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WILEY ISPAD International Society for Pediatric and Adolescent Diabetes

ORAL SESSIONS

Oral Session I - Diabetes Technologies

O01
CGM in healthy children aged 2-8 years

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Objective: To describe glycemic patterns monitored with CGM in healthy children aged 2-8 years.
Methods: Participants were healthy siblings, aged 2-7.9 years, of children with diabetes using CGM. Height and weight were measured by staff at the hospital. HbA1c was measured with DCA Vantage, with reference value 27-42 mmol/mol. Fasting plasma glucose and two-hour postprandial glucose value after a defined meal was measured with Hemocue prior to inclusion. Each child used one Dexcom G4 sensor placed on the arm or the buttock and calibrated according to the manufacturer's instructions. Data were downloaded to the Diasend system and analyzed with SPSS.
Results: 13 healthy children (9 girls) participated, with mean age 5.5 (±1.7; range 2.1-7.9) years, BMI-SDS 0.06 (±0.85; range −1.5-1.6), HbA1c IFCC 32 (±2.7) mmol/mol, and HbA1c NGSP 5.1% (±0.24%). Their fasting p-glucose was 5.0 (±0.40) mmol/l and two-hour postprandial p-glucose was 5.9 (±0.74) mmol/l. They provided 1895 (±107; range 1637-1985) glucose values each.

Mean glucose value was 5.3 (±0.33) mmol/l. Mean glucose variability expressed as SD was 1.0 (±0.21). Altogether 84% (±6.8; range 72-94%) of values were in the range 4-7 mmol/l, while 10% (±7.9%) of values were < 4.0 mmol/l, 3.3% (±3.6%) were < 3.5 mmol/l and 0.77% (±1.2%) were < 3.0 mmol/l. The median frequency of values below 4.0, 3.5, and 3.0 mmol/l was 7%, 2%, and 0%, respectively (range 1-27%, 1-11%, and 0-3%). Nadir glucose 4.5 (±0.31) mmol/l was at 5 a.m. and the highest value was 5.9 (±0.59) mmol/l at 9 p.m. Only 6.2% (±4.4%) of values were > 7.0 mmol/l, while 0.62% (±1.2%) were > 9 mmol/l, and 0.077% (±0.28%) were > 11 mmol/l.
Conclusions: Normoglycemia in children aged 2-8 years as monitored with CGM was 4.6-6.0 mmol/l, with a diurnal pattern of lower plasma glucose in the morning (3.9-5.1 mmol/l) and higher in the evening (4.7-7.1 mmol/l). Glucose values < 4.0 mmol/l were uncommon and values < 3.5 mmol/l were rare.

O02
Overnight glucose control during and after physical activity with closed-loop system GlucoSitter™ in youth with type 1 diabetes

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Objective: The aim of this clinical study was to investigate the safety and efficacy of closed-loop (CL) insulin delivery during physical activity and the night after in children and adolescents with type 1 diabetes (T1D).
Methods: This study is a two-arm, open-label, randomized, in-hospital, crossover, ongoing clinical trial of 20 children and adolescents with T1D. They performed two exercise protocols: moderate (55% of maximal oxygen uptake-VO_2max) physical activity, and a combination of moderate activity with incorporated high intensity sprints (55/80% VO_2max) either on CL (DreaMed GlucoSitter™) or open-loop (OL) in random order. In OL group pump was disconnected during the exercise and basal insulin dose was reduced by 20% for 4 hours after the exercise.
Results: This interim analysis included 10 subjects (5 girls), median age was 15,73 years (IQR:13,43-15,91 years) and median was HbA1c 7,8% (IQR:7,4-8,05%). There was no statistical difference in percentage of time in hypoglycemia below 3,9 mmol/l (1,3% (IQR:0,0-4,65%) for CL and 0,0% (IQR:0,0-0,4%) for OL). Event rate of hypoglycemia below 3,3 mmol/l was low in both groups (3 vs 1 in OL). In the VO2max 55/80% exercise protocol, the proportion of time with glucose values within target range (3,9-10 mmol/l) was significantly higher in the CL (85,9% (IQR:76,1-91,2%) compared to OL (67,8% (IQR:52,2-79,9%, P=0.0488)). Subjects did not spend any time in hyperglycemia above 13,9 mmol/l (0,0% (IRQ:0,0-0,0%) in CL compared to 6,3% (IQR:0,0-16,3%, P=0.0469) in OL). In the VO2max 55% protocol these differences did not reach statistical significance.
Conclusions: CL insulin delivery during and overnight after physical activity was safe and effective in maintaining glucose values in desired range without increased risk of hypoglycemia in the hospital environment.
Trial registration: ClinicalTrials.gov NCT02657083
Disclosure: M.M. received funding from 2015 ISPAD Research Fellowship Grant.

O03
At-home and hotel use of a hybrid closed-loop (HCL) system in a pivotal trial

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Range	Percentage of time in range		
	Run-In (sensor)	Study (sensor)	Hotel (i-STAT)
>300 mg/dL	2.3±4.2	1.7±1.9	1.6±9.38
>180 mg/dL	27.4±13.7	24.5±9.2	25.1±21.24
71 to 180 mg/dL	66.7±12.2	72.2±8.8	72.5±20.53
≤70 mg/dL	5.9±4.1	3.3±2.0	2.4±4.82
≤50 mg/dL	1.0±1.1	0.6±0.6	0.2±0.83

Plus-minus values are means ± standard deviations.

Objectives: A hybrid closed-loop (HCL) insulin delivery system was evaluated to establish its safety in adults and adolescents during unsupervised (home) and supervised (hotel) use.
Methods: Participants with type 1 diabetes for ≥2 years, >6 months' insulin pump use, and no recent severe hypoglycemia or DKA used the Medtronic HCL system, consisting of an investigational glucose sensor and transmitter, and a new pump platform with a control algorithm. After a 2-week run-in phase, all subjects were assigned to a 3-month study phase conducted at home, with a 6-day, 5-night hotel stay that included frequent reference (i-STAT) venous glucose measurements. Endpoints included the% of glucose values below, within, and above the target range of 71-180 mg/dL.
Results: There were no episodes of severe hypoglycemia or DKA. The Table summarizes sensor glucose (SG) values throughout the study and i-STAT values during the hotel stay. The% of in-target SG values (all subjects) increased from 66.7% in the run-in to 72.2% in the study phase, and increased from 60.4% to 67.2% among the 30 adolescents age 14-21, with corresponding decreases in SG values above and below the target range (p< 0.001 for each). SG and i-STAT glucose distributions were in good agreement (Table). The MARD for the sensors compared to i-STAT reference values was 10.3 ± 9.0 (median, 8.2%).
Conclusions: The HCL system was safe and was associated with reductions in the percentage of above- and below-target glucose values. Reference glucose measurements confirmed the results derived from the fourth-generation sensors.
[Distributions of glucose concentrations]

O04
Pivotal trial of a hybrid closed-loop system in adults and adolescents with type 1 diabetes

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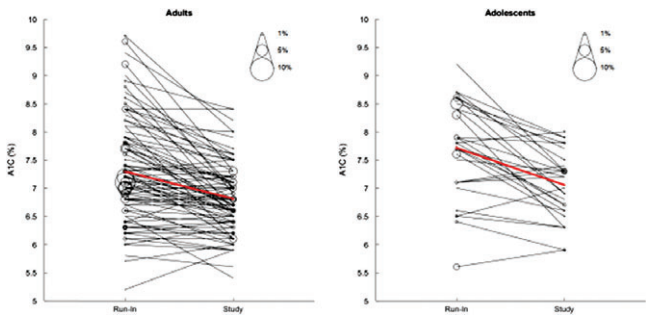

Objectives: A hybrid closed-loop (HCL) insulin delivery system was evaluated to establish its safety for unsupervised use in adults and adolescents.
Methods: Participants with type 1 diabetes for ≥2 years, >6 months' insulin pump use, and no recent severe hypoglycemia or DKA used the Medtronic HCL system, consisting of an investigational glucose sensor and transmitter and a new pump platform with a control algorithm. After a 2-week run-in, all subjects were assigned to a 3-month study phase of system use. Changes in A1C (ΔA1C) and nighttime hypoglycemia prevalence, defined as the percentage of sensor glucose (SG) values ≤50 mg/dL between 10PM and 7AM were determined in 30 adolescents (age 14-21) and 94 adults (age 22-75).
Results: The Figure shows A1C and nighttime hypoglycemia prevalences for adults (Panel A) and adolescents (Panel B) during the run-in and study phases. Bubble sizes correspond to hypoglycemia prevalence and slopes correspond to ΔA1C. Mean A1C fell from 7.3±0.9% to 6.8±0.6% in adults and from 7.7±0.8% to 7.1±0.6% in adolescents. Subjects with nighttime hypoglycemia >1% fell from 34 to 19 (adults) and from 12 to 4 (adolescents). There was no severe hypoglycemia or DKA in 12,389 patient-days. The MARD for the sensors compared to i-STAT reference values was 10.3±9.0% (median, 8.2%).
Conclusions: At-home use of the HCL system was safe during unsupervised home use and was associated with reductions in both A1C and nocturnal hypoglycemia, particularly in adolescents.
[A1C and nighttime hypoglycemia]

O05
Assessing the impact of insulin pump therapy on behaviour, mood, cognition and glycaemia in youth with type 1 diabetes - a randomised controlled trial

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Objectives: In response to parental reports of benefit, we have previously shown improved behaviour, mood & cognition following CSII initiation in a pilot study. This study aimed to re-examine these factors in a randomised controlled trial (RCT).
Methods: RCT at two Australian tertiary centres. Youth with T1D for >1y, aged 7-15y were randomised to intervention ('**I**' -immediate CSII start, n=56) or control ('**C**' -ongoing use of intermittent injections n=45) groups. Baseline assessments of behaviour & mood (BASC-2), cognition (standardised tests of intelligence, attention, memory & executive function) & HbA_{1c} were conducted pre-randomisation and after 4 months (mo). Primary outcome was difference in parent-reported behaviour at 4mo; differences in self-reported behaviour, mood, cognition & HbA_{1c} were secondary outcomes. T-tests & linear mixed model analyses were used.
Results: Mean baseline age & HbA_{1c} were similar (11.2 vs 11.0y; 7.9% vs 7.8% in **I** & **C** grps respectively). Parent-reported behavior problems (Cohen's d 0.41; p< .05) and HbA_{1c} (7.4% vs 8.0%; p=.001) were significantly lower in the intervention grp at 4mo. Mood (parent report) & some aspects of cognition (perceptual reasoning, attention, cognitive flexibility) improved in both groups over the study period but were not different between groups at 4mo (p>0.05). Self-reported behaviour & mood did not differ.
Conclusions: Parent-reported behaviour problems & HbA_{1c} decreased significantly with CSII vs intermittent injections over 4mo. As externalizing behaviour scores have been shown to predict mental health & glycaemic outcomes, this may have long-term benefits;

however effect size here was modest. Improvement in mood and cognition appear to reflect Hawthorn and practise effects respectively rather than any beneficial impact of CSII. This study highlights issues germane to parental attribution of cause and effect in respect to diabetes therapies and reiterates the value of RCT when evaluating such modalities.

O06

Flash glucose monitoring in type 1 and type 2 diabetes patients - the first Indian experience of libre pro

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Objectives: FreeStyle Libre Pro Flash Glucose Monitoring (FGM) technology, a novel automated ambulatory glucose profile (AGP) reporting system has recently been introduced.
Methods: The utility and usability of FGM glucose monitoring system was evaluated in clinically discrete situations including vulnerability to hypoglycaemia and persistent hyperglycemia.
Results: We evaluated the complete data (sensor AGP and clinical profile) of 35 type 2 (n=31) or type 1 (n=4) diabetics -FIRST study. Mean age was 49.3 yrs (T2DM mean 53.3 yrs min 23 max 80 yrs, T1DM mean 20.25 yrs min 10 yrs - max 37 yrs), 19 males, 16 females. Most compelling reasons for flash monitoring were fluctuations in blood glucose with reported episodes of hypoglycaemia (n=22, T2DM=20, T1DM=2) followed by consistent hyperglycemia despite advanced therapeutic care (n=13, T2DM=12, T1DM=1). Mean change in HbA1c (mean −0.19 ±1.5, 95% CI −0.7- 0.3) after three months was not statistically significant (baseline mean 8.3 Vs 3 months mean 8.1; 95% CI −0.9051 to 0.5108, p= 0.98). The change in HbA1c in T2DM (mean ± SEM - 0.16 ± 0.27, n=31) Vs T1DM (mean ± SEM −0.42 ± 1.11, n=4) was not statistically significant (95% CI −0.8 to 2.5, p=0.06). Change in HbA1c in < 60 years (Mean ± SEM 0.20 ± 0.38, n=23) Vs > 60 years (Mean ± SEM −0.18 ± 0.26, n=12) was statistically significant (95% CI −1.14 to 1.18, p=0.01).
Conclusions: The comprehensive data provided complete glycemic profile within short time span of 14 days with actionable snapshot insights into the 'Diabetic Pentad' comprising fasting, post prandial glucose, HbA1c, glycemic variability and hypoglycaemia, to customise the diabetes care approach to address hypoglycaemia and glycemic variability. The flash technology is a convenient, discreet and user friendly innovation in the advancement of ambulatory monitoring to enable physicians' make more informed treatment decisions. This can help personalize diabetes treatment plans, allowing better management of diabetes.

O07

Behavioral supports for parents of very young children with type 1 diabetes (T1D) using continuous glucose monitoring (CGM)

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Objectives: Diabetes management presents unique challenges for parents of very young children with T1D. Diabetes-related distress and hypoglycemia worries are common. Despite increasing use of CGM in this age group, many children do not reach glycemic goals. We tested 4 behavioral interventions designed to reduce distress and hypoglycemia worry and improve glycemic control.
Methods: Parents of 19 children under age 6 (mean age 4.2 ± 1.3) with T1D for an average of 2.3 ± 1.0 years using CGM were enrolled from 3 pediatric diabetes centers across the U.S. Behavioral interventions were assigned based on baseline glucose control or CGM use. Parents received either 4 sessions on managing fear of hypoglycemia and optimizing insulin treatment, or 4 sessions on distress reduction and age-specific developmental demands.

Parents completed the Hypoglycemia Fear Survey, the Glucose Monitoring Satisfaction Scale, and the parent version of the Diabetes Distress Scale before and after the intervention. CGM data (14-day download, before and after) were used to calculate time in target (70-180 mg/dL).
Results: Sixteen families completed 3 or more sessions. Hypoglycemia worries decreased while CGM satisfaction increased; both changes were significant with medium effect sizes (Table 1). Time in target increased from 47% to 54%.
Conclusions: Integrating behavioral supports with CGM use has promise for reducing burden and promoting glycemic target achievement in very young children with T1D.

