

Managing type 2 diabetes in young people

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Drugs for type 2 diabetes in youth

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Welcome

As members will know, an ever-increasing number of young people are being diagnosed with type 2 diabetes mellitus. This disease is more aggressive in children than in adults, and presents specific issues regarding screening, management and co-morbidities. It provides the topical theme of this issue of *ESPE News*.

On **page 7**, William Tamborlane explains how the formation of the Pediatric Diabetes Consortium in the USA came about initially to provide a type 2 diabetes registry, and how it has subsequently begun to address the limiting lack of medical treatment options that have been approved for use in youth.

The Australasian Paediatric Endocrine Group has recently developed guidelines on screening, assessment and management of type 2 diabetes mellitus in young people (**page 8**). Alexia Peña Vargas outlines their importance in supporting patients, particularly those in high risk ethnic groups, including the indigenous Australasian population.

Type 2 diabetes mellitus has complex and devastating co-morbidities, as Orit Pinhas Hamiel describes, as she details research that has taken place into the various complications across a wide range of studies (**page 9**).

We also highlight some articles on type 2 diabetes mellitus from the recently published *Yearbook of Paediatric Endocrinology* (**page 10**). We hope that all these articles bring you up to date with the latest developments in this area.

Of course, since the last issue of *ESPE News*, we have had the privilege of meeting virtually to exchange knowledge and expand our understanding at ESPE 2021 Online, which was incredibly valuable at a time when travel is still restricted. It provided an excellent programme of talks and posters (**page 11**). The Annual Meeting saw the presentation of the ESPE Awards for 2021 as well as those for 2020. You can read about the 2021 award recipients on **pages 4 and 5**. (The 2020 recipients were featured in issue 50.) We congratulate them all!

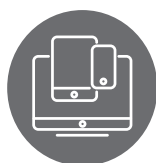
The rest of this issue is packed with news, including details of the new ESPE Taskforce to support early career paediatric endocrinologists (see **page 3**). You can also enjoy hot topics, as well as the latest event and deadline information, as we move, hopefully and gradually, back towards normality.

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AWARDS

2022 ESPE Awards

We welcome your nominations for the 2022 ESPE Awards. These celebrate and recognise the achievements of ESPE members at all stages of their research and clinical careers, wherever they are in the world.



Nominate your colleagues by **10 December 2021**



www.eurospe.org/grants-awards/awards

YOUR SOCIETY

ESPE Annual Review 2020

The ESPE Annual Review for 2020 is now available online, providing an easily digestible round-up and celebration of everything ESPE achieved and was involved in last year. Take a look and you will see how much happened, despite the pandemic.



Find the ESPE Annual Review at www.eurospe.org/about/annual-review



ESPE roles renamed from 2022

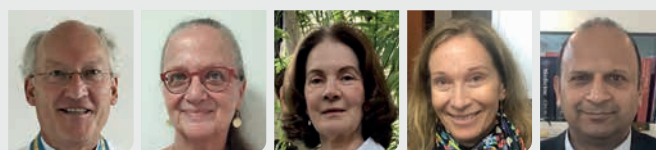
Historically, ESPE has used the term Secretary General where other societies use President. At the recent Annual Business Meeting, it was agreed to bring our terminology in line with the wider community. Thus, after the ESPE Annual Meeting in September 2022, the role of Secretary General will be known as President, while the current role of President will become Annual Meeting Host (with a Deputy Annual Meeting Host). You will begin to see these changes reflected in our communications.

ESPE Clinical Fellowship Spring Initiative on video

This event in April 2021 celebrated 30 years of the ESPE Clinical Fellowship programme. It featured a diverse educational programme, with 3.5 hours of content, which is now freely available online as a bookmarked video for all to view. The event included a wide range of high quality presentations, including cases and research from ESPE Clinical Fellows.



You can watch the event at <https://vimeo.com/536237907/75d19e455f>



See our 2021 award winners on pages 4-5

ADVOCACY

European Health Data Space

The European Commission's plan to create a European Data Space includes the health sector. Its aim is to improve access to health data, to support healthcare delivery, research and policy-making.

ESPE, along with the European Society of Endocrinology, the European Reference Network on Rare Endocrine Conditions (Endo-ERN) and the European Registries for Rare Endocrine Conditions (EuRECa), issued a joint statement welcoming the initiative, but also urging the EU institutions to consider the following points:

- the importance of involving national bodies in the development of EU standards and technical requirements
- the need to maintain patient access and control over personal health data
- the promotion of involvement in research as an incentive to stimulate sharing of health data
- the value of sharing medical data beyond the EU, especially for rare diseases where data are limited.



Read the statement at www.eurospe.org/news/article/16306/european-health-data-space-consultation

CAREERS

New ECPE Taskforce

ESPE's mission is to advance excellence in paediatric endocrinology to benefit children worldwide. That is why ESPE needs to nurture its members in their early careers, so that future opinion leaders are appropriately represented and engaged within the Society.

For this reason, the ESPE Council agreed to create an Early Career Paediatric Endocrinologist (ECPE) Taskforce. The project is led by Rasha Hamza (Egypt), as Chair of the ESPE Education and Training Committee. The Taskforce is chaired by Rade Vukovic (Serbia), and has five enthusiastic and accomplished members from different parts of the world.



Rasha Hamza



Rade Vukovic

The ECPE Taskforce seeks to define how ESPE can best support young paediatric endocrinologists, research their needs, and maximise their engagement, integration and visibility within the Society. It is the first step towards developing a future, wider ECPE group, providing early career members with more chances to actively contribute to ESPE.

