is thus potentially more dangerous, we evaluated the TS feature with respect to the rate and timing of NH.

Methods: A NH event was an interval of >20 min with SG values ≤65 mg/dl that started between 10 pm and 8 am. Early events started between 10 pm and 3 am; late events started between 3 am and 8 am. Subjects with ≥2 NH events in a run-in phase were eligible for randomization. A total of 247 subjects (26 age 16–24, 139 age 25–50, and 82 age 51–70) were randomized to SAP therapy with the TS feature (TS, $n = 121$) or without it (Control, $n = 126$). Early and late NH events during the 2-week run-in and 3-month study phases were characterized.

Results: During the run-in phase, there were 2.1 NH events per patient-week, 67% of which were late. During the study phase, there were 1.8 NH events per patient-week, 65% of which were late. The distribution of early vs. late NH events was unaffected by study group assignment. Subjects in both groups had lower NH rates in the study phase than the run-in phase. In the study phase, the TS group, compared to Control, had significantly fewer NH weekly events (early: 0.5 vs. 0.8, $p < 0.001$; late: 1.0 vs. 1.4, $p < 0.001$), and the mean AUC (mg/dl×min) of those events was significantly less (early: 1,272 vs. 1,871, $p < 0.001$; late: 819 vs. 1,403, $p < 0.001$). In both groups, the AUC of early events was greater than the AUC of late events ($p < 0.001$ for each).

Conclusions: Late NH events were twice as frequent but generally less severe than early NH events. Use of the TS feature was associated with significantly fewer and less severe NH events in both early and late phases of the night.