Hypoglycaemia: a problem with many faces

A Symposium on the occasion of the 54th Annual Meeting of the European Association for the Study of Diabetes

3 October 2018
Berlin, Germany

Brought to you by members of the International Hypoglycaemia Study Group
Welcome and introduction

Simon Heller, BA, MB, Bchir, DM, FRCP
Professor of Clinical Diabetes
University of Sheffield
Director of Research and Development and
Honorary Consultant Physician
Sheffield Teaching Hospitals NHS Foundation Trust
Sheffield, United Kingdom
IHSG Members
Look at how far we’ve come

- **2013**
  - ADA Chicago First Meeting

- **2014**
  - EASD Vienna Symposium

- **2015**
  - IDF Vancouver Meet the Experts

- **2016**
  - HCP Education Slide Deck
  - Classification of Hypoglycaemia Publication
  - WCPD9 Atlanta Symposium

- **2017**
  - IHSG Website Launch
  - EASD Lisbon Symposium
  - IDF Abu Dhabi Symposium

- **2018**
  - HCP and Patient Tools
  - EASD Berlin Symposium
Why hypoglycaemia matters

Higher incidence of hypoglycaemia occurs as patients move closer to HbA₁c treatment targets.

It is an under-recognized problem that deserves increased awareness.

There is a lack of understanding by both professionals and patients.

A better understanding can increase patient quality of life.
A look at today’s symposium

18:50–19:10
Update on hypoglycaemia risk factors
Yingying Luo

19:10–19:30
Hypoglycaemia in children
Tim Jones

19:30–19:50
Hypoglycaemia and the family
Stephanie Amiel

19:50–20:10
Panel discussion
Simon Heller, Yingying Luo, Tim Jones, Stephanie Amiel

20:10–20:15
Concluding remarks
Simon Heller
The International Hypoglycaemia Study Group (IHSG) is supported through a grant by Novo Nordisk A/S and is consistent with its ongoing commitment in diabetes.
Remember, if you have questions for our speakers....

You can **submit questions** at any time by filling out a question card.

Question cards will be collected in between sessions and will be answered during the **panel discussion**.
Update on hypoglycaemia risk factors

Yingying Luo, MD
Associate Professor
Peking University People’s Hospital
Beijing, China
Annual prevalence of severe hypoglycaemia in type 1 and 2 diabetes

SH, severe hypoglycaemia; SU, sulfonylurea.
Prospective hypoglycaemia rates in diabetes worldwide

Annual rate denotes estimated number of events per patient-year. Rates calculated from full analysis set. Novo Nordisk data on file.
Impact of hypoglycaemia

- **Brain**
  - Coma, seizures, cognitive dysfunction, psychological effects

- **Cardiovascular**
  - Myocardial ischemia, cardiac arrhythmias

- **Musculoskeletal**
  - Falls, accidents, fractures, dislocations, driving mishaps

*Increased mortality*
Impact of non-severe hypoglycaemia on QOL

• Reduced QOL in both T1D and T2D\textsuperscript{1}
• QOL significantly affected in T2D patients (HYPO study)\textsuperscript{2}
• Depressive symptoms and inability to carry out daily activities\textsuperscript{3}
• Significant work-time loss in a study of 7 European countries and a multinational survey\textsuperscript{4,5}
• QOL effect is greater for nocturnal than daytime events\textsuperscript{6}

QOL, quality of life.
Impact of hypoglycaemia on adherence

T2D patients on metformin + sulfonylurea

<table>
<thead>
<tr>
<th>Hypoglycaemia Level</th>
<th>Percent of Adherent Patients</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No hypoglycaemia</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>Mild hypoglycaemia</td>
<td>56</td>
<td>0.01</td>
</tr>
<tr>
<td>Moderate/worse hypoglycaemia</td>
<td>46</td>
<td></td>
</tr>
</tbody>
</table>

n=266, 59, 80

Fear of hypoglycaemia: impact on treatment

Prospective study of 100 insulin-naïve adults with type 2 diabetes – personal barriers to starting insulin

- 33% were unwilling to start insulin
- Fear of hypoglycaemia was the most common personal barrier
- Other common barriers included concerns about permanent need for insulin, less flexible regimen, and feelings of failure
Case study: Mr. Lee