Our predecessors in paediatric endocrinology paved the way for our successes, and we aim to do the same for those who follow.

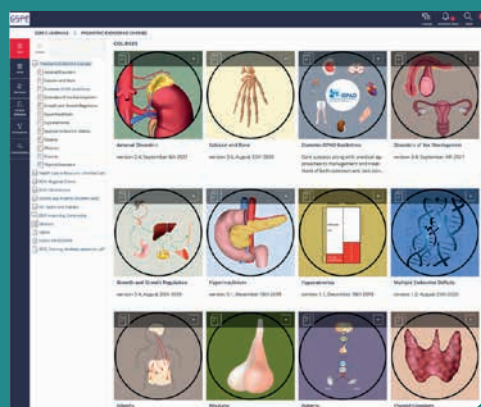
RESOURCES

ESPE e-Learning



New website design

Visit www.espe-elearning.org to see our updated and redesigned site!



Paper on e-Learning

You can find out more about the value of e-Learning in this recent publication:

Transforming education through a global e-learning model for pediatric diabetes and endocrinology Ng *et al.* 2021 *Hormone Research in Paediatrics* doi: 10.1159/000517165.



Access it free of charge at www.karger.com/Article/FullText/517165

Supporting this issue's theme

The category **Diabetes ISPAD Guidelines** under **General Content** offers three chapters accompanied by three cases:

- Type 2 diabetes in youth: Cathy, an 11-year-old girl
- The diagnosis and management of monogenic diabetes in children and adolescents: ensuring a correct diabetes diagnosis
- Management of cystic fibrosis-related diabetes in children and adolescents: Jane and Caleb.



See www.espe-elearning.org
Registration is free of charge

EVENTS

ESPE C&CA School Webinars

All applicants to the ESPE Caucasus & Central Asia School 2021 enjoyed two introductory webinars in October, as a 'starter' course for the physical event.



You can find a report on the webinars at www.eurospe.org/media/2668/espe-candca-webinars-2021-report.pdf

ESPE Award Winners 2021

We congratulate our 2021 ESPE Award winners for their dedication and achievement in the field.



You can find a link to a presentation about our winners at
www.eurospe.org/grants-awards/espe-2021-award-winners

ESPE Andrea Prader Prize



Francis de Zegher (Leuven, Belgium) received the ESPE Andrea Prader Prize, in recognition of his lifetime achievement in teaching and research, outstanding leadership and overall contribution to the field of paediatric endocrinology.

ESPE Outstanding Clinician Award



Orit Pinhas-Hamiel (Tel Aviv, Israel) was presented with the ESPE Outstanding Clinician Award, in recognition of her outstanding clinical contribution to the practice of paediatric endocrinology.

ESPE International Award



Berenice Mendonça (São Paulo, Brazil) received the ESPE International Award. This is presented to an outstanding paediatric endocrinologist from a country outside Europe and the Mediterranean basin.

ESPE International Outstanding Clinician Award



Veronica Mericq (Santiago, Chile) received the ESPE International Outstanding Clinician Award, in recognition of her contribution and commitment to clinical paediatric endocrinology in a country outside Europe and the Mediterranean basin.

ESPE Research Award



Faisal Ahmed (Glasgow, UK) received the ESPE Research Award, in recognition of research achievements of outstanding quality in basic endocrine science or clinical paediatric endocrinology.

ESPE Young Investigator Awards



Sasha Howard



Willem Staels

This award for paediatricians who are still in training or have been no more than 5 years in a senior (principal investigator) role was presented to the following, in recognition of their scientific publications:

- **Sasha Howard** (London, UK), whose award lecture was entitled 'Developmental origins of delayed puberty'
- **Willem Staels** (Brussels, Belgium), whose award lecture was entitled 'Vegf-A mRNA transfection to improve islet graft revascularisation'.

Nominations are now open for our 2022 Awards



Nominate your colleagues by
10 December 2021



www.eurospe.org/grants-awards/awards

ESPE awards

IFCAH-ESPE Grants

The following awards have been made for research into congenital adrenal hyperplasia (CAH):

- **Martijn Finken** (Amsterdam, The Netherlands) for 'Exploring hypothalamus-pituitary-adrenal axis rhythm development across early infancy' (€60 000)
- **Nils Krone** (Birmingham/Sheffield, UK) for 'Establishing novel improved biomarker profiles in CAH' (€110 000)
- **Emanuele Pignatti** (Bern, Switzerland) for 'Targeting androgen release in adrenocortical cells to prevent hyperandrogenism in CAH' (€80 000).

ESPE Research Unit

Lars Säwendahl (Stockholm, Sweden) and colleagues have been awarded the ESPE Research Unit, which supports collaborative research among members, for their project entitled 'Humanin, a novel target to improve bone health in chronic inflammation' (€100 000).

ESPE Clinical Fellowships

Due to the pandemic, selection of clinical fellows has been postponed throughout 2021. It is hoped that the selection process will take place in the coming months for the programme to run again in 2022. All applications have already been received for this allocation and no additional places are available.

ESPE Hormone Research in Paediatrics Prizes

Prizes for papers published in *Hormone Research in Paediatrics* were presented to the following:

- **Malgorzata Wasniewska et al.** (Italy) for 'Growth trajectory and adult height in children with non-classical congenital adrenal hyperplasia' *Hormone Research in Paediatrics* 2020 **93** 173–181 (best original paper)
- **Meera Shaunak et al.** (UK) for 'Isolated 17,20 lyase deficiency secondary to a novel CYB5A variant: comparison of steroid metabolomic findings with published cases provides diagnostic guidelines and greater insight into its biological role' *Hormone Research in Paediatrics* 2020 **93** 483–495 (best 'Novel Insights from Clinical Practice' paper).