[Table 1. Change from pre to post]

O08

Introduction of personal insulin pump 640G therapy with SmartGuard technology reduces the negative impact of diabetes on life comfort of patients with type 1 diabetes

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Objective: The aim of a study was to assess the quality of life(QoL) of the patients suffering from type 1 diabetes(DM1) after introducing personal insulin pump 640G with SmartGuard technology.
Material and methodology: 10 girls and 14 boys (the caregivers in younger children) with well-controlled DM1 (mean HbA1C was 6.7%; 5.8%-8.75%) were examined , age between 2 and 15, mean 8 years. The mean time from diagnosis was 3.7 years. Patient were previously treated with insulin pumps with or without hypoblocade(Medtronic MiniMed EAL-TIME/ Veo). 2-11 months after introducing 640G pump therapy two surveys were conducted: standardized PedsQLTM 3.0 Diabetes which measured the QoL in diabetic patients (Survey I) and the authorial questionnaire (Survey II) which measured the satisfaction of 640G therapy, it consisted of 11 questions, 2 closed and 9 - semi-closed-ended.
Results: The mean scores of QoL in Survey I regarding communication (79%), concerns (60%), treatment (76%) and diabetes (69%) which according to our scale (0-19% very low, 20-39%low, 40-59% moderate, 60-79% high, 80-100% vey high) which means patiens

		mean (SD)		mean comparisons		
Parent Measures	N	pre-	post-	t	p	Cohen´s d
Hypoglycemia worries	16	22.3 (7.31)	18.8 (5.19)	2.26	.04	.59
CGM satisfaction	16	20.9 (3.16)	23.0 (3.08)	2.24	.04	.55
Diabetes distress	16	25.3 (6.56)	23.9 (5.67)	1.26	.23	.32

perceived their QoI high in all categories. The results of Survey II showed gladness and assurance of the patients with 640G pump therapy. Over a half of participants (17 people) certified a serious reduction of both hypo- and hyperglycemia episodes. 8 patients/caregivers highlighted a better coherence between blood glucose(BG) measured by sensor and glucose meter(GM) which enabled them to decrease the frequency of pricking fingers with GM to measure BG and improve quality of life. 11 caregivers noticed greater involvement of children in controlling the disease and also better cooperation with 640G pump itself.

Conclusions: Patients with DM 1 using 640G pump with SmartGuard technology are satisfied with the effects of the therapy and their QoL measured by PedsQL is relatively high regarding this group of patients.

Oral Session II - Diabetes Epidemiology

O09

Maternal obesity as a risk factor for early childhood type 1 diabetes - a nationwide prospective population based study

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Objective: To investigate the possible effects of maternal body mass index (BMI) and gestational weight gain on the subsequent risk of childhood type 1 diabetes.
Methods: Children in the Swedish pediatric diabetes quality register were matched with four controls from the Swedish Medical Birth Register. The children, of whom data on their mother's BMI in early pregnancy and gestational weight gain were available, were included, total 16 179 individuals, 3231 children with type 1 diabetes and 12 948 control children.
Results: Mothers to children with type 1 diabetes were more likely to be obese (p=0.02) and to have diabetes themselves (p< 0.001) as compared to mothers to control children. The gestational weight gain did not differ significantly. In mothers without diabetes maternal obesity was a significant risk factor for type 1 diabetes in the offspring (p< 0.05) but this was not found in mothers with diabetes. Among the children with type 1 diabetes there were a greater proportion of children in the youngest age group (age 0-4) the higher the maternal BMI was. In the oldest age group, 15-19 years of age, the pattern was reversed. These findings were the same both for boys and girls. However, further analysis showed that the observed differences were only seen for non-diabetic mother whereas there was no significant difference if the mother had diabetes. Furthermore, the proportion of obese mothers was highest in the youngest age group, 18.2% compared to 7 % in age group 5-9 years of age 4.6% in age group 10-14 years and 10.3% in the oldest age group.
Conclusions: Maternal obesity, in absence of maternal diabetes, is a risk factor for type 1 diabetes in the offspring, and also influence the age of onset of type 1 diabetes. This emphasizes the importance of a normal maternal BMI to potentially decrease the incidence of type 1 diabetes.

O10

Incidence trends for childhood type 1 diabetes during 1989-2013 in 24 European registries participating in the EURODIAB study

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Objectives: To describe twenty-five year incidence trends for childhood type 1 diabetes in 24 European registries participating in the EURODIAB study.
Methods: All registries operate in geographically defined regions and are based on a clinical diagnosis of type 1 diabetes. Completeness of registration is assessed by capture-recapture methodology and exceeded 90% in most registries. Statistical analysis employed the Joinpoint program to model incidence trends in individual registries by fitting the most appropriate number of line segments connected at join points. Mixed effects Poisson regression was used for pooled analyses with registries defining the random effects.
Results: Twenty four registries in 20 countries registered more than 70,000 new cases diagnosed before the 15th birthday during the period 1989-2013. Joinpoint fitted simple log-linear increasing trends in incidence in 14 registries with a further 7 registries showing different trends in two periods but with a predominant increase. Two registries showed significantly faster rates of increase in boys than girls while eight found differences in rates of increase by age-group with the higher rates of increase in the 0-4yr and 5-9yr age-groups and lowest in the 10-14yr age group. Poisson regression estimated pooled rates of increase across all registers of 3.9%, 3.8% and 3.1% per annum in the three age-groups, respectively. Rates of increase also varied when each five-year period was analysed separately with the lowest rate of increase in the 2004-2008 period.

...Period.....	Annual increase (*95%CI*)
1989-1993	4.9% *(3.1%-6.7%)*
1994-1998	2.9% *(1.2%-4.6%)*
1999-2003	4.6% *(2.9%-6.2%)*
2004-2008	1.4% *(0.1%-2.7%)*
2009-2013	3.3% *(1.3%-5.3%)*

Conclusions: Rates of type 1 diabetes in European children continue to increase in all age-groups although the rate of increase may have reduced in more recent periods. The extent to which birth cohort effects can explain these apparent differences will be assessed.

O11

Risk factors for premature mortality in subjects with childhood-onset type 1 diabetes: data from the population-based Brecon Cohort in Wales, UK between 1979 & 2015

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Objectives: The aim of this study was to examine mortality rates and causes of death among patients diagnosed with type 1 diabetes before their 15th birthday in Wales.
Methods: The BRECON childhood onset type 1 diabetes registry (n=3288), with diagnosis from 1979 to 2013 (capturing >97% of all new cases from 1995), was used to investigate patterns in cause-specific mortality. 43,141 patient-years of diabetes were analysed and 31 deaths were identified. The observed number of deaths was

compared with number of deaths seen among different age groups in Wales, as reported by NHS Wales. Associations of socio-demographic factors with mortality were assessed using Cox proportional hazard models. The proposed risk factors included socio-economic status, the size of centre involved in diabetic care, diabetes duration and gender.

Results: The overall standardised mortality ration (SMR) was 2.3 (95%CI 1.59-3.23), being highest in the age group 15-20 years, at 3.76 (95%CI 1.54-5.09). Increase in the overall SMR has been observed in the age groups 10-20 years. The commonest cause of death was ketoacidosis (n=9), followed by accidents some of which might be attributed to hypoglycaemia (n=5), and suicide (n=4). All deaths occurred among individuals diagnosed during and after puberty (after the age of 10) regardless of diabetes duration, the log-rank statistics is 3135.83 (p-value < 0.001). Higher mortality rates among male subjects have been observed, with hazard ratio of 0.54 (95% CI 0.21-0.99; P=0.048). No statistically significant relationship has been found between the risk of death and diabetes duration, socio-economic status, size of centre involved in diabetic care and family history of diabetes.

Conclusions: Despite advances in diabetic treatment, type 1 diabetes is still associated with higher mortality rates, particularly in the age during transition from paediatric to adult care facilities.

O12
Excess mortality in young persons with type 1 diabetes in Sweden

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Objectives: To study mortality rates and their relation to metabolic control during childhood in young persons (≤29 years) with type 1 diabetes (T1D) diagnosed <18 years of age.

Methods: Data on all 12046 subjects registered in the Swedish pediatric diabetes quality registry, SWEDIABKIDS, from 2006 to 2014 were used. To investigate if any of these subjects had died and the causes of death, data were merged with the Swedish Register for Cause-Specific Mortality. The incidence of death was compared with the incidence in the general population (GP). Last registered HbA1c in SWEDIABKIDS was used.

Results: In total 99 persons ≤29 years of age with T1D were deceased, incidence 0.84/1000, 3.2 times higher than in the GP. Of these 51 had died of a documented diabetes-related cause. Among boys, the excess mortality was 2.1 times higher than in the GP, in girls 4.9 times higher. The highest mortality rate was found in age group 25-29 years and 10-14 years, 5.8 times higher than in the GP. Subjects dead from diabetes related causes had a mean HbA1c 80 ± 30 mmol/mol

(9.5 ± 2.7%). Subjects dead from other causes had a mean HbA1c 65 ± 19 mmol/mol (8.1 ± 1.8%) and those still alive 63 ± 16 mmol/mol (7.9 ±1.5%) (p < 0.001). Corresponding figures for boys were 81 ± 27 (9.5 ± 2.5), 66 ± 19 (8.2 ± 1.7) and 62 ± 15 (7.9 ±1.4), for girls 80 ± 33 (9.5 ±3.0), 64 ± 21

(8.0 ± 1.9) and 64 ± 16 (8.0 ± 1.5). The relation between high HbA1c and excess mortality was most obvious in the highest age group (25-29 years), especially in girls, 110 ± 34 (12.2 ± 3.1), vs 80 ± 25 (9.5 ± 2.3) in boys.

Conclusions: In this cohort of young subjects with type 1 diabetes, there was a high mortality rate compared to the GP. HbA1c was higher in those who died due to the diabetes disease, compared to death by other causes or to subjects still alive. Good metabolic control during childhood seems essential to decrease mortality rates in young adults.

O13
Prediction of type 1 diabetes using a genetic risk model in the diabetes autoimmunity study in the young (DAISY)

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Objectives: Our objective was to evaluate a previously-reported 10-factor weighted genetic model to predict development of type 1 diabetes (T1D) in the Diabetes Autoimmunity Study in the Young (DAISY) cohort. Performance of the 10-factor model (HLA plus nine SNPs) was compared to a more limited model (HLA plus two SNPs) and to HLA alone. We evaluated whether a model derived from first-degree relatives of T1D patients (FDR) would be effective in DAISY participants recruited from the general population (GP) as well as FDR subjects.

Methods: DAISY follows children prospectively for development of islet autoimmunity (IA) and T1D. The 10-factor model included HLA genotype plus SNPs from *PTPN22*, *INS*, *IL2RA*, *ERBB3*, *ORMDL3*, *BACH2*, *IL27*, *GLIS3* and *RNLS* genes. The 3-factor model was restricted to HLA genotype plus *PTPN22* and *INS*. These were applied to the DAISY cohort with complete SNP data (n=1941).

Results: Stratification of participants by 10-factor risk score showed significant differences in risk of T1D over time by Kaplan-Meier analysis: DAISY GP (p=0.00006), DAISY FDR (p=0.0022). The 10-factor and 3-factor models had improved discrimination of T1D outcome over HLA type alone in DAISY GP (p=0.03 and 0.03), but there was no difference in discrimination between these two models. In DAISY FDR, the 10-factor model showed improved performance over HLA (p=0.01) and the 3-factor model (p=0.02).

Conclusions: We have shown that a 10-factor risk model, previously validated in FDR of T1D patients, is able to predict development of T1D in children from the DAISY cohort. A more minimal 3-factor model showed similar performance in predicting development of T1D in GP; however, the 10-factor model had superior performance to both the 3-factor model and HLA alone in FDR. Differences in model performance in children with or without family history of T1D may lead to important insights into risk factors specific to these groups.

O14
Epidemiological trends of youth-onset type 2 diabetes in British Columbia, Canada

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Objective: To describe the trends in incidence and prevalence of youth-onset type 2 diabetes (T2D) in British Columbia (BC), Canada.

Methods: Children < 20 years of age living in BC between April 1st, 2002 to March 30th, 2013 were identified within linked administrative health data (physician billing claims, hospitalization discharge codes, and prescription dispensations). A validated diabetes case-finding definition and algorithm that differentiates T1D and T2D were applied to the linked data. Annual age-standardized incidence [IR] and prevalence rates [PR] were calculated overall, and by sex over the 10-year period. Linear regression was used to test for temporal trends.

Results: In 2002/03, 37 (62% female [F]) new cases of T2D were identified in individuals < 20 years, increasing to 53 (68% F) cases in 2012/13. The overall age-standardized IR (95% CI) per 100,000 was 5.0 (4.49-5.51), while for males and females it was 3.77 (3.15-4.39) and 6.27 (5.16-7.38), respectively. The age-standardized IR (95% CI) of T2D increased from 3.45 (2.43-4.80) in 2002/03 to 5.16 (3.86-6.78) in 2012/13 while in males it increased from 2.53 (1.39-4.36) to 3.23 (1.88-5.24), and in females from 4.43 (2.80-6.73) to 7.21 (5.05-10.05). The sex differences in T2D incidence widened from 2010 onwards. The number of prevalent cases increased from 97 (63% F) in 2002/03 to 219 (63% F) in 2012/13 while the age-standardized prevalence rate (%) increased from 0.009 (0.007-0.011) to 0.021 (0.018-0.023) increasing the overall age-standardized prevalence by 130%. Females had consistently higher prevalence of T2D than males over this period.
Conclusions: The incidence and prevalence of youth-onset T2D is increasing in BC with significant gender differences. Higher rates of T2D in female youth poses a significant risk to future offspring via exposure to hyperglycemia in utero. These data are necessary to guide health service delivery and disease prevention initiatives for youth-onset T2D.

O15
Premature deaths from ischaemic heart disease in childhood and young adult onset type 1 diabetes

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Objectives: Ischaemic heart disease (IHD) is a major cause of death for individuals with type 1 diabetes (T1D). Age at onset of T1D and risk of IHD death was assessed.
Methods: The Yorkshire Register of Diabetes in Children and Young Adults includes under 15s (early onset) diagnosed with T1D in Yorkshire from 1978, and 15 to 29 year olds (late onset) diagnosed in West Yorkshire from 1991. Personal identifiers were linked to Office for National Statistics (ONS) death certification data. Underlying cause of death was validated by a specialist clinician. Standardised mortality ratios (SMRs) were calculated using England and Wales population and IHD death rates between 1978 to 2014 by 5-year age group and sex.
Results: The cohort included 6,209 individuals, with 107,492 person-years of follow-up. Out of 233 deaths, 16 were due to T1D with IHD. Fourteen deaths had early onset (median age at death was 35.1). There were 2 deaths with late onset (median age of death was 43.2). Overall SMR for IHD deaths was 8.5

(95% CI 5.2 - 13.9). SMR for early onset (13.8 (95% CI 8.2 - 23.3)) was non-significantly higher than the SMR for late onset (2.3 (95% CI 0.6 - 9.3)).

[SMRs by onset and age at death]

Conclusions: Death from IHD begin to appear from 20 years old in the early onset group and mortality is non-significantly higher compared with the late onset group. This suggests that childhood T1D may result in unexpectedly early vascular death.

O16
End-stage renal disease in patients with childhood-onset type 1 diabetes diagnosed during 1973-2012

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Objectives: To estimate the cumulative incidence of end-stage renal disease (ESRD) by sex, age at diagnosis and year of diagnosis in a nationwide, population-based cohort with childhood-onset type 1 diabetes (T1D) in Norway.
Methods: Data are based on the nationwide, population-based Norwegian Childhood Diabetes Registry and includes all new-onset cases (age < 15 years) diagnosed with T1D during 1973-82 (n=1,888) and 1989-2012 (n=5,983). The follow-up period was from diagnosis of diabetes to development of ESRD, death, emigration or to September 30, 2013. We estimated the cumulative incidence of ESRD by years since diagnosis of diabetes by linking to the nationwide Norwegian Renal Registry and mortality by linking to the National Population Registry. We assessed cumulative mortality among patients with ESRD.
Results: The cohort was followed for maximum 40 years (mean 16.8 years). During 132,143 person-years, 95 (1.2%) individuals developed ESRD, 58 men and 37 women. Mean years from diagnosis of diabetes to ESRD was 24.7 years (range 12.1-37.8). The cumulative incidence of ESRD was 0.82% (95% CI 0.56-1.21) at 20 years, 3.21% (2.54-4.05) at 30 years and 5.3% (4.22-6.65) at 40 years. There was an increasing trend in cumulative incidence of ESRD over the three age groups at diagnosis (0-4, 5-9 and 10-14 years at diagnosis), p=0.01. No difference in cumulative incidence of ESRD was identified between men and women, p=0.13, nor between the two diagnosis cohorts (1973-82 and 1989-2012), p=0.96. The probability of death 10 years after diagnosis of ESRD was 39.4% (28.4-52.9).
Conclusion: We report relatively low incidence of ESRD among children diagnosed with type 1 diabetes in childhood. Individuals diagnosed at younger age seem to have more favorable outcome.