• Mr Lee: 72 years old, lives alone
• Type 2 diabetes for 15 years
• On metformin 500 mg tid, glimepiride 4 mg qd and NPH 20 U at bed time
• Recent HbA1c: 6.7% (2 months ago)
• Always feels hungry before bed. Sometimes wakes up at 3–5 am and feels palpitations
  • Discomfort always disappears after eating
• Very few SMBG readings
• Past history: CABG 2 years ago
• Personal history: No habit of smoking; drinks beer or alcohol before dinner everyday

CABG, coronary artery bypass grafting; NPH, neutral protamine Hagedorn; qd, once-daily; SMBG, self-measured blood glucose; tid, thrice-daily.
Do you think the patient has good glycaemic control?

A. Yes

B. No
Which risk factors in the case do you think are modifiable?

A. Strict glycaemic control
B. On glimepiride and NPH
C. Alcohol consumption
D. Lack of SMBG
E. All of the above
Risk factors for hypoglycaemia

**Non-modifiable risk factors**
- Older age
- Diabetes duration
- Kidney damage
- History of severe hypoglycaemia
- Emotional disorders
- Patients using CNS depressing agents
- Genetic factors
- Comorbidity

**Modifiable risk factors**
- Poor glycaemic control (include low HbA$_{1c}$ under the ideal target)
- Glucose-lowering medication use
- Alcohol and other substances
- Lack of knowledge
- Limited access to the glucose monitoring devices

Impaired awareness of hypoglycaemia
Non-modifiable risk factors associated with hypoglycaemia

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Cases (N=690)</th>
<th>Controls (N=6900)</th>
<th>Crude OR (95% CI)</th>
<th>Adj OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
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<tr>
<td>20–59</td>
<td>114 (16.5)</td>
<td>2195 (31.8)</td>
<td>1.00 (reference)</td>
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<td>60–74</td>
<td>231 (33.5)</td>
<td>3012 (43.6)</td>
<td>1.55 (1.22–1.95)</td>
<td>1.19 (0.90–1.56)</td>
</tr>
<tr>
<td>≥75</td>
<td>345 (50.0)</td>
<td>1693 (24.5)</td>
<td>4.26 (3.39–5.36)</td>
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CI, confidence interval; CVD, cardiovascular disease; OR, odds ratio.
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<tr>
<td>Renal failure prior to index date</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>No</td>
<td>323 (46.8)</td>
<td>4971 (72.0)</td>
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<tr>
<td>Yes</td>
<td>367 (53.2)</td>
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<tr>
<td><strong>Cognitive impairment/dementia prior to index date</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>626 (90.7)</td>
<td>6726 (97.5)</td>
<td>1.00 (reference)</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>Yes</td>
<td>64 (9.3)</td>
<td>174 (2.5)</td>
<td>4.19 (3.08–5.71)</td>
<td><strong>2.00 (1.37–2.91)</strong></td>
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CI, confidence interval; CVD, cardiovascular disease; OR, odds ratio.
Glucose fluctuation and hypoglycaemia

**HbA₁c of 7.5%**

- **mg/dL**: 90, 108, 126, 144, 162, 180, 198, 216, 234, 252
- **mmol/L**: 5, 6, 7, 8, 9, 10, 11, 12, 13, 14

**Day**: 1, 9, 18, 27, 36, 45, 54, 63, 72, 81, 90

---

**HbA₁c of 7.5%**

- **mg/dL**: 90, 108, 126, 144, 162, 180, 198, 216, 234, 252
- **mmol/L**: 5, 6, 7, 8, 9, 10, 11, 12, 13, 14

**Day**: 1, 9, 18, 27, 36, 45, 54, 63, 72, 81, 90
Hypoglycaemia may occur at all levels of glucose control.

Unadjusted

<table>
<thead>
<tr>
<th>HbA$_1c$ category (%)</th>
<th>Relative risk of hypoglycaemia (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6</td>
<td>1.09 (0.88, 1.30)</td>
</tr>
<tr>
<td>6–6.9</td>
<td>1.00 (1.00, 1.00)</td>
</tr>
<tr>
<td>7–7.9</td>
<td>1.09 (1.00, 1.13)</td>
</tr>
<tr>
<td>8–8.9</td>
<td>1.30 (0.90, 1.25)</td>
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<tr>
<td>≥9</td>
<td>1.28 (1.01, 1.09)</td>
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Adjusted for age, sex, race

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Fully adjusted

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CI, confidence interval.