ESPE Research Fellowship

Ruth Ming Wai Kwong (London, UK) has been awarded the ESPE Research Fellowship, which enables talented young scientists, investigators and paediatric endocrinologists to conduct research at leading institutions worldwide. She received it for her project entitled 'Interrogating the role of SGPL1 in adrenal/testicular development and acute steroidogenesis' (€140 000).

Let ESPE support your career

Apply for an ESPE grant – see www.eurospe.org/grants-awards

ESPE Research Unit Grant



Lars Säwendahl, recipient of the 2021 ESPE Research Unit Grant

This collaborative research grant aims to foster, facilitate, co-ordinate and identify topics for high quality research in paediatric endocrinology, for both physicians and scientists.

The grant of €100 000 is for 2 years (up to €50 000 per year). It covers salary, materials and consumables, small items of equipment, collaborative visits and overheads that should be less than 10% of the total value.



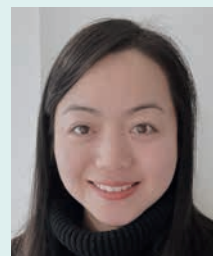
Preliminary applications
1 November 2021–15 February 2022

Those fulfilling the preliminary criteria will need to submit a final application by **20 April 2022**



Find full details at
www.eurospe.org/grants-awards/grants/research-unit

ESPE Research Fellowship



Ruth Ming Wai Kwong, recipient of the 2021 ESPE Research Fellowship

The Research Fellowship enables talented early career scientists, investigators and paediatric endocrinologists to conduct research at leading institutions worldwide.

€125 000 is available for up to 2 years of research training in a centre of excellence, for those intending to pursue a career in paediatric endocrinology. It will also cover living expenses. An additional €15 000 is available for consumables (reasonable travel and laboratory expenses).



Applications accepted
1 January–20 April 2022



Find full details at
www.eurospe.org/grants-awards/grants/research-fellowship

Bringing you recent highlights from the world of research

Polycystic ovary syndrome in women born preterm

Some studies have shown an increased risk of early pubarche, early menarche and polycystic ovary syndrome (PCOS) in girls born small for gestational age. However, little is known about the association between preterm birth and PCOS. This Finnish study by Paalanne *et al.* included 74 women born very or moderately preterm (<34 weeks of gestation), 127 women born late preterm (34–36 weeks of gestation) and 184 women born at full term. Their mean age was 23.2 years.

Women born preterm had higher testosterone, lower sex hormone-binding globulin and a higher free androgen index than controls. Furthermore, women born late preterm had a threefold increased risk of having PCOS according to clinical and biochemical signs. Women born late preterm also had a significantly higher waist circumference than controls and were more hyperinsulinaemic and insulin-resistant than women born at term. These are contributing factors to hyperandrogenism and pathogenic features of PCOS.

This study supports the association of early life factors, including prematurity, with the development of PCOS in later life.



Read the full article at Paalanne *et al.* 2021 *European Journal of Endocrinology* 185 279–288

Epidemiology and genetic analysis of idiopathic T1DM

Idiopathic diabetes is a subcategory of type 1 diabetes mellitus (T1DM) characterised by the absence of autoantibodies. The underlying molecular mechanisms are still poorly understood.

Over a 2-year period, Abdel-Karim and colleagues carried out a prospective study of 1157 patients with T1DM who were under the age of 18 years. Autoantibodies (GAD65, IAA, IA-2A and ZnT8) were measured and, in cases where they were absent, genetic evaluation was performed to rule out monogenic diabetes. It was found that 53 patients (4%) had idiopathic T1DM, and around 33% of these had a history of diabetic ketoacidosis. The C peptide level was low in 56.6% and normal in 43.4%. Additionally, it was found that C peptide levels were higher and the requirement for insulin was lower in the idiopathic diabetic cohort.

Thus, accurate diagnosis is essential for management and prognosis, as some reports also mention a higher cardiovascular risk in the long term in these patients.



Read the full article at Abdel-Karim *et al.* 2021 *Journal of the Endocrine Society* doi: 10.1210/jendso/bvab131

Childhood radiotherapy induces chronic adipose dysfunction

Thanks to great advances in treatment, the 5-year survival rate for all paediatric patients with cancer now exceeds 80%. Childhood cancer survivors, however, have an increased risk of developing type 2 diabetes mellitus (T2DM) and cardiovascular disease, specifically in individuals who underwent total body irradiation (TBI) or abdominal radiotherapy (RT). The underlying molecular mechanisms for this association are not known.

Huang *et al.* examined adult survivors of childhood cancer, who had previously been treated with abdominal RT or TBI, and compared them with individuals treated with chemotherapy only (CHM) or healthy controls. They included individuals with no prior T2DM or obesity to detect early changes in gene expression of adipose tissue by RNA sequencing.

The biggest differences were observed between individuals with TBI compared with CHM or healthy controls, with upregulation of inflammatory markers and dysregulation of adipocytokine expression. This suggests adipose tissue dysfunction in individuals with a history of TBI, which negatively impacts their cardiometabolic health.