Age at death (years)	Early onset Observed	Expected	SMR (95% CI)	Late onset Observed	Expected	SMR (95% CI)
20 to 24	2	0.04	50 (12.5, 199.9)	0	0.01	0
25 to 29	2	0.09	22.6 (5.6, 90.2)	0	0.04	0
30 to 34	3	0.16	18.9 (6.1, 58.5)	0	0.11	4.9 (0.7, 34.6)
35 to 39	2	0.25	8 (2, 31.8)	1	0.21	0
40 to 44	3	0.28	10.6 (3.4, 33)	0	0.27	0
45 to 49	2	0.15	12.9 (3.2, 51.7)	0	0.18	0
50 and over	0	0.02	0	1	0.05	19.5 (2.7, 138.3)
Total	14	1.02	13.8 (8.2, 23.3)	2	0.86	2.3 (0.6, 9.3)

Oral Session III - Education and Psychosocial Issues

O17

Empowering children and young people (CYP) with diabetes - SEREN, a new structured education programme in Wales, UK. $S_{tructured}E_{ducation:}R_{eassuring}E_{mpowering}N_{urturing}$

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Education in diabetes is a fundamental component of self-management. Health care systems that have structured education from diagnosis have demonstrated improving trends in HbA1c. Within Wales, education for CYPs was delivered in an informal way and this deficiency was highlighted in the National Paediatric Diabetes Audit year on year. While structured education is being delivered across some parts of the UK, there is no overarching programme covering the entire age range of CYPs with diabetes, from diagnosis to transition to adulthood.

Objectives: Following basic training in the principles of structured education, a working group that consisted of Health Care Professionals (HCPs) and parent representatives was set up in 2013, to develop such a programme. The philosophy of the programme has been to "Empower the CYP and family to manage diabetes from diagnosis right through and including transition to adult services".

Methods: Work commenced based on education materials that were already being used within Wales. It draws on shared interactive and age appropriate resources and is aligned to the education key stages for the UK (1, 2, 3+4). The resources include an interactive story board, age based workbooks and activities. The detailed curriculum for the educators which is accompanied by an education/assessment record will enable standardisation of diabetes education across Wales. The programme is accompanied by a quality assurance process with formal evaluation being planned.

The first module "Diabetes at Diagnosis" for age 11 years+, piloted in September 2015 helped to refine these resources.

Conclusion: The first phase of the programme was launched in March 2016 after training of HCPs. The other key stages (with a Welsh translation) will follow and additional modules such as sport, pumps, annual updates and transition to comprehensive school and adulthood are planned.

We would like to take the opportunity to share our journey with you.

O18

How is diabetes training for persons taking care of children with type 1 diabetes in kindergarten and school delivered and funded? Results from a survey in Germany

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Objective: After onset of type 1 diabetes support for integration in kindergarten, day care and school is crucial. A structured, but also individualised, diabetes training for all persons caring for the child should be performed by the local diabetes team. In close cooperation with the parents diabetes specific knowledge should be addressed to avoid fears and to secure reintegration. Lacking a statutory rule diabetes education is provided in different ways in different regions of Germany.

Methods: The working group "inclusion" within the German association for pediatric diabetology has conducted a nationwide survey. A questionnaire of 16 Items with categorized answers regarding conduct and financial coverage (most frequently, in second line, rarely) was sent to 91 pediatric diabetes treatment centers.

Results: 66 pediatric diabetes centers (treating about 9700 children with diabetes) all over Germany (representing all 16 federal states) answered the questionnaire completely. Most frequently (90%) qualified members of a pediatric diabetes team conduct the training locally at the school, kindergarten or day care centre. This initial diabetes education is financed for about 80% in kindergarten or day care centers and about 70% in schools either by funding, honorary commitment, or is subsidized from hospital sources. In summary a diabetes training is particularly ensured by personal or private initiative or has to be covered by support of the local clinic with all the problems that occur in consultations with the hospital administration.

Conclusion: The working group inclusion therefore calls for a mandatory financial regulation for diabetes training of persons that care for children in school, kindergarten and day care in Germany. This training is required for integration and care of children with diabetes outside of their usual home care.

O19

Individual quality of life in parents of youth with type 1-diabetes: exploration of life domains in a context of Chilean rural area

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Introduction: Parental involvement are very important in the management of type1-diabetes (T1D) during the childhood. It may cause parental distress and contribute to diminish parent quality of life (QoL). The aim of this study is to investigating the individual, as oposed to predetermined, QoL in parents of children with T1D, in the specific and unexplored context of rural Chilean area.

Materials and Methods: We conducted an exploratory study with a methodological mixed design, during 2014-2015, composed by two phases: (1) The first phase consisted on the exploration of the most important domains of parents QoL through 12 interviews. (2) The second phase investigated the QoL of 21 parents through an evaluation adapted from the Shedule for the Evaluation of Individual Quality of Life -Direct Weighting interview, which allows respondents to nominate and evaluate their own quality of life domains.

Results: 11 life domains were identified through the first phase. During the second phase, the most frequently nominated life domains were "family", "finances","child health", "psychological well-being" and "access to physician trained in diabetes care" respectively, ranked in terms of importance, domains were "family", "child health", "social network", "psychological well-being", and "access to physician trained in diabetes care"; ranked in order of satisfaction, domains were "family", "social network", "psychological weel-being", "beliefs" and "finances". Total QoL scores ranged from 43.1 - 97.7 M= 72.0, SD=14.3.

Conclusions: Parents nominated many life domains not identified by WHO definition or classic Parent QoL questionnaire related to the child T1D. These findings are underscoring that parent QoL is multidimensional, with domains which can depend of the geographic place, like public health system charateristics. These findings should be replicated with larger sample to be able to associate theses findings to demographic and diabetes characteristics.

O20
New finding-PSEUDOHYPOGLYCEMIA

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India leads in the prevalence of Type I Diabetics according to latest statistics. A large chunk of these people lies below the poverty line to whom affordability and accessibility is a huge issue. They do not have access to a comprehensive Diabetic team.

We have created our own **D**iabetes **A**t **U**r **D**oorstep **(DAUD)** team consisting of diabetic educators who visit the rural remote areas and provide diabetic education, insulin and check Random blood sugar by creating a checklist.

The most peculiar finding was sub-optimal insulin dosage due to fear of hypoglycemia (Pseudo-hypoglycemia). It appeared as if the Type I kids have adapted to constant hyperglycemia state of RBS more that 200 mg/dl. The moment there is normoglycemia the patient starts developing hunger, weakness, perspiration at RBS less than 140 mg/dl.

This could be attributed to lack of availability of strips (cost issue) for SMBG, illiteracy, diabetic Education and lack of untrained health Professionals to deal with this. Or else a child may be anemic or suffering from nutritional deficiency etc. On mental aspect it can be anxiety, personality disorder, hysteria where a patient reports relief of symptoms after eating. In such cases glucose level is within reference range while patient is symptomatic.

The end result of this is missed insulin shots, avoidable shocking &weight gain. Education of patient and family, training of HCP can play a major role in improving this situation. Monitoring & making strips & glucometer available at affordable rates along with proper guidance on diet & exercise through project like DAUD can make a revolutionary change.

O21
Association between hypothalamus-pituitary adrenal axis activity and anxiety in prepubertal children with type 1 diabetes

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Background: Animal models of insulin-dependent diabetes show hyperactivity of hypothalamus-pituitary adrenal (HPA) axis, independently of hypoglycaemia. Few data exists regarding type 1 diabetes (T1D) in children.

Objective: To describe HPA axis activity according to the anxiety levels in prepubertal T1D children.

Method: Prepubertal T1D children and siblings of T1D children (controls) were included. State-Trait Anxiety Inventory (STAI) test was performed at inclusion. Glucocorticoids metabolites (LCMS)/creatinine ratio on nocturnal urines and morning salivary cortisol (SC) were measured at home during 5 consecutive days without identified nocturnal hypoglycaemia. Expressed results were mean of the five samples for each child. Tetrahydrocortisol (THF) + allo-THF/tetrahydrocortisone (THE) ratio (ie THFs/THE ratio) was considered as an estimate of type 1 11β-hydroxysteroid dehydrogenase (11β-HSD1) activity.

Results: Forty-nine T1D children (mean age 9.0+/−1.7 yrs) and 26 controls (9.3+/−1.4 yrs) were recruited. STAI scores were not different between T1D children (29.7+/−6.6) and controls (33.0+/−7.8). Total glucocorticoid metabolites/creatinine were decreased in T1D children vs controls (552+/−170 vs 673+/−170 µg/mmol, p< 0.01). THFs/THE was increased in TD1 children vs controls (0.46+/−0.10 vs 0.41+/−0.09, p=0.02). Salivary cortisol at awakening and 30 minutes after awakening (SC+30) were not different between groups. In both groups, STAI scores were associated with SC+30 when adjusted for BMI (controls b=−1.1, p=0.03; T1D children b=−1.0, p=0.04). STAI score was associated with THFs when adjusted for BMI in T1D children (b=−0.05, p=0.03) but not in controls.

Conclusion: Subtle changes of HPA axis activity, independently of recognized hypoglycemia, are present in prepubertal children with T1D, particularly for nocturnal glucocorticoid synthesis, 11β-HSD1 activity and its associations with anxiety.

O22
Does sleep matter? Associations between child sleep, glycemic control and parental wellbeing in the T1D Exchange Clinic Registry

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Objective: Sleep is a modifiable risk factor that may have physiological and behavioral impacts on diabetes outcomes, yet little is known about the impact of sleep disturbance in children with type 1 diabetes (T1D). The current study sought to describe sleep patterns in children with T1D and their parents and to examine associations between sleep quality (SQ), diabetes outcomes, and parental wellbeing.

Methods: Parents of children 2-12yo (n=515, mean age 9yrs, 47% female, 86% non-Hispanic white, mean age at diagnosis 4yo, mean A1c 7.8±0.9%, frequency of blood glucose monitoring (BGM) 7.4±2.4 times/day) from the T1D Exchange clinic registry (50 sites) completed internet-based surveys on their child's sleep patterns (Children's Sleep Habits Questionnaire (CSHQ)), their own sleep patterns (Pittsburgh Sleep Quality Inventory (PSQI)), fear of their child having a hypoglycemic event, their emotional wellbeing, and nocturnal monitoring habit. Clinical and demographic information were collected. Data were analyzed using general linear regression models.

Results: Mean sleep duration was below the recommended amount for all age groups (10.9 hrs/night in 2-4yo, 9.5 in 5-12yo, 6.5 in parents). Further, 67% of children and 53% of parents met the criteria for poor SQ (CSHQ>41;PSQI>5). Children with poor SQ had higher A1c (7.9% vs 7.6%; P< 0.001). Frequency of BGM (overall and nocturnal) was not associated with child SQ (mean 7.6 times/day vs. 7.4 in poor/good quality;P=0.56). Children's poor SQ was also associated with worse parental wellbeing and parental SQ (P< 0.001 for both). Child and parental SQ were worse when parents exhibited more fear of hypoglycemia (P< 0.001 for both)), but were not associated with frequency of nocturnal BGM (P=0.66 and p=0.35, respectively).

Conclusion: Sleep disturbances may negatively impact glycemic control in T1D, and may offer a potential target for interventions to improve outcomes in children with T1D and to reduce parental stress.

O23
Psychological flexibility in adolescents with type 1 diabetes

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Objectives: Type 1 diabetes (T1D) is challenging to manage, requiring a complex set of diabetes-related behaviors. Adolescents with T1D are at increased risk of deteriorating diabetes management, metabolic control and quality of life (QoL). Moreover, during adolescence, parental-controlled care gradually shifts to self-management. Therefore, the identification of protective factors specific for this developmental stage becomes particularly relevant. Psychological flexibility (PF), a construct derived from Acceptance and Commitment Therapy (ACT), refers to an individual's ability to act in alignment with life values and long-term goals (e.g. health, good family relations) in the presence of interfering (negative) thoughts, emotions and bodily sensations.

The aim of the study was to examine the association between PF and diabetes management, metabolic control and emotional functioning in adolescents with T1D.

Methods: A total of 104 adolescents with T1D (age range: 12-18, mean: 14.83 years, 53% male) and their parents completed questionnaires online and at home, measuring PF (diabetes-related PF, general cognitive and emotional fusion, general experiential avoidance), adherence and general QoL. The analyses controlled for HbA1c levels (mean HbA1c = 7.7%).

Results: After controlling for gender and age, hierarchical regression analyses revealed a significant contribution of diabetes-specific PF in explaining adherence ($Adj.R^2$=.15, p=.002) and QoL ($Adj.R^2$=.20, p< .001), but not metabolic control (HbA1c). General PF significantly contributed to the explanation of metabolic control ($Adj.R^2$=.07, p=.008) and QoL ($Adj.R^2$=.15, p< .001), but not adherence.

Conclusions: Our findings demonstrate that being able to act in line with personal values and long-term goals is associated with better diabetes management and control and better QoL. Overall, PF shows promise as a potentially protective characteristic against the burden of self-management in adolescents with T1D.

O24
The challenge of transition: adolescent and parent attitudes towards transition and adolescent diabetes services

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Objectives: Healthcare professionals often make decisions about how adolescents engage with adolescent diabetes services (e.g. if seen alone, when to transition, etc.) by consulting with parents rather than adolescents. This study assessed and compared the attitudes of adolescents and their parents on different aspects of adolescent diabetes services.

Methods: 82 adolescents aged >12 years (41 males), and their parents (n=82) separately completed an anonymous questionnaire examining attitudes towards aspects of adolescent diabetes services. Comparison of attitudes was undertaken using chi-squared/logistic regression for categorical variables and t-tests/ANOVA for continuous variables.

Results: Significant differences were found between adolescents' and parents' attitudes towards readiness for transition (p< 0.001) and age of transition (p< 0.001). Adolescents preferred an earlier age of transition compared to parents. Significant differences were also found between both groups in their attitudes towards the age when adolescents

a. should first be seen by the doctor on their own (p< 0.01), and when to discuss
b. alcohol (p< 0.01) and
c. sexual health (p< 0.001).

Adolescents preferred to discuss these issues individually, while parents preferred to be present in the room (p< 0.001, p< 0.01 respectively). Optimal diabetes clinic frequency was every three-months for both groups but adolescents with poorer control (HbA1c>8%) preferred to be seen every six-weeks (p< 0.05). Older adolescents (>15yrs) preferred to begin the process of transition later (i.e. after completion of second level education) compared to younger adolescents (p< 0.001).

Conclusions: Adolescents and their parents differ significantly in their attitudes towards a number of different aspects of adolescent diabetes services. When making decisions about adolescents' diabetes care it is important that adolescents, as well as their parents, are included in the decision making process.