Impact of IAH on hypoglycaemia at different times

CGM, continuous glucose monitoring; IAH, impaired awareness of hypoglycaemia.
Impact of IAH on severe hypoglycaemia


IAH, impaired awareness of hypoglycaemia; SH, severe hypoglycaemia.

<table>
<thead>
<tr>
<th></th>
<th>Normal awareness</th>
<th>Impaired awareness</th>
</tr>
</thead>
<tbody>
<tr>
<td>% patients with SH episode(s)</td>
<td>26%</td>
<td>66%</td>
</tr>
<tr>
<td>SH episodes/patient year</td>
<td>0.5</td>
<td>2.8</td>
</tr>
</tbody>
</table>

*p* < 0.01

*p* < 0.001
Risk factors to be considered in special situations


Individuals who had no episodes of hypoglycaemia before Ramadan

Individuals who had episodes of hypoglycaemia before Ramadan

Hypoglycaemia during Ramadan

<table>
<thead>
<tr>
<th>Region</th>
<th>Individuals with no episodes (%)</th>
<th>Individuals with episodes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asia</td>
<td>32.6</td>
<td>2.7</td>
</tr>
<tr>
<td>Middle East</td>
<td>19.2</td>
<td>3.3</td>
</tr>
<tr>
<td>North Africa</td>
<td>8.7</td>
<td>42.5</td>
</tr>
<tr>
<td>Europe</td>
<td>34.4</td>
<td>5.3</td>
</tr>
<tr>
<td>Total</td>
<td>34.9</td>
<td>5.0</td>
</tr>
</tbody>
</table>

Asia, Middle East, North Africa, Europe, Total.
Which risk factors in the case do you think are modifiable now?

A. Strict glycaemic control
B. On glimepiride and NPH
C. Alcohol consumption
D. Lack of SMBG
E. All of the above

MPH, neutral protamine Hagedorn; SMBG, self-measured blood glucose.
Risk factors for Mr. Lee

Non-modifiable risk factors
- Age
- Diabetes duration
- Comorbidity

Modifiable risk factors
- Limited knowledge about hypoglycaemia
- Alcohol consumption
- No SMBG
- Glucose target
- Insulin dosage
Do you think this patient is at high risk?

A. Yes

B. No
Recognize the high risk population

IHSG has developed a hypoglycaemia risk assessment infographic

Available at: www.ihsgonline.com
Clinical approach to hypoglycaemia

- Establish hypoglycaemia as a key outcome in diabetes care along with HbA$_1^c$
- Identify risk factors for hypoglycaemia:
  - Conventional risk factors for hypoglycaemia
  - Risk factors for reduced hypoglycaemia awareness and HAAF
- Patient and clinician education around intensive glycaemic therapy
  - Insulin, monitoring, risk factors, prevention, etc
- Technologies

HAAF, hypoglycaemia-associated autonomic failure.
Modifiable risk factors for Mr. Lee

- Provide diabetes education
- Limit the alcohol consumption
- Educate Mr. Lee to use glucose monitoring device
- Elevate the glucose target
- Stop SU and change NPH to long-acting insulin analogue
Take home messages

• Hypoglycaemia is a major problem for both type 1 and 2 diabetes patients globally
• Hypoglycaemia has many short-term and long-term impacts on patients
• Identifying high-risk populations using tools such as that provided by the IHSG may minimize the risk of hypoglycaemia
• Recognizing and modifying the risk factors of hypoglycaemia may improve disease control for the patients
Remember, if you have questions for our speakers....