Read the full article at Huang *et al.* 2021 *JCI Insight* doi: 10.1172/jci.insight.153586

Cognition and white matter microstructure in congenital hypothyroidism

This observational study by Perri *et al.* examined the cognitive function and white matter microstructure, observed by magnetic resonance imaging (MRI), in children with congenital hypothyroidism. They compared 39 affected children with 39 healthy children and found that 10% of those with permanent hypothyroidism had an IQ score <70 and 28.6% had an IQ score of 71–84. There were particular effects on processing speed, visual attention, reading speed, calculations and numerical knowledge, which were lower than the control group.

Family history was also relevant, with a lower IQ value, working memory index and processing speed in children of mothers with Hashimoto's and those with a family history of thyroid disorders. MRI demonstrated white matter microstructural abnormalities which correlated with the clinical and cognitive findings.

Despite timely diagnosis and treatment, children with congenital hypothyroidism remain at risk of white matter abnormalities and neurocognitive impairment. Further work is needed to look into the association between maternal thyroid disease and cognitive outcomes.



Read the full article at Perri *et al.* 2021 *Journal of Clinical Endocrinology & Metabolism* 106 e3990–e4006

New medications for type 2 diabetes mellitus in youth

William Tamborlane explains the relative lack of drugs used to treat adolescent type 2 diabetes mellitus, and the steps that are being taken to remedy this situation.

A current lack of approved drugs

There are many reasons why a limited number of new drugs are currently approved for use in adolescents with type 2 diabetes mellitus (T2DM).

First of all, T2DM is a relatively 'new' disease in paediatrics, initially described in the 1990s. Metformin was the first and only drug approved by the US Food and Drug Administration (US FDA), in 1999, for use in T2DM in youth. This was on the basis of a small, randomised clinical trial. Insulin was also approved for use by young people with T2DM, but this was based on its effective use in adults with T2DM and in children with T1DM, not a randomised controlled study in adolescents.

Rosiglitazone and glimepiride failed as initial monotherapies versus metformin in T2DM in youth. Prior to the recent approval of liraglutide,¹ no new drugs had been approved for use in paediatric T2DM on the basis of a randomised study for more than 20 years.

A major reason why many of the new drugs approved for adult use have not been approved in paediatrics is that adolescents with T2DM are difficult to recruit for trials. For example, low-income disadvantaged parents are less readily engaged with research and often can't afford to miss work so that their children can be screened for these studies. Adolescents with T2DM often miss clinic visits and are lost to follow-up. Their compliance with taking meds and carrying out other diabetes-related tasks is poor. Many patients are also excluded due to behavioural problems, depression, other psychiatric disorders and use of atypical anti-psychotic drugs.

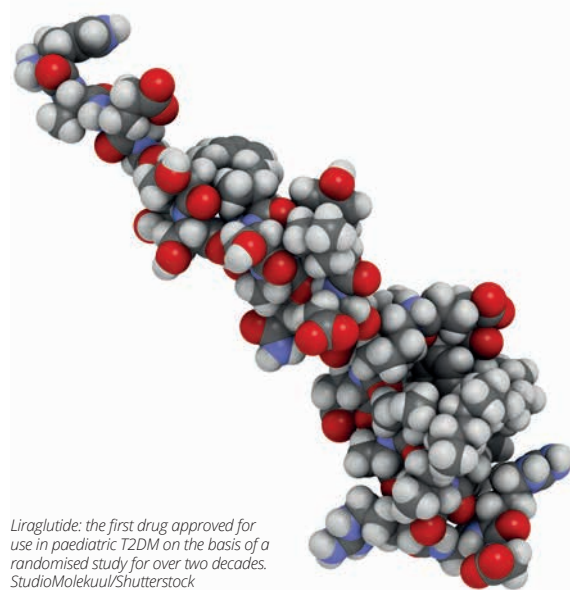
Another recruitment problem includes the relatively small number of cases with T2DM who are 10–17 years



William Tamborlane

“

More recently, the Pediatric Diabetes Consortium's primary aim has been to improve the care of adolescents with T2DM by making drugs with proven effectiveness in adults available to them”



Liraglutide: the first drug approved for use in paediatric T2DM on the basis of a randomised study for over two decades. StudioMolekuul/Shutterstock

old. It is estimated that there are fewer than 25 000 youth cases under 18 years of age in the USA. Only about 200 adolescents with T2DM are listed in the UK registry and there are fewer than 1000 with T2DM in the German/Austrian T2DM Registry. In addition, many adolescents who are screened for participation in T2DM trials are excluded, due to a variety of modifiable and non-modifiable exclusions.

Improving drug availability

However, a major turning point has been reached by the formation of the Pediatric Diabetes Consortium (PDC) of the 60 leading US paediatric diabetes treatment centres. The initial aim of the PDC was to establish the first paediatric T2DM registry in the USA. More recently, its primary aim has been to improve the care of adolescents with T2DM by making drugs with proven effectiveness in adults available to them.²

This has been accomplished by the collaboration of a large number of US paediatric endocrine centres to evaluate the efficacy and safety of new drugs for adolescents (10–17 years of age) with T2DM. In addition, the PDC Executive Committee has negotiated template trial budgets with industry and contract research organisation sponsors, which have been offered to each PDC centre that enrolls in a trial. The PDC has also established monthly Oversight Committee calls with investigators and study co-ordinators at all centres that are enrolled in each clinical trial.

The PDC has already accomplished its primary goal by participation in the studies highlighted in the panel (left).

We strongly believe that the results of these and future randomised clinical trials will transform the care of young people with T2DM in the future.