Oral Session IV - Diabetes Chronic Complications and Associated Diseases

O25

Fas and Fas ligand expression in children and adolescents with type 1 diabetes mellitus

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Background: Early identification of risk factors and prevention of diabetes complications are of paramount importance in children and adolescents. Fas and its ligand are typical members of the tumor necrosis factor (TNF) receptor superfamily. Fas/Fas ligand (Fas/FasL) interactions may be related to augmentation of proliferation and inflammatory response. The role of soluble forms, sFas and sFasL in diabetes remains to be fully elucidated.
Aim: To detrmine the levels of sFas and sFasL in children and adolescents with type 1 diabetic patients and their relation to inflammation, glycemic control and microvascular complications.
Methods: Eighty children and adolescents with type 1 diabetes were divided into 2 groups according to the presence of micro-vascular complications and compared with 40 age- and sex-matched healthy controls. High sensitivity C-reactive protein (hs-CRP), HbA1c, urinary albumin creatinine ratio (UACR) as well as soluble Fas (sFas) and sFasL levels were measured.
Results: sFas and sFasL levels as well as Fas/FasL ratio were significantly higher among patients with and without complications compared healthy controls and the highest levels were found among patients with complications. sFas/sFasL ratio was significantly increased in relation to nephropathy (microalbuminuria), peripheral neuropathy or retinopathy. Significant positive correlations were found between both sFas and sFasL levels and each of disease duration, systolic and diastolic blood pressure, fasting blood glucose, HbA1c, triglycerides, total cholesterol, UACR and hs-CRP ($p< 0.05$). The cutoff value of sFas/sFasL ratio at 7.27 pg/mL could differentiate patients with and without micro-vascular complications with a sensitivity of 85% and specificity of 90%.
Conclusions: Elevated sFas/sFasL ratio in type 1 diabetic patients with micro-vascular complications suggests that inflammation and apoptosis are involved in the pathogenesis of these complications.

O26

Circulating angiopoietin-2 levels in young patients with type 1 diabetes mellitus: a link between inflammation, micro-vascular complications and subclinical atherosclerosis

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Background: Angiopoietin-2 is a growth factor involved in the pathophysiology of different vascular and inflammatory diseases such as arteriosclerosis. Carotid or aortic scans provide non-invasive screening tools for assessment of preclinical atherosclerosis in high-risk children.
Aim: We assessed serum angiopoietin-2 in children and adolescents with type 1 diabetes mellitus as a potential marker for diabetic vascular complications in relation to glycemic control, inflammation and vascular structure.
Methods: Sixty patients with type 1 diabetes were divided into 2 groups according to the presence of micro-vascular complications and compared with 30 healthy controls. High-sensitivity C-reactive protein (hs-CRP), hemoglobin A1c (HbA1c), urinary albumin creatinine ratio, serum angiopoietin-2 levels, carotid and aortic intima media thickness (CIMT and AIMT) were measured.
Results: CIMT, AIMT and serum angiopoietin-2 levels were significantly increased in patients with and without micro-vascular complications compared with controls and the highest levels were in patients with complications ($p< 0.001$). Serum angiopoietin-2 was higher in patients with microalbuminuria than normoalbuminuric group ($p< 0.001$). The cutoff value of serum angiopoietin-2 at 900pg/mL could differentiate patients with and without micro-vascular complications with a sensitivity of 92.3% and specificity of 100%. The cutoff values for CIMT and AIMT to detect micro-vascular complications were determined. Multiple regression analysis showed that fasting blood glucose, HbA1c, hs-CRP, CIMT and AIMT were independently related to angiopoietin-2.
Conclusion: The relation between angiopoietin-2 and assessed parameters of vascular structure in type 1 diabetes reflects a state of subclinical atherosclerosis and highlights the role of disturbed angiogenesis and vascular inflammation in the occurrence of diabetic complications.

O27

Achieving clinical guideline goals is associated with better insulin sensitivity (IS) and cardiopulmonary health in youth with type 1 diabetes (T1D)

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Objective: Most youth with T1D do not meet the American Diabetes Association (ADA) and International Society for Pediatric and Adolescent Diabetes (ISPAD) targets for HbA1c, blood pressure (BP), lipids, and BMI. We hypothesized that ISPAD/ADA goal achievement would be associated with better IS and cardiopulmonary health in youth with T1D.
Methods: We assessed the cross-sectional relationship between ISPAD/ADA goal achievement, IS and cardiopulmonary health in youth with T1D from the RESISTANT (n=86) and EMERALD (n=41) studies (n=127; age 15.7±2.2 years, 52% girls). IS was measured by glucose infusion rate during a hyperinsulinemic-euglycemic clamp. Cardiopulmonary fitness was measured as peak oxygen consumption (VO_2peak/kg) during cycle ergometry. EMERALD and RESISTANT had different cycle ergometry protocols, thus VO_2peak analyses were stratified by cohort. Goal achievement was defined as HbA1c< 7.5%, BP< 90th percentile, LDL-C < 100mg/dL, HDL-C >35mg/dL, TG < 150mg/dL and BMI < 85th percentile. Participants were stratified into 3 groups: achieving 1-3 goals (n=52), 4 goals (n=48) and 5-6 goals (n=27). Differences between groups were examined with generalized linear models.
Results: IS was lower in participants who met 1-3 goals (5.24±3.40 mg/kg/min) vs. those who met 4 goals (7.41±4.13 mg/kg/min, $p=0.04$) and those who met 5-6 goals (8.45±4.28 mg/kg/min, $p=0.003$), and remained significant after adjustments for sex and Tanner stage. The difference in IS between participants who met 1-3 goals and 5-6 goals remained significant after adjusting for BMI ($p=0.03$). VO_2peak was lower in participants in RESISTANT who met 1-3 goals (25.84±4.63mL/kg/min) vs. those who met 4 goals (33.01±7.81mL/kg/min, $p=0.01$) and those who met 6 goals

(33.18±4.44mL/kg/min, p=0.004). Similar and significant relationships were observed in EMERALD participants for VO_2peak.
Conclusions: In youth with T1D, ADA/ISPAD goal achievement was associated with better IS and cardiopulmonary health.

O28
Prevalence of subclinical entheseal involvement in children and adolescents with type 1 diabetes: a case-control study

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Objectives: At the best of our knowledge, no data about enthesis ultrasonographic evaluation in young patients with type 1 diabetes(-T1D) have been reported. The prevalence of subclinical entheseal involvement in children and adolescents with T1D was studied using a high frequency ultrasound probe.
Methods: We evaluated 23 children and adolescents (12 M), with T1D, ages 9-18 years (mean±SD, 13.9±2.5 years), disease duration 1-10 years, without any clinical sign or symptom of musculoskeletal involvement. A control group consisting of 28, sex (12 M) and age-matched (14.2±2.8 years), was also evaluated. Both patients and controls underwent an ultrasound examination (ESAOTE MyLAB 70 6-18 MHz linear array transducer). Brachial triceps, femoral quadriceps, Achilles, plantar fascia, and proximal and distal patellar entheses were all scored using the 0-136 Madrid Sonographic Enthesis Index (MASEI).
Results: None of the patients had a MASEI score suggesting early spondyloarthritis involvement but their average score was significantly higher than controls (4.65 ± 4.4 vs 3.04 ± 1.9, p=0.009). No difference has been observed about enthesis with power Doppler score ≥2 or with dishomogeneous echo structure in both patients with T1D and controls. Patients with T1D showed significantly more calcification than controls (43.5% vs 8.7%; p=0.0046). In patients with T1D a significant correlation between the total MASEI score and diabetes duration was observed (p=0.004), while no correlation was observed between the total MASEI score and age (p=0.85) or HbA1c (p=0.15).
Conclusions: In a recent review, the hypothesis that in T1D patients the excess of advanced glycation end products may be the cause of tendon damages has been suggested. In our study we observed a higher total MASEI score and calcifications in patients with T1D than in controls. This finding is new in patients with T1D and needs to be confirmed in larger group and during follow-up.

O29
Celiac disease in 52,721 youth with type 1 diabetes: ethnicity is not associated with glycaemic control nor therapy

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Objectives: Celiac disease (CD) affects ~5% of youth with type 1 diabetes (T1D). We examined international differences in CD prevalence and clinical characteristics of patients with T1D+CD vs T1D only.
Methods: Data sources: DPV (Germany/Austria), T1DX (US), NPDA (England/Wales) and ADDN (Australia). The analysis included youth age < 18 yrs with a visit between Apr 2013 and Mar 2014. Linear and logistic regression were used to assess the relationship between T1D+CD vs T1D and A1C, therapy and growth, adjusting for sex, age, ethnicity and T1D duration.
Results: Biopsy-confirmed CD was present in 1835 youth, diagnosed at median age 8 yrs [IQR 5.0-11.0], with CD diagnosed before T1D in 5.5%. Comparing T1D+CD vs T1D, patients were younger at T1D diagnosis: 5.4 yrs [2.9-8.7] vs 7.0 [4.0-10.2], fewer were male (41 vs 53%), non-white (15 vs 18%) or overweight/obese (34 vs 37%), all p< 0.01. Height SDS was lower (mean 0.29±1.2 vs 0.48±1.2, adjusted p< 0.001). Stratified by ethnicity, A1C was comparable in T1D+CD vs T1D: white 8.3 vs 8.3%; non-white 8.3 vs 8.5% and CSII use was similar: white: 43 vs 39%, non-white: 33 vs 33% (all p>0.05). Characteristics are shown in the table.
Conclusions: Differences in CD rates and T1D duration at CD diagnosis may reflect international variation in screening/diagnostic practices, and/or CD risk. Although fewer patients with CD are non-white, the association between CD and A1C or diabetes therapy reassuringly does not appear to be related to ethnicity.
[Characteristics of youth overall and by registry]

O30
Celiac disease screening in asymptomatic type 1 diabetes mellitus patients across North America and Europe

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	Overall	DPV	T1DX	NPDA	ADDN
Number	52,721	24,611	7,536	17,152	3,422
Age at visit	13.2 [10.0-15.7]	12.8 [9.4-15.4]	13.0 [10.0-15.0]	14.1 [11.0-16.1]	12.9 [9.6-15.3]
Age at T1D diagnosis	7.0 [4.0-10.2]	7.3 [4.2 - 10.6]	6.0 [3.0-9.0]	7.0 [3.8-10.1]	6.9 [4.0-10.1]
Duration at visit	4.9 [2.6-7.9]	3.8 [1.5-7.0]	6.0 [3.0 - 8.0]	5.7 [3.6-8.5]	4.3 [1.9-7.5]
Non-white (%)	18.2	20.4	20.9	12.2	31.7
CSII (%)	37.0	43.0	60.5	17.7	40.1
CD (%)	3.5	3.2	1.9	3.8	7.7
Age <5 yrs at CD diagnosis (%)	23.0	23.3	17.2	-	26.3
CD within 2 yrs after T1D diagnosis (%)	54.2	55.5	27.4	-	69.1

Objective: Medical associations recommend screening for celiac disease (CD) in at-risk groups, as type 1 diabetes mellitus (T1DM). There is a lack of consensus among guidelines on who and how to screen. We aim to evaluate current practices and factors influencing and limiting the screening of CD in asymptomatic T1DM patients across North America and Europe.
Methods: A web-based survey was sent to paediatric endocrinologists and paediatricians with an expertise in T1DM in Canada, United States and Europe. Physicians were contacted through the following associations: Pediatric Endocrine Society (PES), International Society for Pediatric and Adolescent Diabetes (ISPAD), Canadian Pediatric Endocrine Group (CPEG) and European Society of Pediatric Endocrinology (ESPE).
Results: A total of 381 participants responded to our survey. Two hundred and twenty nine (60.1%) were from the United States, 90 (23.6%) from Europe, 48 (12.6%) from Canada and 14 (3.7%) from others countries. Almost 21% of Canadians claimed never screen asymptomatic T1DM patients for CD, compared to 0.4% of Americans

(p< 0.001) and 0.0% of Europeans (p< 0.001). When asked about the possible consequences of not treating asymptomatic CD patients, 22.2% of Canadians reported no possible consequence compared to 5.7% of Americans (p< 0.001) and 5.6% of Europeans (p=0.01). A proportion of 37.5% of Canadians don't agree that screening for CD in asymptomatic patients with T1DM can reduce their morbidity, compared to 12.0% of Americans (p< 0.001) and 14.4% of Europeans (p=0.06). A proportion of 56.3% of Canadians think that the recommendations from their endocrine associations are unclear regarding screening for CD in asymptomatic patients with T1DM, compared to 34.5% of Americans (p=0.01) and 19.8% of Europeans (p< 0.001).
Conclusion: We noted a clear difference in practices, mostly between Canadians and others responders. A unification of guidelines would be needed.

O31
Inflammatory bowel disease in children and adolescents with type 1 diabetes: a multicenter analysis from the German-Austrian DPV database

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Objectives: The association between type 1 diabetes (T1D) and other autoimmune comorbidities such as celiac disease and thyroiditis is well known. Therefore, we investigated clinical characteristics of the autoimmune overlap of T1D and inflammatory bowel disease (IBD). Does the course of T1D differ in patients suffering from both diseases?
Methods: Data of 65.147 young patients with T1D below the age of 18 years (mean age 14 ± 3.86 years, mean diabetes duration 5.41 ± 4.2 years) of 379 centres in Germany and Austria participating in the DPV initiative (Prospective Diabetes Follow-up) were analysed.

We used multiple regression models to analyse differences in metabolic control, acute complications, insulin dose and steroid intake in patients with T1D and IBD compared to those with T1D only. Severe hypoglycaemia was defined as requirement for need of outside help.
Results: Out of 65.147 children and adolescents, 63 children were diagnosed with IBD: 33 with ulcerative colitis, 26 with Crohn´s disease, 4 with undetermined colitis.

Mean BMI-SDS in patients with T1D and IBD was −0.153 ± 0.115 whereas in patients with T1D only BMI-SDS was 0.273 ± 0.004 (p = 0.0002). However, patients with T1D and IBD had a significantly higher use of steroids (0.223 ± 0.053 versus 0.009 ± 0.0003, p < 0.0001) and a significantly higher rate of severe hypoglycaemia (0.328 ± 0.073 versus 0.158 ± 0.002, p = 0.001). No differences were found in HbA1c levels and insulin dose, neither differences in rates of ketoacidosis.
Conclusions: Although children and adolescents with T1D and IBD take steroids more often, they suffer from severe hypoglycaemia more frequently and have a lower BMI. This may be due to malabsorption caused by chronic intestinal inflammation.

O32
Liver stiffness by transient elastography as a non-invasive tool for detection of hepatopathy-induced fibrosis in pediatric patients with type 1 diabetes

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Aim: To identify the effect induced by hepatopathies of different etiologies among children and adolescents with T1DM using transient elastography (TE) and its relation to glycemic control.
Methods: One hundred patients with T1DM (at least 5 years disease duration) were studied stressing on liver function tests, fasting lipid profile, HbA1c, hepatitis C virus (HCV)-RNA using PCR, serum immunoglobulins, autoimmune antibodies; Anti-nuclear antibody (ANA), Anti-smooth muscle Antibody (ASMA), and Anti-Liver Kidney microsomal antibody (anti-LKM) using indirect immunofluorescence methods. Pelvi-abdominal ultrasound was performed and TE was done for patients with elevated ALT, HCV, positive autoimmune antibody and/or abnormal ultrasound findings. Liver biopsy was done when indicated after parental consent.
Results: 31% of patients were found to have one or more abnormalities; clinical hepatomegaly in 8%, elevated ALT in 10%, HCV in 6%, autoimmune hepatitis (AIH) in 11% (10 were positive for ASMA and 2 were positive for ANA while anti-LKM antibodies were negative) and abnormal hepatic ultrasound in 20% (5 AIH, 2 HCV, 1 Mauriac Syndrome, 9 non-alcoholic fatty liver disease and 3 non-alcoholic steatohepatitis). Mean liver stiffness in those 31 patients was 7.0 ± 2.1 kPa (range, 3.1- 11.8 kPa); 24 were Metavir F0-F1, 7 were F2-F3 while none were F4. Type 1 diabetic patients with abnormal ultrasound had significantly higher FBG, HbA1c and total cholesterol than those with normal liver

(p< 0.05). Patients with AIH had higher HbA1c than those with negative autoimmune antibodies (p=0.012). Liver stiffness was significantly higher in patients with abnormal ultrasound compared with normal liver (p=0.039). Significant positive correlations were found between liver stiffness and HbA1c and ALT.
Conclusions: Hepatic abnormalities are prevalent in young patients with T1DM and related to poor metabolic control. TE provides a reliable method for detection of hepatopathy-induced fibrosis.