Raise your hand to have question cards collected

Questions will be answered during the panel discussion
Hypoglycaemia in children

Tim Jones, MBBS, FRACP, MD
Clinical Professor
Head of the Diabetes & Obesity Research team
University of Western Australia
Crawley, Australia
Childhood is not limited to one stage

Infancy, toddlerhood, early childhood, preadolescence, adolescence, post-adolescence, emerging adult...
Children are not simply “small adults”

- Physiology is different and organs are in development
Children are not simply “small adults”

- Physiology is different and organs are in development
- Behaviours differ and change over time
Children are not simply “small adults”

- Physiology is different and organs are in development
- Behaviours differ and change over time
- Differing social contexts: family, school, other adults, culture
Children are not simply “small adults”

- Physiology is different and organs are in development
- Behaviours differ and change over time
- Differing social contexts: family, school, other adults, culture
- Diabetes and its treatment may differ from adults
Children have a unique physiology

- Insulin sensitivity changes with age
- Adolescents have different counterregulatory hormone responses than adults
  - They may trigger counterregulation at a higher blood glucose level than adults
- Few studies performed in very young children

Symptom responses during hypoglycaemia

- Children with T1DM, poor control
- Non-diabetic children
- Non diabetic adults

Baseline Symptom score

Plasma glucose (mM)
The childhood brain is developing

Maturation occurs from the back to the front of the brain

Brain development in youth (5–20 years old)

- Diabetes
- Hypoglycaemia
- Hyperglycaemia

Maturing of brain areas

Children’s behaviour can be unpredictable
Children’s behaviour can be unpredictable

- Nobody can make a toddler eat who doesn’t want to eat
- Hypoglycaemic symptoms may be behavioural
- All young children may require assistance for hypoglycaemia
- Children may feign hypoglycaemia
- Hypoglycaemia may be a source of embarrassment for adolescents
- Risk taking, experimentation
- Mental health
Children have caretakers
Children have caretakers
Children often have to be left in the care of other adults.
• Physiology is different and organs are in development
• Behaviours differ and change over time
• Differing social contexts: family, school, other adults, culture
• Diabetes and its treatment may differ from adults
Children are not simply “small adults”

- Physiology is different and organs are in development
- Behaviours differ and change over time
- Differing social contexts: family, school, other adults, culture
- **Diabetes and its treatment may differ from adults**
  - 85–95% type 1 diabetes
  - C-peptide negative
  - Fewer complications
Hypoglycaemia frequency: DCCT

Severe events per 100 patient years

- Adolescents
  - Intensive: 120
  - Conventional: 30
- Adults
  - Intensive: 100
  - Conventional: 20
Nocturnal hypoglycaemia: CGM detected

- Of all events, 25% were longer than 2 hours
- Hypoglycaemia more prolonged in adolescents vs adults
- Mean time <3.4 mmol/l was 81 mins

Data are median, error bars 25-75th centile, 36,000 study nights.
Severe hypoglycaemia rate and HbA$_{1c}$ % by registry and calendar year

DPV, Diabetes-Patienten-Verlaufsdocumentation; SH, severe hypoglycaemia; WACDD, Western Australian Children Diabetes Database.

Haynes, Holl et al, Unpublished
Severe hypoglycaemia rate and HbA\textsubscript{1c} in 3 contemporary pediatric cohorts

<table>
<thead>
<tr>
<th>HbA\textsubscript{1c} % category</th>
<th>Mean SH rate (per 100 patient years)</th>
</tr>
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<tr>
<td>&lt;7</td>
<td>3</td>
</tr>
<tr>
<td>7.0–&lt;8.0</td>
<td>4</td>
</tr>
<tr>
<td>8.0–&lt;9.0</td>
<td>5</td>
</tr>
<tr>
<td>≥9.0</td>
<td>6</td>
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DPV, Diabetes-Patienten-Verlaufsdocumentation; T1DX, Type 1 Diabetes Exchange; WACDD, Western Australian Children Diabetes Database.
Contemporary pattern severe hypoglycaemia: contributors to changes

- Data: importance of recording hypoglycaemia
- Patient education
- Improved understanding of counter-regulation and hypoglycaemia precipitants
- More physiological insulin delivery through pumps and insulin analogues
- Increased glucose monitoring
Historically

- Severe: coma and convulsion
- Moderate: hypoglycaemia associated with cognitive impairment requiring assistance from someone else for recovery
Severe events: definitions in childhood

Historically

• Severe: coma and convulsion
• Moderate: hypoglycaemia associated with cognitive impairment requiring assistance from someone else for recovery