William V Tamborlane

Professor and Chief of Pediatric Endocrinology,
Yale University School of Medicine, Connecticut, USA

References

1. Tamborlane et al. 2019 *New England Journal of Medicine* **381** 637–646.
2. Van Name et al. 2020 *Diabetes Technology and Therapeutics* **22** 330–336.

Trials with PDC participation

AstraZeneca:

- Exenatide by once weekly injection (approved)
- Oral dapagliflozin (recently approved for youth and young adults with T2DM by the European Medicines Agency)
- Phase III dapagliflozin and saxagliptin versus placebo study (nearing completion of randomisation)

Boehringer Ingelheim:

- Dinamo phase III empagliflozin and linagliptin versus placebo (nearing completion of enrolment)
- Dinamo Mono study (in early recruitment phase)

Novo Nordisk:

- Liraglutide by daily injection (approved)
- Oral semaglutide (in early recruitment phase)

Takeda:

- Phase III alogliptin versus placebo study (nearing completion)

Type 2 diabetes mellitus: Australasian guidelines

Alexia Peña Vargas updates us on the Australasian Paediatric Endocrine Group guidelines on screening, assessment and management of type 2 diabetes mellitus in young people.



Alexia Peña Vargas

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Tighter diabetes targets should be set for all children. This is due to the accelerated rate of developing diabetes complications and the higher mortality rate compared with patients with T1DM and adult-onset T2DM”

The first Australasian guidelines for children with type 2 diabetes mellitus (T2DM) were developed to support healthcare providers in relation to screening and care of children with T2DM.¹ They were developed in the context of the increased incidence of T2DM in children, particularly in high risk ethnic groups, and the higher diabetes complication rate in paediatric T2DM compared with adult T2DM.²

The guidelines emphasise the challenges and details of screening and management of children from indigenous backgrounds in Australia and New Zealand, which were not included in previous international paediatric guidelines.³ Specific screening for indigenous children in comparison with non-indigenous individuals is shown in the Table. This took into account the need for early identification of these children, using feasible approaches, as they are at high risk of suboptimal control and early diabetes complications.¹

Recommendations

In addition to the guidance for screening (see Table), the guidelines include the following recommendations.

1. Diabetes antibodies testing should be undertaken at diagnosis, and consideration should be given to **genetic testing**, if diabetes is present in two or more consecutive generations and diabetes autoantibodies are negative.

2. Diabetes education should be delivered by a specialised multidisciplinary team with expertise in managing paediatric

T2DM. It should be individualised, family-centred and developmentally and culturally appropriate.

3. Blood glucose monitoring should be individualised according to treatment and need to improve glucose levels.

4. Tighter diabetes targets (glycated haemoglobin (HbA_{1c}) 48mmol/mol [$\leq 6.5\%$]) should be set for all children. This is due to the accelerated rate of developing diabetes complications and the higher mortality rate compared with patients with T1DM and adult-onset T2DM.^{2,4} This target HbA_{1c} should be achieved without hypoglycaemia and/or undue treatment burden.

5. Advice on lifestyle should include optimising weight, a healthy diet, 60 minutes of moderate to vigorous physical activity per day, limitation of recreational screen time to ≤ 2 hours/day and quality sleep of 8–11 hours' duration, according to age.

6. Metformin up to 2g/day should be used as the first-line medication in children with mild presentation or in those who are diagnosed after screening.

7. Insulin should be the first-line treatment for patients who present with diabetes ketoacidosis, hyperglycaemic hyperosmolar state or ketosis. It should be added to metformin where glycaemic targets have not been achieved or maintained with metformin monotherapy.

8. Newer medications approved for adults with T2DM should be considered if target diabetes control is not achieved with reasonable adherence to treatment and under the guidance of a paediatric endocrinologist. Even though this recommendation had limited evidence to support it, there is emerging evidence of the effectiveness of glucagon peptide-like receptor agonists (liraglutide) in adolescents with T2DM.⁵

9. Complications and co-morbidities should be screened for at diagnosis and during follow up, including obesity, retinopathy, nephropathy, neuropathy, psychosocial issues, reproductive disorders, liver disease, obstructive sleep apnoea, hypertension and dyslipidaemia.

10. Transition of adolescents with T2DM to a diabetes multidisciplinary care team including an adult endocrinologist should be arranged for their ongoing care. This particularly applies to those who have co-morbidities and/or those who are taking insulin. This allows earlier use of newer oral or injectable medications and early intervention for diabetes complications.

The guidelines also highlight the need for ongoing research into childhood T2DM, as the evidence used to provide recommendations was limited.¹

Alexia S Peña Vargas

Paediatric Endocrinologist, Endocrinology and Diabetes, Women's and Children's Hospital, and Associate Professor, University of Adelaide, Australia

References

1. Peña et al. 2020 *Medical Journal of Australia* **213** 30–43.
2. Bjornstad et al. 2021 *New England Journal of Medicine* **385** 416–426.
3. Zeitler et al. 2018 *Pediatric Diabetes* **19** Suppl 27 28–46.
4. Reynolds et al. 2018 *Journal of Diabetes and its Complications* **32** 545–549.
5. Tamborlane et al. 2019 *New England Journal of Medicine* **381** 637–646.

Table. Australasian recommendations for T2DM screening in children and adolescents.