Oral Session V: Diabetes Genetics, Immunology and Environmental and Monogenic diabetes

O33
DIAGNODE: autoantigen (GAD-alum) given into lymph-nodes together with oral vitamin D to preserve beta cell function in Type 1 diabetes. A pilot trial

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Residual beta cell function in Type 1 diabetes (T1D) is clinically very important, but no intervention without too serious risks/adverse events has so far been efficacious. GAD-alum sc has been promising but not enough effective. Vitamin D might help to gain additional efficacy. Furthermore, in allergy allergen administration into lymph-nodes seems more effective than sc administrations. For the first time this administration route is tried in an autoimmune disease, T1D.

Objectives: To evaluate the safety as well as clinical and immunological response of giving GAD-Alum (Diamyd) directly into lymph nodes in combination with oral vitamin D (2 000 IE/day).

Patients and Methods: DIAGNODE-1 is a single-center open-label pilot Phase I trial designed to enroll approximately 9 subjects between 12-30 years of age, T1D duration < 6 months , positive for GAD65- antibodies (GADA) and a fasting C-peptide ≥0.12 nmol/L. They get Vitamin D 2000 U/d Day 0-120 and 4 µg GAD-alum into an inguinal lymph-node Day 30, 60 and 90. So far 7 patients have been recruited and 4 have been followed for 6 months . The immune response has been evaluated by measurement of GADA, and the effect of GAD_{65} stimulation on cytokines in cell supernatants, cell proliferation and T cell phenotypes, and beta cell function has been evaluated by Mixed Meal Tolerance Tests.

Results: The treatment has been feasible and well tolerated, without any concern regarding safety during the first 6 months follow-up. From baseline to 6 months the C-peptide AUC (nmol/l) decreased 2% and 29 % respectively in two patients, and increased 32% and 6% respectively in two patients, with a pronounced Th2-deviation of the immune system.

Conclusion: A low dose GAD-alum given into lymph-node in recent onset T1D is feasible, tolerable, seems to be safe, and gives a strong Th2-deviation of the immune response which together with Vitamin D might preserve beta cell function.

O34
Detection of a viral footprint in the pancreatic islets of newly diagnosed T1D patients: results from the DiViD study

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Objectives: The Diabetes Virus Detection (DiViD) study has suggested the presence of chronic enteroviral infection in pancreatic tissue collected from 6 of 6 live adult patients with newly diagnosed T1D. The aim of the present study was to compare the gene and protein expression of selected virus-induced pathogen recognition receptors and interferon stimulated genes in DiViD islets vs age-matched non-diabetic (ND) controls.

Methods: RNA was extracted from laser captured islets and Affymetrix Human Gene 2.0 ST arrays used to obtain expression profiles. The presence and localisation of viral response proteins were examined by triple immunofluorescent labelling in 4um sections of pancreatic tissue.

Results: PKR expression did not differ between T1D and ND islets at the level of total RNA but a subset of β-cells displayed markedly increased PKR protein levels. These cells corresponded to those previously shown to contain the viral protein, VP1. RNA encoding MDA5 was increased significantly in T1D islets. At the protein level, Mda5 staining was seen in α- and certain β- cells in both T1D and ND islets. In addition, an uncharacterized subset of islet cells expressed intense MDA5 staining and these were more prevalent in DiViD cases. STAT1 RNA was elevated in T1D islets vs ND and was exclusively increased in β-cells at the protein level. Both classical and non-classical HLA Class I molecules were also increased at the RNA and protein levels in T1D islets. MxA RNA was upregulated in T1D vs ND islets and was detected exclusively in T1D β-cells at the protein level.

Conclusion: The increases in PKR, MxA, HLA-I and STAT1 seen in β-cells in T1D provide clear evidence of the activation of IFN signalling pathways. As such, these data strengthen the hypothesis that chronic enteroviral infection contributes to the development of islet autoimmunity in T1D.

O35
Increased prevalence of type 1 diabetes among patients with 18q deletion syndrome may be associated with a deficit in T regulatory cells

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Objectives: Several patients with the chromosome 18q del syndrome (MIM#601808) are reported to suffer from autoimmune disorders and immunoglobulin deficiency (mainly IgA deficiency). The aim of the study was to evaluate the prevalence of type 1 diabetes (T1DM) among patients with 18q del syndrome of Caucasian origin.

Methods: Medical registries and social media were used to recruit the patients. Microarray oligonucleotide comparative genomic hybridization (aCGH) (Agilent, USA) was used to confirm initial diagnosis. Lymphocyte phenotyping for the assessment of CD127low/CD25/CD4/CD3 T regulatory cells using a FACS CANTO II flow cytometer (BDBioscience, USA) was performed. FoxP3 expression was confirmed using nuclear factor FoxP3 staining kit supplied by eBioscience (USA).

Results: Twenty three patients aged 3-31 years (median 13 years) were included into the study. 18q aberrations varied from small interstitial deletions of about 8 Mbp (18q22.3-q23) to large deletions of about 55 Mbp encompassing 18q11.2-q23. Of the patients 3/23 had early onset T1DM (diagnosed at 7 months, 3.5 and 4 years, respectively) with OR(95%CI)=40.9(9.5-175.8) comparing the prevalence of type 1 diabetes among pediatric patients in the region of Lodz district (142/100 000 individuals < 18 years). In 9 of 23 patients hypothyroidism/autoimmune thyroiditis was present. Immunological studies, performed in 16 out of 23 patients, revealed complex serum immunoglobulin deficiency in 4/16 patients. In general, IgA deficiency was detected in 3/16, IgE def in 2/16, IgM def in 4/16, IgG def in 4/16, IgG1 def in 1/16, IgG3 def in 1/16 and IgG4 def in 6 out of

16 patients. Interestingly, all recruited patients had Treg deficiency with low intracellular expression of crucial transcription factor FoxP3 in this subset (<15%).
Conclusions: Relatively high prevalence of type 1 diabetes among patients with 18q deletion syndrome may be associated with a deficit in T regulatory cells.

O36
The microbiome in children with islet autoimmunity: bacteriome profiling and virome sequencing in stool samples from Finnish DIPP study

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Objectives: We set out to explore the stool bacteriome profiles in the context of early-onset islet autoimmunity, taking into account the interactions with the virus component of the microbiome.
Methods: Stool samples were longitudinally collected from 18 infants and toddlers with islet autoimmunity that started at the median age of 17.4 months, and from 18 tightly matched controls from the Finnish Diabetes Prediction and Prevention (DIPP) birth cohort. Three stool samples taken 3, 6 and 9 months before the first detection of autoantibodies in serum of the case child were analysed by bacteriome profiling, and virome sequencing. The risk of islet autoimmunity was evaluated in relation to bacteriome diversity, composition of the bacteriome profiles at various taxonomic levels, correlations between abundances of bacteriophages and bacteria, and prominent unknown motifs in the virome.
Results: The abundance of five bacterial operational taxonomic units (OTUs) was significantly decreased in children with islet autoimmunity as compared to controls, with the most prominent distortion observable in OTUs belonging to *Bacteroides vulgatus*, *B. thetaiotaomicron* (corrected P values < 0.001) and *Bifidobacterium bifidum* (p=0.0014). The diversity, or the composition at taxonomic levels of bacterial phyla, classes or genera, showed no differences between cases and controls. One of the bacteriophage signals, the *CrAssphage*, showed a tendency towards an association with islet autoimmunity, and correlated with *Bacteroides dorei* and *B. thetaiotaomicron*.
Conclusions: The results confirm previous findings that an imbalance within the prevalent *Bacteroides* genus is associated with islet autoimmunity. The detected quantitative relation of the novel "orphan" bacteriophage *CrAssphage* with two prevalent species of the *Bacteroides* genus serve as an example of the bacteriome-virome interactions whose complex nature we are only beginning to appreciate.

O37
Early childhood infections precede development of β-cell autoimmunity and T1D in children with HLA-conferred disease risk

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Objective: To assess the relationship between early childhood infections and islet autoimmunity in children with HLA-conferred risk for type 1 diabetes (T1D).
Methods: Seven hundred ninety-seven children with HLA-conferred susceptibility to T1D (51.4% males) from Finland (n=387), Estonia (n=324) and Russian Karelia (n=86) were followed from birth up to the age of 3 years. Children attended clinical visits at the age of 3, 6, 12, 18, 24, and 36 months. Serum samples for analyzing five T1D-associated autoimmune markers (IAA, GADA, IA-2A, ZnT8A, and ICA) were collected and health data, including data on past and ongoing infections, were recorded during the visits.
Results: Children who seroconverted to autoantibody positivity during the follow-up (n=47, 5.9%) had their first infection at a younger age than children with no signs of islet autoimmunity (median 4.0 vs. 5.0 months; p=0.007). They had also more infections during the first year of life (3.5 vs. 3.0; p< 0.001). By May 2016, seven children (0.9%; one from Estonia, one from Russia, and five from Finland) had been diagnosed with T1D. Their median age at diagnosis was 3.7 years (range 2.4-6.4 years). Compared to their non-diabetic peers, children who progressed to T1D were younger at their first infection (2.2 vs. 4.9 months; p=0.004) and had more infections during the first 2 years of life (both years 6.0 vs. 3.0; p=0.001 and p=0.027, respectively). By the age of 3 years, children progressing to T1D had double the cumulative number of infections when compared to their non-affected peers (17.5 vs. 9.0; p=0.007). These findings were not explained by the HLA genotype or the country of origin.
Conclusions: Early childhood infections may play an important role in the pathogenesis of T1D. On the other hand, the current findings may reflect early immunological aberrancies in children developing T1D at a young age.

O38
Early successful hematopoietic cell transplantation (HSCT) in a boy with IPEX syndrome caused by novel c.721T>C *FOXP3* mutation

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Objective: IPEX (MIM #304790) is rare and fatal, X-linked immune dysregulatory disorder caused by mutation in transcription factor FOXP3 that result in either quantitative or functional deficiencies of Tregs causing autoimmune disease and allergic inflammation. HSCT is the only curative therapy available for IPEX patients.
Case presentation: Presented boy was born at 38th GW with birth weight 3380 g and birth length 50 cm. Three maternal brothers died in early infancy due to malabsorption. At six weeks patient presented with hyperglycaemia (38 mmol/L) and severe ketoacidosis at onset of type 1 diabetes (T1D), GAD antibodies were highly positive (>120 kIU/L). Subsequently he developed atopic dermatitis and progressive failure to thrive due to diarrhea. The total parenteral nutrition (TPN) and intravenous insulin infusion was initiated. At the age of three months he underwent HSCT from an unrelated HLA-matched donor. The HSCT course was uncomplicated, the outcome was favorable: gastrointestinal and skin symptoms fully resolved, the boy is fed orally and thriving well. C-peptide remained undetectable (<3.33 pmol/L) and insulin administration is needed. At the current age of six months, his T1D is well controlled by CSII (HbA1c 45 mmol/mol) with daily insulin requirements of 0.63 IU/kg.
Methods and Results: Direct sequencing of *FOXP3* gene revealed a novel c.721T>C (S241P) mutation in the proband, his mother and

sisters. A The quantity of Tregs in our patient was in normal range (9.0%), but in immunosuppressive assay his Tregs failed to suppresses proliferation of effector T cells if compared to healthy controls.
Conclusions: We describe a previously unreported c.721T>C (S241P) mutation in *FOXP3* gene. To our knowledge the patient is the youngest reported patient with IPEX who underwent successful HSCT. We suggest that an early genetic diagnosis followed by early HSCT offers the greatest potential to correct disease process and thereby minimize end-organ damage.

O39
Binational Swiss-Lithuanian study "genetic diabetes in Lithuania"

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Objectives: To examine markers of β-cell autoimmunity in a cohort of young (0-25 years) patients with type 1 diabetes (T1D). To perform genetic testing in islet autoantibody negative diabetes cohort.
Methods: Study subjects were investigated for autoimmune markers of T1D (GAD65, IA-2, IAAs, ICAs), coexistence of other autoimmune diseases (thyroid, celiac disease). Diabetes control was assessed by levels of HbA1C, clinical examination, lipid profile, presence of diabetic complications. Patients with negative pancreatic antibodies (Ab's) were selected for genetic investigation. Genetic analysis was performed in Switzerland by high throughput sequencing from DNA selected for all coding and splicing regions of 483 genes involved in diabetes, glucose homeostasis or pancreas development, captured by bait using Haloplex technology.
Results: Our cohort consisted of 1211 subjects covering all pediatric diabetes patients (<18 years, n=861), and 70% of adult patients younger than 25 years at diabetes diagnosis (n=350). All positive Ab's were found in 25.4%, 1 or 2 positive Ab's in 66.5%, and all negative Ab's - in 8.1% of cases. 147 cases of non-autoimmune diabetes were identified during the overall project. We included probands positive for insulin autoantibodies, because Ab's were tested after introduction of insulin therapy. 25.9% of genetic tests of 147 subjects (3% of 1211) revealed polymorphisms and mutations. 36.7% variants in potential diabetes genes with high predicted pathogenicity (would increase monogenic diabetes to 7.5% of the entire cohort). GCK mutation was found in 13.6%, HNF1A in 4.8%, other known genes (HNF4A, KLF11, INS, KCNJ11, ABCC8) in 7.5%, and negative in 37.4% of the entire cohort. 10% of the 147 subjects had actionable changes and were subjected to a treatment change.
Conclusions: This binational project revealed high rate of positive results. This led to optimization of treatment and further follow-up of such patients.

O40
Glucokinase mutations in pediatric patients with impaired fasting glucose

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Aims: We aimed to detect the Glucokinase frequency in two cohorts describing clinical manifestations and identified variants. We also intent to predict the effect of the novel mutations to correlate molecular defects and clinical manifestations.
Methods: Totally 100 unrelated Italian families with incidental hyperglycaemia were enrolled and subdivided in two cohort applying strict and mild criteria of Maturity Onset Diabetes of the Young selection. Genetic testing was performing by Sanger Sequencing GCK gene of all participants.
Results: 53 Italian families with 41 different mutations affecting the GCK gene and co-segregating with the clinical phenotype of GCK/MODY were identified. All mutations were found in heterozygous state. In cohort 1 we detected GCK defects in 32/36 subjects (88.9%) selected with full stringent MODY criteria of diagnosis while in cohort 2 GCK defects were found in 21/64 subjects (32.8%) with no fully stringent MODY criteria of diagnosis.
Conclusion: Our study enlarge the wide spectrum of GCK defects adding 23 novel variants. The application of strict recruitment criteria resulted in a higher GCK/MODY prevalence (88.9%) never previously reported for the Italian population. In order to reduce the proportion of missed cases it could be useful to perform genetic test even if one or more clinical parameters for MODY clinical diagnosis are missing. Computational analysis could be useful to understand the effect of the change on protein functionality, especially when the novel identified variants is a missense change and/or parents' DNA is not available.

Oral Session VI: Diabetes Care

O41

Long-term improvement and sustainability of HbA1 outcome in children and youth with type 1 diabetes: the diabeter experience

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Diabeter is a comprehensive care model that has established healthcare management for Type 1 diabetes (T1D) children and adolescents characterized by a strong focus on personalized care and usage of technology. Central in this approach is Vcare, a disease management system that monitors >200 outcome parameters. Upon every upload of glucosemeter or insulinpump data, Vcare generates personalized treatment overviews and therapy advice (Ther@pymail). We hypothesized that this personalized approach results into better clinical outcome. Only 15-30% of pediatric T1D reach the ISPAD HbA1c target of < 7.5% (59mmol/mol)(McKnight,Diabet.Med **32**(8):1036).