ISPAD 2018 guidelines

• Severe: event with severe cognitive impairment requiring external assistance by another person to actively take corrective action
• Severe hypoglycaemic coma: event associated with seizure or loss of consciousness

### Impact of hypoglycaemia among young people

<table>
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<tr>
<th>Short-term</th>
<th>Long-term</th>
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<tbody>
<tr>
<td>• Unpleasant symptoms</td>
<td></td>
</tr>
<tr>
<td>• Mood and behaviour changes</td>
<td></td>
</tr>
<tr>
<td>• Social embarrassment</td>
<td></td>
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<tr>
<td>• Cognitive deterioration</td>
<td></td>
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<tr>
<td>• Driving</td>
<td></td>
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<tr>
<td>• Work performance</td>
<td></td>
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<tr>
<td>• School performance</td>
<td></td>
</tr>
<tr>
<td>• Sport</td>
<td></td>
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<tr>
<td>• Accidents</td>
<td></td>
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<tr>
<td>• Seizure</td>
<td></td>
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<tr>
<td>• Death</td>
<td></td>
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<td>• Fear of hypoglycaemia</td>
<td></td>
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<tr>
<td>• Reduced Quality of Life and family stress</td>
<td></td>
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<tr>
<td>• Weight gain</td>
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<tr>
<td>• Reduced physical activity</td>
<td></td>
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<td>• Restrictions on employment</td>
<td></td>
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<tr>
<td>• Driving licensing restrictions</td>
<td></td>
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<td>• Personal relationships impaired</td>
<td></td>
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<tr>
<td>• Brain development concerns</td>
<td></td>
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What are the main concerns about having hypoglycaemia?

Passing out and dying

Going so low that I go into a coma, and no waking up.

Being alone.
Unpleasant symptoms
Embarrassment
Fear of death
Fear of unknown
Concern about hyperglycaemia
Loss of function, concentration
Case history

Patient characteristics

- 10 years old, female
- Type 1 diabetes for 12 months
- MDI therapy
- HbA$_{1c}$ 6.7%
Case history

Patient characteristics

- 10 years old, female
- Type 1 diabetes for 12 months
- MDI therapy
- HbA1c 6.7%

- Nocturnal seizure at 2 am, treated with im glucagon
- Previous day at the beach on holiday

im, intramuscular; MDI, multiple daily injection.
Case history

Patient characteristics

- 10 years old, female
- Type 1 diabetes for 12 months
- MDI therapy
- HbA₁₀ 6.7%
- Nocturnal seizure at 2 am, treated with im glucagon
- Previous day at the beach on holiday
- 2nd seizure 3 months later
- No obvious clinical predisposing factors

im, intramuscular; MDI, multiple daily injection.
### Clinical factors associated with hypoglycaemia

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<th>Risk factors</th>
<th>Co-morbidities</th>
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<td>Impaired hypoglycaemia</td>
<td>Celiac disease</td>
</tr>
<tr>
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<td>awareness</td>
<td></td>
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### Clinical factors associated with hypoglycaemia

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</table>
At the next clinic visit 3 months later:

- HbA$_{1c}$ 8.6%
- No further severe events
Fear of hypoglycaemia can be a major obstacle to improving glycaemic control.
Fear of hypoglycaemia can be a major obstacle to improving glycaemic control

Excessive fear leading to inappropriate management:
- Often makes child eat a large snack at bedtime: 13%
- Often avoids leaving child alone (age >13 years): 11%
Role and limitations of technology in children

- Children and technology
- Parents early adopters
- Must be practical
- Unexpected consequences of uses
Severe hypoglycaemia rate is lower with a CSII regimen

Injections

CSII

Mean SH rate (per 100 patient years)

0 2 4 6 8 10 12

TIDX  DPV  WACDD

*p<0.05.
CSII, continuous subcutaneous insulin infusion; DPV, Diabetes-Patienten-Verlaufsdokumentation; SH, severe hypoglycaemia; TIDX, Type 1 Diabetes Exchange; WACDD, Western Australian Children Diabetes Database.
Severe hypoglycemia