	Indigenous population	Non-indigenous population
Age	Any child ≥ 10 years (or at onset of puberty, whichever occurs earlier)	
Target screening indications	One of the following risk factors: <ul style="list-style-type: none"> • overweight or obese (BMI ≥ 85 or ≥ 95 percentile and/or waist circumference to height ratio > 0.5) • maternal history of diabetes or gestational diabetes during the child's gestation • first degree relative with T2DM • signs of insulin resistance (acanthosis nigricans) • other conditions associated with obesity/metabolic syndrome (hypertension, dyslipidaemia, fatty liver disease, polycystic ovary syndrome) • use of psychotropic medications 	In those who are overweight or obese (BMI ≥ 85 or ≥ 95 percentile) AND have one or more additional risk factors: <ul style="list-style-type: none"> • maternal history of diabetes or gestational diabetes during the child's gestation • first degree relative with T2DM • signs of insulin resistance (acanthosis nigricans) • other conditions associated with obesity/metabolic syndrome (hypertension, dyslipidaemia, fatty liver disease, polycystic ovary syndrome) • use of psychotropic medications • race and ethnicity (South Asian, South East Asian, Middle Eastern, North African and Latino)
Screening method	Point of care HbA _{1c}	HbA _{1c} or OGTT
Screening frequency	Every year	Every 2–3 years or earlier if excessive weight gain

BMI, body mass index; HbA_{1c}, glycated haemoglobin; OGTT, oral glucose tolerance test.

Complications of type 2 diabetes mellitus in youth

Orit Pinhas-Hamiel draws together the latest data to illustrate the complexity and devastating, far-reaching effects of this condition in young people.



Orit Pinhas-Hamiel

“

These devastating sequelae indicate that the course of T2DM in adolescents affects almost all organs of the body ... Integrated aggressive medical interventions are needed”

Now, nearly three decades since the first publications, type 2 diabetes (T2DM) in children and adolescents is well established as a global problem. Increased numbers of affected adolescents and longer diabetes duration have yielded prospective studies with appropriate control groups. Compelling data comprising mixed ethnic populations arise from multicentre studies in the USA (TODAY/TODAY2 and the SEARCH for Diabetes in Youth), and studies from Canada and Australia. The limited data from Europe and Asia suggest similar trends.

Young people with T2DM experience a wide range of complications and co-morbidities (Table 1). Acute complications include diabetic ketoacidosis, which can lead to recurrent admissions,¹ hyperosmolar hyperglycaemic non-ketotic syndrome, and severe hypoglycaemic events, which have been reported in 2.6% of cases.

The Figure shows the prevalence of complications compared with adolescents with type 1 diabetes (T1DM). Table 2 (page 10) summarises data showing the prevalence of microvascular complications and co-morbidities at diagnosis and at follow-up from several registries.

Macrovascular complications

T2DM is a major risk factor for cardiovascular disease (CVD), including myocardial infarction and stroke. Markers for early CVD, including carotid intima-media thickness, peripheral arterial stiffness and vascular endothelium, were reportedly higher than in adolescents with obesity and normal weight, even after short disease duration. The event rate for all adjudicated heart, vascular and cerebrovascular events was 6.4/1000 patient-years, which is triple the cardiovascular event rate seen in adults in the Diabetes Control and Complications Trial.

Table 1. Complications and co-morbidities of T2DM in adolescents.

Cardiovascular disease	Long term impact on offspring
Decreased bone mineral density	Nephropathy
Decreased cognitive function	Neuropathy
Depression, low quality of life, anxiety	Polycystic ovary syndrome
Eating disorders	Retinopathy
Fatty liver	

Diverse co-morbidities

Co-morbidities impair the global health and quality of life of adolescents with T2DM and include the following.

- **Cognition** – Poorer scores have been reported in several neurocognitive domains, particularly in executive functioning and memory. Differences in brain grey matter volume, white matter volume and microstructural integrity were shown in imaging studies.²
- **Decreased bone mineral density** – An age-related decline in bone z scores suggests an adverse impact of diabetes on bone mass attainment during puberty.³
- **Disordered eating behaviours** – At a mean age of 14.0 years, 6% had clinical and 20% had subclinical levels of binge eating.⁴
- **Depression** – About one-fifth endorse elevated depressive symptoms and about one-fifth endorse thoughts of self-harm.⁵
- **Pregnancy** – T2DM during pregnancy poses a long term impact, including increased risk for T2DM in offspring, in addition to the known neonatal and maternal complications.⁶

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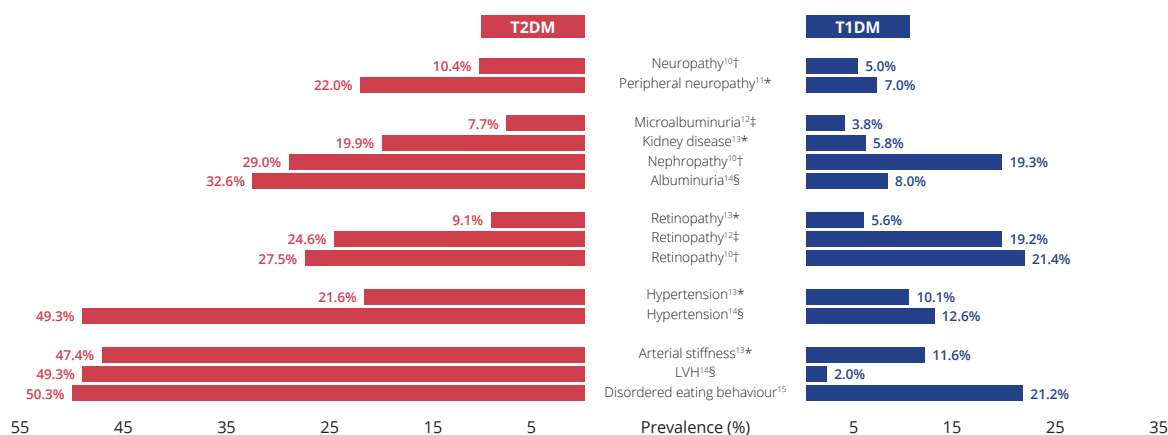