Method: A retrospective analysis, with HbA1c as primary outcome parameter was conducted in patients treated in the clinic (2006-2015), comparing the period before/after introduction of Ther@pymail (2012). HbA1c outcome was expressed as percentage of patients reaching the ISPAD HbA1c target. Patient's contacts (face-to-face, phone, email) with or without Ther@pymail were collected and expressed as per patient per year.

Results: The addition of Ther@pymail to the Diabeter care model resulted in 45-50% of patients reaching ISPAD target, despite the increased number of patients treated. Results were independent of treatment-modality.

[diabeter4]

Conclusion: The Diabeter model can improve and sustain over time clinical outcome in pediatrics T1D. Providing automated personalized advice by Ther@pymail can further improve HbA1c outcome.

O42

Home telemedicine increases the number of type 1 diabetes care visits attended by young adults

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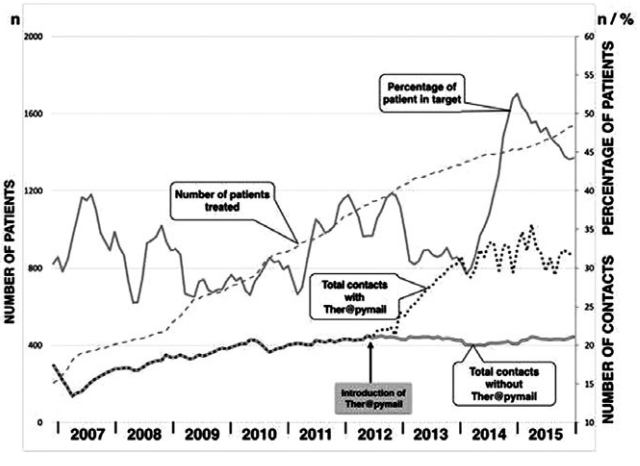

Objectives: To determine adherence to essential components of T1D care: visit attendance, device downloads and A1C measurement in young adults with T1D enrolled in a home telemedicine trial (CoYoT1).

Methods: Visits occurred every 3 months for 1 year with 3 home telemedicine visits and 1 in-person clinic visit. Prior to each visit, participants were instructed to download their T1D devices from home and obtain A1C at a local laboratory.

Results: 45 young adults (M_{age}=19.8±1.6 years; 56% female) with T1D ($M_{diabetes\ duration}$=8.6±4.6 yrs.) participated. At least 72% of participants downloaded their T1D devices and >80% completed A1C (Table 1). In the year prior to study enrollment, participants completed 2.5±1.2 in person T1D clinic visits. With access to home telemedicine, participants completed significantly more T1D clinic visits (M=3.3±1.1;

t= −3.563; p< 0.001) compared to the number of T1D visits attended in the prior year. The proportion of participants who completed ≥4 T1D visits/year, as recommended by ADA, significantly improved from 22% to 67%; McNemar c^2 p < 0.001.

Conclusions: Providing young adults with T1D care visits via home telemedicine increases visit frequency. Additionally, data needed for quality T1D care was successfully obtained for the majority of home telemedicine visits. Offering home telemedicine for young adults may be a successful way to increase clinical care engagement during this transitional stage.

[Adherence to T1D Care Components via Telemedicine]

O43

New challenges in pediatric diabetes care: frequency and medical treatment of type 1 diabetes among current refugees in Germany and Austria

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Objectives: For German and Austrian pediatric diabetes teams a new challenge is the care of refugees from Afghanistan, Syria, Iraq and Iran. We studied type 1 diabetes (T1D) outcome of these patients using real-life clinical care data from Germany/Austria.

Methods: 38104 T1D patients (<21y) from the multicenter diabetes patient follow-up registry, DPV, were studied. Patients born in Afghanistan, Syria, Iraq or Iran were classified as refugees. In refugees the first year of care was studied, for native patients (child and parent born in Germany/Austria) the most recent year. To compare groups, multivariable regression adjusted for age, sex, diabetes duration was used (SAS 9.4).

Results: 175 patients were born in Afghanistan, Syria, Iraq or Iran. They were younger (median [IQR]: 12.6 [9.4-15.3] vs 15.3 [11.7-

	Visit 1 Total N=45	Visit 2 Total N=45	Visit 3(in person visit) Total N = 45	Visit 4 Total N = 45
# Completed Visits	45(100%)	39(87%)	35(78%)	32(71%)
# T1D Device Downloads	38(84%)	29(75%)	32(91%)	23(72%)
# A1Cs Completed	41(91%)	36(92%)	35(100%)	26(81%)

17.5] y, p< 0.001), more often male (62.9 vs 53.2%, p< 0.001), but age at diabetes onset was comparable (8.5 [5.7-11.4] vs 8.6 [4.9-12.0] y) to native children. Table 1 summarizes medical care after demographic adjustment. BMI-SDS (KiGGS) did not differ between groups (0.21±0.07 vs 0.27±0.01).

[Medical care of refugees with T1D]

Conclusions: A relevant number of pediatric refugees from Syria, Iraq, Iran and Afghanistan have diabetes. Compared to native children, refugees are faced with several challenges in diabetes therapy and outcome: language barriers, different health beliefs or therapeutic concepts in the home country, or access barriers within the health care system might be contributing factors.

O44

Factors affecting health-related quality of life and adherence to diabetes care in paediatric patients with type 1 diabetes mellitus in Spain: results from the CHRYSTAL study

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Objectives: CHRYSTAL (Costs and Health Related qualitY of life Study for Type 1 diAbetes meLlitus paediatric patients in Spain) was an observational study conducted in 2014 in patients ages 1-17 years with type 1 diabetes mellitus (T1DM). The objective of this analysis was to evaluate the association between diabetes-specific health-related quality of life (HRQoL), adherence to diabetes care, demographics, and diabetes-related factors.

Methods: The study included 2 patient-reported outcomes (PROs): the Diabetes Module of the Pediatric Quality of Life Inventory (PedsQL) and the Self Care Inventory-Revised (SCI-R). The PedsQL measures HRQoL and is composed of 28 items, assessing diabetes symptoms, treatment barriers, treatment adherence, worry, and communication. The SCI-R measures adherence to diabetes care and is composed of 15 items, assessing diet, glucose monitoring, medication administration, exercise, low glucose level, and preventive/routine aspects of self-care. A stepwise regression procedure was used to evaluate the association between each PRO score and the main variables related to T1DM, including HbA1c levels, number of hypoglycaemic episodes, puberty status, and sociodemographic factors.

Results: A total of 275 patients participated in the study. The main factors significantly affecting PedsQL total scores were the number of severe hypoglycaemic events in the last 12 months (β= −3.997, p=0.046) and age of the child (β= 0.471, p=0.031). Age was also associated with the SCI-R total score (β= −1.174, p< 0.001).

Conclusions: For children and adolescents with T1DM in Spain, severe hypoglycemic events and lower age were significantly related to lower overall self-reported HRQoL. Higher age was associated with lower adherence to diabetes care. Health care providers should consider these interactions as part of their regular practice of managing diabetes in order to address specific patients' needs.

	T1D		
	native children	with Syrian, Iraqi, Iranian, or Afghan origin	p-value
N	37,929	175	-
HbA1c, %	8.16±0.01	9.21±0.12	<0.001
SMBG, per day	5.25±0.01	4.04±0.15	<0.001
insulin pump, %	39.9	6.6	<0.001
insulin dose, IU/kg/d	0.86±0.002	0.98±0.02	<0.001
hypoglycemic coma, per 100 pat.year	2.8±0.1	5.7±1.7	0.022

O45

Correlation between hypoglycemia, glycemic variability and C-peptide preservation after alefacept therapy in patients with type 1 diabetes: analysis of data from the ITN T1DAL trial

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Objective: In natural history studies, maintenance of higher levels of C-peptide (C-pep) secretion correlates with a lower incidence of major hypoglycemic events in patients with type 1 diabetes (T1D), but it is unclear whether this is true for drug-induced C-pep preservation.

Methods: We analyzed hypoglycemic events & glycemic control data from the T1DAL study (alefacept in new-onset T1D) which demonstrated significant C-pep preservation at 1 & 2 years. We performed a post hoc analysis using mixed models of the relationship between the meal-stimulated 4-hour C-pep area under the curve (4-hr AUC) & rates of major hypoglycemia, measures of glycemic control and variability, & an index of partial remission.

Results: Data from 49 participants (33 in the alefacept group, 16 in the placebo group) were analyzed at baseline & 12 & 24 months. The 4-hr AUC at baseline & at 1 year was a significant predictor of the number of hypoglycemic events during the ensuing 12-month interval (p=0.030). There was a strong relationship between the 4-hr AUC & glucometer SDs (p< 0.001), highest readings (p< 0.001), & lowest readings (p=0.03), all measures of glycemic variability. There was a strong inverse correlation between the 4-hr AUC & two measures of glycemic control: HbA1c & average glucometer readings (both p< 0.001); & between the 4-hr AUC & IDAA1C values (p< 0.001), as well as a strong correlation between IDAA1C values & glucometer SDs (p< 0.001), suggesting that reduced glycemic variability is associated with a trend toward partial remission.

Conclusions: Measures of glycemic variability & control, including rates of hypoglycemia, are significantly correlated with preservation of C-pep regardless of whether this is achieved by immune intervention with alefacept or natural variability in patients with new-onset T1D. Preservation of endogenous insulin production by an immunomodulatory drug may confer clinical benefits similar to those seen in patients with higher C-pep secretion.

O46

Change in prevalence of impaired awareness of hypoglycemia in a population-based clinic cohort of youth with type 1 diabetes

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Objectives: Impaired awareness of hypoglycemia (IAH) is a serious complication of insulin therapy associated with an increased risk for severe hypoglycemia (SH). IAH prevalence has been documented in youth with Type 1 diabetes (T1D) however improvement in management and reduced rates of SH raise the question as to whether there has been a change in the prevalence of IAH. The aim of this study was to determine the change in prevalence of IAH in a population-based cohort of adolescents with T1D on contemporary therapy.
Methods: Children > 12 years of age with T1D documented their responses to hypoglycemia based on the modified Clarke questionnaire. The prevalence of IAH was also analysed in a similar population-based cohort using the same questionnaire in 2002. The clinical details of the participants and the number of SH events in the year preceding the survey were determined from the Western Australian diabetes database.
Results: The modified Clarke questionnaire was administered to 413 children in 2002 and to 444 children in 2015 with similar baseline demographic characteristics. The prevalence of IAH was 33% in 2002 and 21% in 2015 ($z = 3.703$, $p < 0.001$). A lower HbA1c, younger age at diagnosis and longer duration of diabetes correlated with IAH in the 2002 cohort but not in the 2015 cohort. There was a significant decline in the rates of SH in 2015 compared to 2002 ($p < 0.001$) despite a reduced HbA1c in 2015. IAH increased the risk of SH 3 to 4 fold in both cohorts (IAH vs aware: 52 vs 16 events/100pt years in 2002 and 8 vs 2 events/100pt years in 2015).
Conclusions: The study demonstrated a reduction in IAH across a similar population using the same questionnaire in 2002 and 2015. The associated risk profile for IAH has also changed. Although IAH has reduced, IAH is still prevalent in a substantial minority of adolescents with T1D and is associated with an increased risk of SH. Identification of these individuals is an important component of T1D management.

O47

The SWEET Initiative: targeting harmonized diabetes care through high quality data registry from 48 centers worldwide

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Objective: SWEET ("Better control in Pediatric and Adolescent diabetes Working to CrEat CEnTers of Reference (CoR)") is a non-profit entity endorsed by ISPAD aiming to create an extensive network of certified CoRs for childhood diabetes in order to ensure high quality care.
Methods: Electronic documentation of at least 150 pediatric patients with diabetes annually, with subsequent upload of anonymized data to a common database is a main prerequisite. The SWEET dataset consists of 37 clearly definable items that reflect adherence to ISPAD's guidelines. Data can be uploaded either through the DPV software that is adapted for a multilingual group or in other electronic formats. The results of data analysis are conveyed to members through biannual benchmarking reports. In collaboration with NHS Diabetes, peer review visits to applying centers are organized so as to assess compliance with the SWEET quality criteria. Smaller or partly compliant as yet centers can participate as collaborative ones (CC).
Results: To date, 48 centers (CoRs & CCs) from 33 countries in 5 continents have contributed data for 28,667 patients. In 2015, 19.131 patients (51,6% males, median age 14,2 y, T1D: 96.0%, T2D: 1.1%, other forms: 2.9%) with 69,028 visits were recorded. Median HbA1c was 7.8% with 39.1%, 41.4%, and 19.4% of patients having HbA1c < 7.5%, 7.5-9% and >9%, respectively. One third of all centers achieve a median HbA1c < 7.5%. Regarding treatment modality, 41,2% of all patients were pump users. Severe hypoglycemia and DKA rates were low in all centers. Data completeness rates have significantly increased over time.
Conclusions: SWEET aims at an improved and more uniform care for people with diabetes through comparing processes and outcomes among participating members. Benchmarking has highlighted the importance of complete and accurate data to achieve meaningful interpretation. Annual meetings further enhance collaboration on scientific projects, exchange of experience and innovation.

O48

Characteristics of young adults with type 1 diabetes (T1D) who attain HbA1c target in the global TEENs study

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Objectives: Increasing evidence documents that many young adults with T1D are vulnerable to poor glycaemic control, mental health problems, loss to medical follow up and acute complications. Little is known about those young adults who reach an A1c of < 7% (ADA). We aimed to identify demographic, treatment and family/psychosocial factors among a subgroup of the 1648 participants, 18-25 y/o in the global TEENs study with A1c < 7%.
Methods: Data were collected from 219 centres, 20 countries. A1c was measured uniformly using A1cNow™ (Bayer). Demographic, family and treatment factors were collected by interview, survey, and record review. Participants completed 2 psychosocial measures—the PedsQL™ 3.0 Diabetes Module and the PAID (Problem Areas in Diabetes). The cohort was split into 3 A1c groupings: < 7% [<53mmol/mol] (N=299, 18.1%); 7-< 9 % [53-74 mmol/mol] (N=850, 51.6%); ≥ 9 %.[>75 mmol/mol] (N=499, 30.3%). 299 young adults with A1c< 7% were compared with the other 2 A1c groups. Significant (p< .001) predictive characteristics of the 299 young adults with A1c< 7% were identified using multivariate logistic regression adjusted for region.

Results: Young adults with A1c < 7% were more likely to have a university degree and to be working. Regarding treatment characteristics, they were more likely to use carbohydrate counting, exercise more days per week, check BG more frequently per day, use pump therapy, and miss fewer insulin doses per week. Young adults at target had less diabetes family conflict and reported lower diabetes emotional burden and higher diabetes-related quality of life.

Conclusions: In the TEENs sample, young adults at target A1c< 7% used contemporary diabetes management methods—approaches that can potentially be used by those above target. Associations between target A1c and lower family conflict, as well as better psychosocial functioning, are likely bi-directional relationships.

This study was supported by Sanofi.

Oral Session VII : DM2 & DM in Developing Countries

O49

Pharmacokinetic (PK) and pharmacodynamic (PD) profile of the SGLT2 inhibitor empagliflozin (Empa) in pediatric patients with type 2 diabetes (T2D)

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Objectives: The newest class of oral hypoglycemic agents, SGLT2 inhibitors, offers promise for treatment of pediatric patients with T2D. Prior to pivotal safety and efficacy trials, data on pediatric PK/PD are needed.

Methods: In a single dose study, 27 children and adolescents, aged 10-17 years, with T2D were randomly assigned to receive either 5 mg, 10 mg, or 25 mg of Empa. Eligibility criteria included HbA1c ≤10.5% (91 mmol/mol), treatment with diet and exercise and/or stable dose of metformin and/or stable basal or MDI insulin. Primary endpoints included PK data (area under the curve [AUC], maximum plasma concentration [C_{max}], time to C_{max} [t_{max}], and half-life [$t_{1/2}$]). Secondary PD endpoints included changes in urinary glucose excretion [UGE] and fasting plasma glucose [FPG] at 24 h postdose.