Figure. Long-term complications in children and adolescents with T2DM versus T1DM. *SEARCH, USA: adolescents with T2DM (n=272) and T1DM (n=1746); †India: adolescents with T2DM (n=889) and T1DM (n=3252) (mean disease duration 3.1 years); ‡Swedish National Diabetes Registry: adolescents with T2DM (n=1413) and T1DM (n=3748) (mean disease duration 3.5 years); §Canada: adolescents with T2DM (n=322, duration 2.3) vs T1DM (n=199, duration 7.2 years). LVH, left ventricular hypertrophy.

Continued from page 9

Multiple complications

Data are still limited on the prevalence of multiple complications in single adolescents with T2DM. Data from the TODAY study on 500 participants at a mean age of 26.4±2.8 years and mean duration since diagnosis of 13.3±1.8 years showed that at least one complication occurred in 60.1% of the participants, two complications occurred in 21.3%, and 7.1% had three.⁷ Major complications such as blindness, amputations and dialysis have been reported,⁸ as well as serious cardiovascular events.⁷

Mortality

During a median follow-up of 5.3 years, the mortality rate for T2DM was higher than for T1DM: 185.6 versus 70.6 deaths/100 000 patient-years.⁹ It was 2.4-fold higher than expected in the general population. Females had higher mortality rates than males. The leading underlying causes of death were motor vehicle accidents, accidental poisoning and intentional self-harm.

These devastating sequelae indicate that T2DM in adolescents affects almost all organs and is more aggressive than T1DM, T2DM in adults, and simple obesity. Integrated aggressive medical interventions are needed.

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Table 2. Prevalence of microvascular complications and co-morbidities at diagnosis and at follow-up.

Study	n	Disease duration	Prevalence (%)						
			Hypertension	Nephropathy	Neuropathy	Retinopathy	NAFLD	Dyslipidaemia	Elevated LDL
Meta-analysis (international) ¹⁶	4363	0–7.8 years	25.0	22.0					
Hong Kong ¹⁷	391	Presentation	22.5	12.8			38.0	35.0	
DPV Registry* (Germany) ¹⁸	510	2.1 years		4.2					
PDC* (USA) ¹⁹	598	2 (0.7–4.2) years	31.0	6.0			5.0	44.0	
TODAY (USA)	523	7.8±5.8 months	13.6	13.0			3.3	33.0	3.0
		<2 years	19.0	6.0	6.0	4.9			
		4–5 years	33.8	18.0		13.7			
TODAY2 (USA) ^{7,20}	500	13.3±1.8 years	67.5	54.8	32.4	51.0		51.6	12.4

LDL, low density lipoprotein; NAFLD, non-alcoholic fatty liver disease; *PDC, Pediatric Diabetes Consortium.

Yearbook of Paediatric Endocrinology 2021

The recently published Yearbook features publications from across the breadth of our field. Here are a few on the subject of type 2 diabetes mellitus (T2DM), which is the theme of this issue of *ESPE News*.

Adolescent BMI and early-onset type 2 diabetes among Ethiopian immigrants and their descendants: a nationwide study

Simchoni *et al.* 2020 *Cardiovascular Diabetology* doi: 10.1186/s12933-020-01143-z

The impact of immigration on risk of early-onset T2DM (before age 40) was assessed in 93 806 native Israelis and 27 684 Israelis of Ethiopian origin (mean age 17.5 years). After adjustment for sociodemographic confounders, the hazard ratios for T2DM among Ethiopian men with normal and high BMI were 3.4 (2.3–5.1) and 15.8 (8.3–30.3) respectively, compared with third-generation Israelis with normal body mass index. For Israeli-born Ethiopian men, the hazard ratios increased to 4.4 (1.7–11.4) and 29.1 (12.9–70.6) respectively.

Multisite examination of depression screening scores and correlates among adolescents and young adults with type 2 diabetes

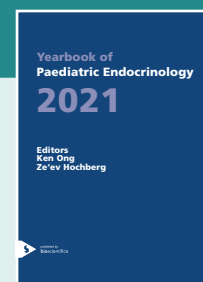
Monaghan *et al.* 2021 *Canadian Journal of Diabetes* doi: 10.1016/j.jcjd.2021.01.011

The presence of depressive symptoms was assessed in 197 adolescents and young adults (aged 12–24 years) with T2DM. Of these, 19% reported elevated depressive symptoms and 19% admitted thoughts of self-harm. Older age, shorter diabetes duration, higher glycated haemoglobin, being non-Hispanic white, more blood glucose checks per day and being prescribed oral medications were associated with more depressive symptoms.

Bone mass and density in youth with type 2 diabetes, obesity and healthy weight

Kindler *et al.* 2020 *Diabetes Care* doi: 10.2337/dc19-2164

This cross-sectional study compared bone mineral density (BMD), lean body mass and abdominal visceral fat among 180 individuals with T2DM, 226 with obesity and 238 with normal weight, aged 10–23 years. The findings suggest that T2DM in youth may have a detrimental effect on bone accrual during the critical window of peak bone mass attainment, irrespective of obesity. Individuals with T2DM and with increased abdominal visceral fat tended to have lower BMD.