Results: Of the 39 patients screened for participation, 27 (67% female, 44% White) were randomized and completed the study; mean (± SD) age was 14.1±2.0 years, body weight 96.7±23.5 kg, BMI 35.5±6.7 kg/m^2, z-BMI 3.0±0.8, eGFR 165.8±25.8 ml/min/1.73m^2, HbA1c 7.0±1.2%, UGE 8.8±22.1 grams/24 h, and FPG 139±56 mg/dL. For PK results, t_{max} occurred within 1-2 hours and $t_{1/2}$ was on average 7-8 hours; C_{max} and AUC increased with higher doses. For PD results, baseline and FPG adjusted mean increase in UGE was 53, 73, and 87 grams/24 h and baseline adjusted mean decrease in FPG was 15.5, 16.6, and 20.4 mg/dL for the 5, 10, and 25 mg doses, respectively. There were no severe adverse events and 1 - investigator-reported drug-related event (dehydration).

Conclusions: Exposure (AUC and C_{max}) and $t_{1/2}$ were comparable in pediatric and adult patients with T2D. There were dose-dependent increases in UGE and comparable decreases in FPG. A single dose of Empa in pediatric patients with T2D was well tolerated, with PK/PD and safety results similar to adult studies.

O50

A phase IIb, randomised, double-blind, placebo-controlled study of the DPP-4 inhibitor linagliptin (Lina) in pediatric patients with type 2 diabetes (T2D)

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	Lina 1 mg/day	Lina 5 mg/day	Placebo
N	10	14	15
Age (years)	14.0 ± 1.8	14.3 ± 2.1	13.7 ± 2.0
Weight (kg)	75.3 ± 19.3	84.8 ± 25.1	78.2 ± 21.8
BMI (kg/m^2)	28.0 ± 5.2	33.0 ± 8.0	29.2 ± 6.0
HbA1c (%)	8.22 ± 0.93	7.87 ± 0.98	7.60 ± 0.92
FPG* (mg/dL)	160.5 ± 53.6	150.8 ± 48.0	149.0 ± 39.6

*Fasting Plasma Glucose

Objectives: To study efficacy, safety, pharmacokinetics (PK) and pharmacodynamics (PD) of Lina in youth with T2D.

Study design: Double-blind, randomised controlled parallel group study comparing Lina 1 and 5 mg with placebo in patients with T2D aged 10-17 years. Primary efficacy endpoint was change from baseline in HbA1c after 12 weeks of treatment and key PD endpoint was DPP-4 inhibition at trough at steady-state.

Results: Baseline characteristics by treatment group are shown in Table. Compared to placebo, there was a dose-dependent reduction in mean HbA1c levels of 0.48% and 0.63% with Lina 1 mg and 5 mg, respectively, associated with corresponding falls in mean FPG of 5.6 mg/dL and 34.2 mg/dL. The% of median DPP-4 inhibition was 38% with Lina 1 mg and 79% with Lina 5 mg. Geometric mean trough levels of Lina were 3.80 nmol/L and 7.42 nmol/L in the 1 mg and 5 mg groups. These values were slightly higher than in adult patients and further PK analysis suggests that the higher exposure is mainly caused by higher plasma DPP-4 concentrations in the study population. There were no drug-related adverse events during treatment with either dose of Lina.

Conclusions: Lina was well tolerated and induced dose-dependent DPP-4 inhibitions that were accompanied by corresponding reductions in HbA1c and FPG in youth with T2D. The results are consistent with the clinical efficacy and safety profile that has been reported for Lina in adult patients with T2D, favoring Lina 5 mg over 1 mg.

[Baseline characteristics (mean ± SD)]

O51

Transfer from pediatric to adult care for U.S. youth with type 2 diabetes: the SEARCH for diabetes in youth study

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Objective: To describe factors associated with transfer from pediatric to adult care and poor glycemic control after transfer among youth with type 2 diabetes (T2D).

Methods: Youth with T2D were included if they had a baseline SEARCH visit in pediatric care at < 18 years and ≥1 SEARCH follow-up visit at 18-25 years. At each visit, HbA1c and BMI were measured; sociodemographic and provider data (pediatric/adult/no care) were self-reported. Predictors of transferring from pediatric care and association between transfer and poor glycemic control

(HbA1c ≥9%) at follow up were explored with multiple logistic regression.

Results: 145 T2D youth (38.6% male, 75.2% minority, 88.6% obese) were included. Most (n=115, 79%) reported transfer to adult care; a substantial proportion (n=26, 22.6%) reported no care at follow up. There were no major differences between those who reported transfer to adult care vs. no care at follow up, with the exception of insurance status (15.7 vs. 72.7% uninsured, p< 0.001). Increasing age

[OR=1.3 per yr, p=0.02] and baseline HbA1c [OR=1.5 per 1%, p =0.01] were each associated with increased odds of leaving pediatric care at follow up, independent of sex, transfer age, and race/ethnicity. Conversely, leaving pediatric care was associated with a 6.8 higher odds (p=0.001) of poor glycemic control at follow up, independent of baseline HbA1c, sex, transfer age, race/ethnicity, and whether participants reported transfer to adult care vs. no care at follow up.

Conclusions: Most youth with T2D transfer from pediatric to adult care between 18-25 years; however some report no care at this point. Worsening glycemic control in childhood is associated with increased likelihood of leaving pediatric care, and leaving pediatric care is associated with poor glycemic control in young adulthood regardless of baseline control. Our findings highlight a need for better preparation and support surrounding transition from pediatric to adult care for youth with T2D.

O52

"Flatbush diabetes": ketosis prone type 2 diabetes presenting with hyperglycaemic hyperosmolar state, ketoacidosis and severe hypernatraemia

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Introduction: Type 2 diabetes (T2D) affects 1.5% of UK children with diabetes. The case of a child presenting with severe diabetic ketoacidosis (DKA) and hyperglycaemic hyperosmolar state (HHS) at first presentation of T2D is described.

Case description: A 12-year-old Afro-Caribbean boy presented with collapse, preceded by polyuria, polydipsia, enuresis and aggression. He had been drinking>3L of sports drinks daily but had vomited for 24h.

Examination signs: Kussmaul breathing; tachycardia; 4 sec capillary refill; GCS 11. He was obese with acanthosis nigricans.

Investigations showed severe hyperglycaemia and hypernatraemia (glucose 95 mmol/L, ketones 6.4 mmol/L, HbA1c 122 mmol/mol, corrected sodium 179 mmol/L). Blood gas confirmed severe DKA.

Management: Fluid resuscitation was commenced, followed by 8% rehydration volume over 48h with 0.05 units/kg/h IV insulin. Ketonaemia resolved in 24h and the patient was in an 8L positive fluid balance after 48h of rehydration.

Following this, isotonic fluid (0.9% NaCl) was gradually reduced to 0.45% NaCl when serum sodium failed to fall. When possible, sodium-free oral fluids were introduced to titrate with IV fluids. Sodium and fluid balance reviewed 4 hourly prevented rapid sodium fall.

CT head at presentation showed no cerebral oedema. Agitation and confusion improved only with correction of hypernatraemia at day 8.

Progress: Due to signs of insulin resistance and known paternal T2D, metformin was commenced in parallel with subcutaneous insulin. Anti-IA2 and anti-GAD antibodies were negative. Insulin was stopped at week 10, when HbA1c was 45 mmol/mol.

Discussion: Children with T2D can present with both DKA and HHS, posing additional management challenges.

Flatbush diabetes (ketosis-prone T2D) classically affects patients of African ethnicity

Glucose-rich sports drinks contribute to extreme hyperglycaemia and hypernatraemia, and may precipitate HHS.

Hypernatraemia must be gradually corrected to prevent cerebral oedema.

O53

Comparison of treatment regimes in children with type 2 diabetes and its effect on glycaemic control

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Objective: To compare change in HbA1c at 1-year among different treatment groups of patients with T2D who were initiated on insulin-only, oral-only or combined insulin & oral therapy.

Methods: Retrospective review of data from diabetes registry of patients diagnosed with T2D. Treatment is categorized into single versus combination therapy, while single therapy group includes oral-only or insulin-only.The change in HbA1c within treatment groups was analysed using SPSS version 19.0 & values reported as mean±SD.

Results: Out of 70 patients,18 were started on insulin-only, 30 on oral-only & 22 on combination therapy. Mean HbA1c at diagnosis was significantly lower in patients on single therapy than those on combination therapy [9.47±3.18 vs.12.4±1.42%; p< 0.001], while mean HbA1c was lower in oral-only than insulin only [7.91±2.06 vs. 12.2±2.95%; p< 0.001].Patients on combination therapy are younger than those on single therapy (p=0.021). Mean weight at diagnosis was significantly higher in those on oral-only vs. insulin only [75.5±21.1 vs. 55.8±18.0 Kg ; p=0.004].There was no correlation between race, gender or C-peptide level and choice of therapy. Reduction in HbA1c at 1-year was seen across all treatment groups (Graph 1), but was more in combination than single therapy and more in insulin-only than oral-only group.

[Graph 1:Compariosn of mean change in HbA1c]

Conclusion: All types of treatment regimens help to achieve glycaemic control in T2D but combination & insulin-only therapy is more effective than oral-only.

O54

A new approach to compare between different screening tests for type 2 diabetes and prediabetes in overweight and obese children

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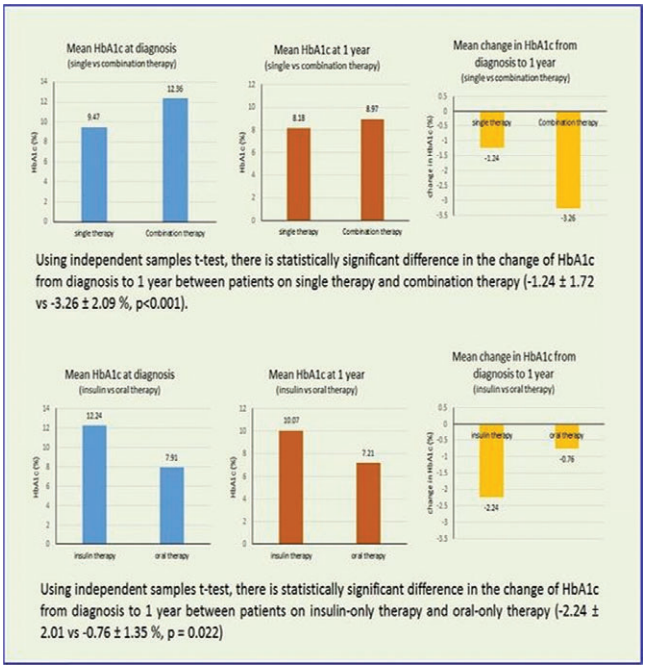
Objectives: In children, studies appear to show that A1C has lower sensitivity when compared to fasting plasma glucose (FPG) or oral glucose tolerance test (OGTT) as "gold standard". However, FPG and OGTT have themselves never been validated in children. The analysis in these studies is confounded, as the tests under study are themselves being used as the 'gold standard'. When defining one test arbitrarily as the gold standard, any other test, by definition, will not measure up.

We compared the three tests not to a 'gold standard', but to a final diagnosis reached through combining the results of more than one test.

Methods: Fifty four children aged 5-15 years with BMI ≥85th percentile were recruited into the study. For all participants, FPG, 2h-PG on the 75-g oral glucose tolerance test (OGTT) and A1C were performed.



If two different tests are both above the diagnostic threshold, this confirms the diagnosis. On the other hand, if a patient has discordant results on two different tests, then the test result that is above the diagnostic cut point should be repeated. The diagnosis is made on the basis of the confirmed test.

Sensitivity and specificity were calculated for the 3 tests. The k coefficient was calculated as a measure of agreement.

Results: One male obese child had T2DM, 36 showed normal glucose tolerance, while 17 children had pre-diabetes.

A1C was the most sensitive test (86.67%) followed by FPG (62.5%). Both FPG and 2h-PG had equal specificities (97.3%) while A1C had a lower specificity of 84.21%.

Fair agreement existed between FPG and both 2h-PG (**k**=0.215; 95% CI −0.086 to 0.516) and A1C (**k**=0.330; 95% CI 0.069 to 0.591) diagnoses. While, there was poor agreement between A1C and 2h-PG diagnoses (**k**=0.179; 95% CI −0.052 to 0.410).

Conclusions: A1C could be a valid screening test for prediabetes in overweight and obese children and further studies are needed.

O55
Association between waist circumference and magnesium, phosphorus and uric acid in indigenous Argentinean children

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Background: Studies in adults show that central obesity increases the likelihood of Type 2 diabetes (T2DM).

Objective: To determine the association between waist circumference (WC) and non-traditional risk factors such as magnesium, phosphorus, and uric acid in indigenous children living at high altitudes.

Methods: A total of 354 (166 M) indigenous school children, aged 9.6 ± 2.3 years, were enrolled in a cross-sectional study in November 2011. Central obesity was defined as WC ≥ 90th percentile according to age and sex. Low magnesium (Mg) and phosphorus (P) levels were defined as serum Mg < 1.8 mg/dL and P < 2.4 mg/dL. Hyperuricemia was defined as serum uric acid > 7 mg/dL.

Results: The prevalence of central obesity was 6.8% (24/354). None of the children had hyperuricemia or low P levels. HypoMg was identified in 21.7% (57/263). There was a significant association between WC (z-score) and Mg (r-015), uric acid (r0.28), P(r-0.30), HOMA-IR (r0.49), Triglycerides (r0.24), and HDL-C (r0.24). However, calcium, sodium, and potassium were not significantly associated with WC. As z-WC quartiles increased Mg and P levels significantly decreased, whereas uric acid levels increased. Multiple linear regression analysis showed that z-WC was associated significantly and directly with uric acid (B0.31), triglycerides (B0.004), and HOMA-IR (B0.35); and inversely with Mg (B-0.83) and phosphorus (B-0.25), adjusted for confounding variables (R2 0.34).

Conclusion: Our results indicate that central obesity was significantly and inversely associated with Mg and P and directly with uric acid in indigenous school children. This underlines the importance of early WC screening of children and early intervention. The interventional methods include healthy lifestyle education and supplementation of micronutrients. Therefore, supplementation with Mg and/or P could decrease the likelihood of central obesity and future T2DM in this community.

O56
Activity of the antioxidant enzyme paraoxonase in indigenous versus urban Argentinean children

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Background: We have previously found that indigenous children from San Antonio de los Cobres (SAC) had lower HDL levels than Buenos Aires (BA) urban children. Among the different antiatherogenic functions exerted by HDL, its antioxidant capacity is mainly attributed to the enzyme paraoxonase 1 (PON1), which is synthesized by the liver and circulates in plasma bound to HDL. Serum PON1 activity was found to be reduced in a number of pathological conditions including cardiovascular disease and type 2 diabetes.

Objective: To compare PON1 activity in indigenous SAC versus urban BA children.

Methods: A cross-sectional study compared 150 (67 males) SAC versus 93 (47 males) urban BA children (6-16 years) between October and November 2015. Anthropometric data, lipid levels, and PON1 activity were measured in both groups.

Results: The prevalence of overweight/obesity was significantly lower in SAC (26/150; 17.3%) than in BA (30/93; 32.6%). However, the prevalence of low HDL was significantly higher in SAC (14/150; 9.5%) than in BA (4/93; 4.3%); and the prevalence of high triglycerides was significantly higher in SAC (28/150; 18.7%) than in BA (4/93; 4.4%). Comparisons of BMI percentile (59 vs 66); triglycerides (120 *vs.* 78 mg/dL), HDL-C (45 *vs.* 51 mg/dL) and Apo B (83 *vs.* 70 mg/dL) levels, as well as PON-1 activity

(170 vs 203 IU/L) showed significant differences in mean levels in SAC compared with BA. In separate linear regression models, adjusted for sex, age, and BMI, SAC children had 44 mg/dL higher triglyceride

(p< 0.001), 6.6 mg/dL lower HDL (p< 0.001) and 14 mg/dL higher Apo B (p< 0.001) levels, and 45 IU/L lower PON1 activity (p< 0.001) compared with BA children.