Download the Yearbook free of charge at www.espeyearbook.org/media/13007/espeyearbook2021.pdf

Hypothalamic dysfunction in childhood

ESPE Science Symposium 2022

Princess Máxima Center, Utrecht,
The Netherlands, 7–8 October 2022

This 2-day event will discuss the aetiology of genetic and acquired hypothalamic dysfunction in childhood, its consequences and new ways of management to improve outcome.

We will also focus on building new networks and collaboration within ESPE and Europe, together with patient organisations and Endo-ERN.

Keynote lectures include:

- **The hypothalamus from an evolutionary point of view**
Dick Swaab, The Netherlands
- **Appetite-regulating hormones in hypothalamic obesity**
Hoog-Wei Gan, UK
- **Congenital disorders of hypothalamic dysfunction associated with hypopituitarism** Mehul Dattani, UK
- **Endocrine disorders in Prader-Willi syndrome: a model to understand and treat hypothalamic dysfunction** Maithe Tauber, France
- **Hypothalamic syndrome in craniopharyngioma** Hermann Müller, Germany
- **Hypothalamic dysfunction and hypothalamitis: a novel autoimmune endocrine disease?** Fahrettin Kelestimur, Turkey
- **Radiation therapy and preserving hypothalamic function** Geert Janssens, The Netherlands
- **Neurosurgical challenges in children with hypothalamic tumours** Eelco Hoving, The Netherlands
- **Hypothalamic dysfunction requires individualised treatment** Hanneke van Santen, The Netherlands

Registration information will be available soon. We look forward to welcoming you to the 2022 ESPE Science Symposium.



Find out more at
<https://bit.ly/sciencesymposium2022>



Next ESPE Connect Webinar



IGF-1 deficiency: knowns and unknowns, a case-based symposium

27 January 2022, 16.00–17.30 (CET)

Moderator: Michel Polak (France)

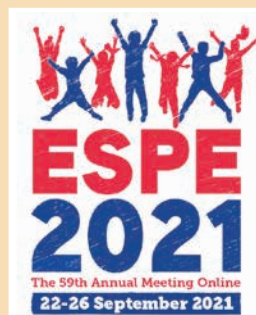


www.eurospe.org/education/webinar-series

Success for ESPE 2021 Online

22–26 September 2021

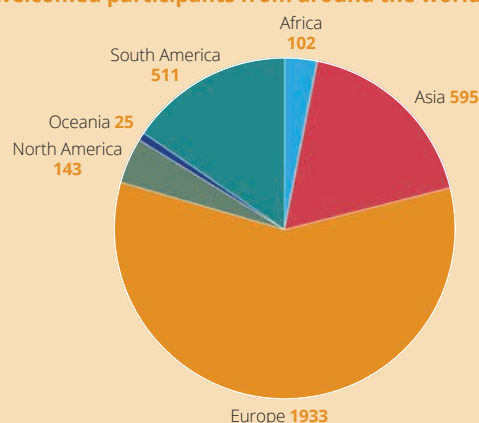
'Lifelong endocrine care through collaboration, discovery and innovation'



Over 3000 delegates registered for this year's online ESPE Annual Meeting. They enjoyed a mixture of interactive sessions with live Q&A, including:

- 8 plenary lectures
- 13 symposia
- 7 'Meet the Expert' sessions
- 2 controversy sessions
- 2 'How do I?' sessions
- 8 ESPE Working Group sessions
- 2020/2021 Award sessions
- 3 Yearbook sessions
- Live poster tours

We welcomed participants from around the world:



Thanks are due to Mehul Dattani, Poonam Dharmaraj and all the other members of the Programme Organising Committee for arranging such an engaging and interesting programme.

All presentations are available to view by registered delegates until May 2022.



To access the sessions see <https://venue.events-nextechar.com/landing?show=espe2021>



You can find the abstracts at <https://abstracts.eurospe.org/hrp/0094>

Future meetings

See www.eurospe.org/meetings for details of all future meetings



11th International Meeting of Pediatric Endocrinology
19–22 March 2022
Buenos Aires, Argentina



60th Annual ESPE Meeting
15–17 September 2022
Rome, Italy



61st Annual ESPE Meeting
September 2023
The Hague, The Netherlands



62nd Annual ESPE Meeting
September 2024
Marseille, France



OTHER EVENTS

2021

European Thyroid Association Webinar: Guideline on Paediatric Thyroid Nodules and Carcinoma
15 December
(See <https://bit.ly/ZoomRegisterHere>)

2022

ESPE Connect Webinar IGF-1 Deficiency
27 January

ESPE Winter School Online
26 February–1 March

ESPE Caucasus & Central Asia School
Date to be confirmed
Tbilisi, Georgia

ESPE Maghreb School
Date to be confirmed
Casablanca, Morocco

ASPED-ESPE Endocrine Academy
Details to be confirmed

DEADLINES

DECEMBER

ESPE Awards 2022 nominations – 10 December 2021

Maghreb School Steering Committee Vacancy applications – 13 December 2021

JANUARY

ESPE Winter School Online applications – 10 January 2022

Early Career Scientific Development Grant applications – 31 January 2022

FEBRUARY

ESPE Research Unit preliminary applications – 15 February 2022

APRIL

ESPE Research Unit final applications – 20 April 2022

ESPE Research Fellowship applications – 20 April 2022

All dates, deadlines and plans are being constantly reviewed in light of COVID-19

For more information about vacancies on ESPE Committees and how to apply, see www.eurospe.org/about/vacancies



European Society for Paediatric Endocrinology

Improving care of children with endocrine diseases by promoting knowledge and research

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ESPE Newsletter

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