Conclusion: This study shows that SAC children had an unfavourable lipid profile and lower PON1 activity compared with BA children. These findings suggest that this community may be at higher risk for earlier cardiovascular disease and type 2 diabetes.

Oral Session VIII - Nutrition and DM in Developing Countries

O57
Is the glycaemic response from fat in meals dose dependent in chidren with T1DM? Interim analysis of 11 patients

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Background: Management of people with T1DM on intensive insulin therapy (IIT) uses algorithms based on the meal carbohydrate (CHO) content (MCC) to calculate prandial insulin dose. Typically, these calculations do not consider the meal content of fat or protein.
Objective: To determine if the postprandial blood glucose (BG) response to varying fat content is dose dependent when standard insulin bolus is given based on MCC.
Methods: Randomised repeat testing of 11 patients with T1DM >1 year duration, aged 8-18 years on ITT. A test meal was given on 6 consecutive nights in random order without insulin 4 hours after the regular evening meal; 5 test meals varying in fat content (3, 13, 25, 38, 50g), but without CHO/protein, and one 20g CHO meal with no fat/protein. A continuous glucose monitoring system was used to assess BG levels (BGL) at 10 minute intervals for 8 hours afterwards. The relationship between the fat loads in the meals and the mean change in postprandial BGL were analysed.
Results: The graph illustrates the change in BGL from baseline (Y axis) versus time in minutes (X axis), following test meal consumption (each meal = different colour).

[Mean post prandial BGL excursion over time]

Conclusions: In 11 patients studied to date, there was no significant dose response to fat consumed without CHO in either the early or late postprandial period indicating that fat does not cause the immediate increase in BGL seen with CHO. More data are needed from this ongoing study to accurately determine the full impact.

O58
Impact of advanced carbohydrate counting method on oxidative stress and metabolic control in children and adolescents with type 1 diabetes (DM1) on multiple daily injection (MDI) therapy

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Objectives: Advanced (third level) carbohydrate counting (CC) is a key strategy in diabetes care, especially for people on intensive insulin regimens. With advanced CC, DM1 patients learn how to use insulin-to-carbohydrate ratios, thus acquiring dietary flexibility and a better quality of life. The aim of this study was to assess the effects of the advanced CC method on metabolic control and oxidative stress in children and adolescents with DM1.
Methods: Thirty-five DMI subjects (2 to 23 years old), who followed a basic CC method for their dietary planning, received individualized nutritional consultation sessions on advanced CC. Anthropometric measurements, HbA1c, lipidemic profile, antioxidant defense mechanisms using the FRAP assay and malondialdehyde (MDA) as an index of lipid peroxidation estimated by the TBARS method, were evaluated at baseline and one year after the nutritional counseling.
Results: At the beginning of the study, all participants were on a basal-bolus insulin regimen using MDI and had never received advanced CC guidance. At baseline, their body fat mass, estimated by BIA, was significantly correlated with HbA1c (r=0.486, p=0.01) and with the levels of MDA (r=0.432, p=0.05). One year after advanced CC counseling, HbA1c decreased significantly by 0.5918±0.83% (p≤0.001) and HDL increased by 3.58±8.5 mg/dl, (p=0.04). Also, MDA decreased significantly from 4.27±2.58 to 2.55±2 μM, (p=0.02) and FRAP increased, but without statistical significance, from 0.14±0.05 to 0.35±0.27 M, (p=0.072).
Conclusions: Advanced carbohydrate counting in children and adolescents with type 1 diabetes is a method that may help in the attainment of greater glycemic and metabolic control, as measured by HbA1c, increased HDL and significantly decreased oxidative stress, and may play a role in decreasing the risk of diabetic complications.

O59
Greater postprandial glucose excursions and inadequate nutrient intake in youth with type 1 diabetes and coeliac disease

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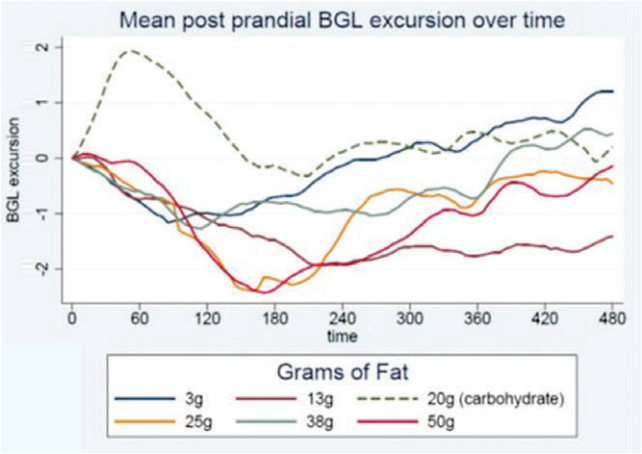
Objective: To compare daily glycemic profiles and nutrient intake in youth with type 1 diabetes (T1D) and coeliac disease (CD) vs T1D only.
Methods: Case control study of 10 youth with T1D+CD and 7 with T1D, who wore blinded continuous glucose monitoring systems (CGMS) for 6 days, with 5-minutely BGLs downloaded at study end. Main meal BGLs (pre-meal, peak, 2-hr post meal) and time to reach peak BGLs were compared between T1D and T1D+CD using Mann-Whitney U tests. Participants consumed a gluten free cereal and milk test meal for 3 days and kept weighed food diaries, which were analyzed for nutrient intake and compared to national dietary recommendations.
Results: Overall, 222 main meals were identified from CGMS traces (median 16, range 8-18 meals per patient). Youth with T1D+CD vs T1D only had shorter time to peak BGL (77 vs 89 mins, p=0.03), higher peak (9.3 vs 7.3mmol/L,-p=0.001) and higher 2-hr post prandial BGL (8.4 vs 7.0 mmol/L, p=0.01), despite similar pre-meal BGLs (9.2 vs 8.6 mmol/L, p=0.28), insulin to carbohydrate ratios (11.1 vs 10.4, p=0.84) and insulin sensitivity factors (3.3 vs 2.7, p=0.54) and



HbA1c (7.5% vs 8.0% / 58 vs 64 mmol/mol, p=0.34). For the test breakfast, the difference between post-meal BGL and peak BGL post-meal was significantly correlated with longer CD duration (R = 0.53, p=0.01). Caloric and macronutrient intake did not differ between T1D+CD vs T1D, however, collectively the majority had inadequate dietary calcium (76%), folate (71%) and fiber (53%) intake, with excessive saturated fat (12% total energy intake) and sodium (>2,000mg/day) intake.

Conclusion: A gluten free diet is associated with greater glycemic excursions in youth with T1D+CD. Youth with T1D did not meet ISPAD guidelines for saturated fat, fiber and sodium dietary intake. Clinical management should address both glycemic variability and dietary quality to increase calcium and fiber, and reduce saturated fat and sodium intake.

O60

Carbohydrate counting from onset of diabetes reduced insulin requirements but increased weight in children and adolescents

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Objective: The aim was to evaluate if carbohydrate (CHO) counting improved glycemic control and anthropometrics compared to conventional treatment, one and two years after onset of diabetes in children and adolescents. A secondary aim was to explore patients and caregivers perception of insulin dosage to meals with focus on efficacy, time consumption and adherence.

Methods: 371 subjects were included and divided into two groups, based on whether onset of diabetes occurred before or after the introduction of CHO counting as standard treatment method in our clinic. Data was collected retrospectively from the Swedish pediatric quality registry (Swediabkids). HbA1c, body mass index standard deviation score (BMI-sds) and total daily insulin were calculated at three months, one and two years. Occurrence of severe hypoglycemia was also measured. A web-based questionnaire provided information on perception of carbohydrate counting, answered by 78 subjects.

Results: CHO counting reduced insulin requirements (p< 0.001) and eliminated differences in insulin requirements between pump- and pen users as well as between boys and girls. Glycemic control was not improved by CHO counting one and two years after diabetes onset (p=0.233, p=0.295). An adverse effect was increased body mass index standard deviation score (BMI-sds) (p=0.044), especially amongst girls (p=0.038). Patients found CHO counting effective and time efficient. Learning CHO counting from onset increased adherence.

Conclusion: CHO counting lowers insulin requirements with maintained glycemic control. Contradictory, greater weight gain was found in the carbohydrate counting group, especially among girls. A plausible explanation is that CHO have taken focus off protein- and fat intake in combination with a more liberal approach to energy dense foods, causing excess energy intake. The strength of CHO counting does not lie in its ability to lower HbA1c-values but as a helpful tool, which patients are happy to use.

O61

Costs to governments of type 1 diabetes care in youth in less-resourced countries - three scenarios for different income levels

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Objectives: Evidenced-based tools are needed to help persuade governments in less-resourced countries to provide adequate youth diabetes health care. We developed 3 scenarios for differing country income levels, calculating the annual cost of care/child needed to achieve a healthy life year, and comparing that to Gross Domestic Product (GDP)/capita as per WHO's CHOICE approach.

Methods: Scenario (S)1: low-income Least Developed Country (LDC), e.g. Mali. Child/adolescent supplied with human insulin and syringes. Self-monitoring blood glucose (SMBG) frequency: 2/day.

S2: low-income non-LDC country, e.g. Tanzania. Child/adolescent supplied with human insulin and syringes. SMBG frequency: 3/day.

S3: upper-middle income country, e.g. Azerbaijan. Child/adolescent supplied with analog insulin and pens. SMBG frequency: 4/day.

Costs of insulin, syringes/pens, SMBG, ketone strips, HbA1c, complications screening, outpatient and inpatient care were determined from publications, known international costs, and local investigations. A healthy life year was assumed for 10+ years with this care. The cost was compared to GDP/capita.

Results: Projected estimated annual costs were S1: (US)$761, S2: $1,067, S3: $1,980. Annual costs in Mali were $740 (105% GDP/capita), Tanzania $889 (93%), Azerbaijan $1,980 (26%). Expressed as a % total cost, supplies were 48%, 48%, 60% in S1, S2, S3 respectively; laboratory/complications 10%, 7%, 4%; and health service delivery 42%, 45%, 36%.

Conclusions: This is a straightforward approach to determining costs of youth diabetes care that will be useful for advocacy to governments. Next, the research team will quantify the healthy life years gained for these 3 scenarios, and conduct a cost-effectiveness analysis in line with WHO CHOICE, where the indicative level for a very cost-effective intervention resulting in a healthy life year is < 100% GDP/capita.

Standard youth diabetes care can be provided at a relatively low cost, even in low-income countries.

O62

Type 1 diabetes care and outcomes in rural low income settings in India using family support strategies

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Objective: Patient outcomes are hard to achieve in rural settings because of lack of education in the family, lack of financial resources and unavailability of specialized care. This a study of 100 children supported by Udaan, an NGO based in Aurangabad, India to identify low-cost strategies that can improve patient outcomes within these constraints, bringing them at par with those observed in developed countries.

Methods: 100 Udaan supported children with Type 1 diabetes were studied. 30 children were below 10, 34 were between 10-14, and 36 were between 15-20 years of age. Average income of a family was about 100 USD / month. Families were provided conventional insulin, Glucometer and 50 strips a month to minimize the cost of care. The average education level of mothers was below 9th grade with 15% being illiterate. In place of traditional written material, weekly interactive learning programs were provided to parents and/or children. Each family attended an average of 15 sessions a year. To address the lack of access to specialized care (there is no pediatric endocrinologist in the region and the nearest doctor is about 50 km away), Udaan ran 24 hour helplines for diabetes support, which each family used approximately 22 times a year.

Results: Average HbA1c level for the 100 children was 8.37%, at par with values observed in developed countries. Of the 100, 9 children

achieved scores below 7%, 24 between 7-8%, 38 between 8-9% and 29 children had HbA1c levels between 9-10%.
Conclusion: 100 children with Type 1 diabetes from rural, low income, low literacy families with no access to specialized care were able to achieve average HbA1c levels of 8.37%, at par with those observed in less resourced-constrained settings. They achieved this cost-effectively, using conventional insulin and less than 50 glucometer strips a month, overcoming access and literacy constraints through 24 hour helplines and localized education support provided by Udaan, an NGO for children with diabetes.

O63
Diabetes support groups in Ghana, 3 years of diabetes youth care

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Introduction: The prevalence of diabetes in adults in Ghana is estimated to be 3.35%. The prevalence of diabetes mellitus in Ghana among the young is not known. Management of diabetes is multidisciplinary and also involves a lot of support for the young person and the family as a whole.

Started in 2012, Diabetes Youth Care has the main aim of filling the unmet social support of these young ones and their families.
Problem statement: There are few support groups for and young people living with diabetes in Ghana.
Aim: To assess impact of support network Diabetes Youth Care on young ones living with diabetes in Ghana.
Objective: To determine the influence of monthly support group meetings.
Method: Assessment of the support network was done by analyzing the attendance and behavior at the monthly, support group meetings and the number of admissions due to acute complications.
Results: The support network initially began with 5 young ones under the age of 30 and has grown to over 100 across the country. The young ones have been empowered with the knowledge about managing diabetes and are able to identify acute complications, manage them to prevent death.

Most of the young ones living with diabetes were in a better position to tell their friends and family about diabetes and also educate them about immediate measures to take when they develop acute complications.

A website created by the support network encourages the young ones living with diabetes to share their real life stories to encourage each other, educate and create awareness about diabetes in young people. This has led to some of them becoming peer educators and mentors to the younger ones with diabetes.
Conclusion: Support network groups are vital in the management of diabetes in young people as they serve as a point of information and education about diabetes. Diabetes Youth Care has been a positive impact in the life of these young ones living with diabetes and that of their families.

O64
Follow-up of successful community mobilisation with women's groups to assess impact on growth of children aged two to four years in Bangladesh

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Objectives: Community Mobilisation (CM) with women´s groups (WG) practising participatory learning and action are a cost-effective strategy to improve neonatal survival in low-resource settings, with a reduction In neonatal mortality in Bangladesh by 38%. The long term effect, if any, has yet to be established. We studied differences in anthropometric outcomes at ages two to four years of children to examine the impact.
Methods: In a cross-sectional survey, anthropometric measures (height, weight, and abdominal, head, chest, mid upper arm circumferences, triceps and sub-scapular skinfold thickness) in children born to women who had been directly exposed to CM were compared at ages 2-4 years with a random sample of age-matched children, whose mothers were not exposed to the intervention.. Maternal weight and height and BMI were recorded. Data were analysed as z-scores and results stratified by maternal BMI.
Results: 2587 children. were inducted. Children whose mothers were underweight at the time of the survey, and were exposed to WGs interventions had significantly larger z-scores for HC (z-score increase of 0.22 (95% CI 0.08, 0.36), p=0.002), AC (0.23 (0.05, 0.42), p=0.013) and MUAC (0.13 (0.00, 0.25), p=0.045) than children whose mothers were not exposed to the intervention. Children with overweight mothers, exposed to the interventions,had significantly smaller weight-for-age (−0.23 (−0.43, −0.04), p=0.018) and weight-for-length (−0.17 (−0.33, −0.00), p=0.047) z-scores compared to control children. Results for weight-for-length z-scores also showed a significant differential effect depending on the child's gender.
Conclusion: Beneficial growth effects on the offspring of the most under-nourished mothers in particular, could have a lasting effect on diabetes and lifelong cardio-metabolic susceptibility. These findings offer a potential public health approach to reducing cardiometabolic risk through a population-level intervention in early developmental life.