<table>
<thead>
<tr>
<th></th>
<th>Insulin pump (N=49)</th>
<th>Sensor-augmented pump with LGS (N=46)</th>
</tr>
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<tbody>
<tr>
<td>Baseline: actual event rate in preceding 6 months</td>
<td>5</td>
<td>6</td>
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<tr>
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<td>25.5 (9.4, 55.6)</td>
<td>22.0 (7.1, 51.3)</td>
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<tr>
<td>Endpoint: actual event rate in preceding 6 months</td>
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<td>0</td>
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<td>Endpoint: rate per 100 patient-years</td>
<td>26.7 (5.5, 77.9)</td>
<td>0 (0, 29.23)</td>
</tr>
<tr>
<td>Incident rate difference from baseline to endpoint</td>
<td>17.8 (3.1, 32.4)</td>
<td>0.019</td>
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CGM, continuous glucose monitoring; LGS, low glucose suspend.
### CGM with automated suspension with hypoglycaemia

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**Incident rate difference from baseline to endpoint**

- **p-value**: 0.019

---

CGM, continuous glucose monitoring; LGS, low glucose suspend.

Reduction in hypoglycaemia with predictive suspension in adolescents: an RCT

PLGM, predictive low-glucose management; SAPT, sensor-augmented pump therapy.
The potential role for technology in fear of hypoglycaemia

- Most studies have focused on glycaemic outcomes with technology
- The burden and fear of hypoglycaemia are key factors limiting optimal glycaemic control
- **Technological advances have the potential to reduce this burden**
Does real-time CGM with remote monitoring reduce hypoglycaemia fear and improve quality of life?

- Children with T1D, <12 years old
- Psychosocial measures primary outcome
Does real-time CGM with remote monitoring reduce hypoglycaemia fear and improve quality of life?

- Children with T1D, <12 years old
- Psychosocial measures primary outcome

RT CGM, real-time continuous glucose monitoring.

Visit 1
- Completion of questionnaires
  - Run in: RT CGM training

Visit 2
- 3 months
  - RT CGM and standard of care insulin therapy
  - Standard care insulin therapy only

Visit 3
- 3 months
  - Completion of questionnaires
  - Standard care insulin therapy only
  - RT CGM and standard of care insulin therapy

Visit 4
- Completion of questionnaires + interview
Reduced fear of hypoglycaemia, improved family functioning and parent HRQL

**p<0.01; ***p<0.001.

HRQL, health-related quality of life; RT CGM, real-time continuous glucose monitoring.

Less parental stress and anxiety leads to better sleep

*\( p < 0.05; \) **\( p < 0.01.\)

RT CGM, real-time continuous glucose monitoring.

Burckhardt M et al, Diabetes Care (in press).
Less parental stress and anxiety leads to better sleep

* $p<0.05$; ** $p<0.01$

RT CGM, real-time continuous glucose monitoring.

Children are not just small adults and go through stages of development
Summary

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Hypoglycaemia and fear of hypoglycaemia have a major impact on diabetes care, the child and the family
Summary

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Hypoglycaemia and fear of hypoglycaemia have a major impact on diabetes care, the child and the family.

With education and applied knowledge, the incidence of hypoglycaemia can be reduced but not abolished.
Summary

Children are not just small adults and go through stages of development.

Hypoglycaemia and fear of hypoglycaemia have a major impact on diabetes care, the child and the family.

With education and applied knowledge, the incidence of hypoglycaemia can be reduced but not abolished.

Technology offers further promise to reduce the incidence and impact of hypoglycaemia in the young.
Remember, if you have questions for our speakers....

Raise your hand to have question cards collected.

Questions will be answered during the panel discussion.
Hypoglycaemia and the family

Stephanie Amiel, MD, FRCP
Professor of Diabetes Research
King’s College London
London, United Kingdom
The person with diabetes = the family with diabetes
Hypoglycaemia and the family

- Effect of hypoglycaemia on spouses
- Effect on other family members/caregivers
- Fear of hypoglycaemia and the family
- Strategies to mitigate deleterious effects
- Technology impact in families
Hypoglycaemia and the family

• Effect of hypoglycaemia on spouses
• Effect on other family members/caregivers
• Fear of hypoglycaemia and the family
• Strategies to mitigate deleterious effects
• Technology impact in families
Having a partner improves diabetes outcomes

- Cross sectional postal survey of 2419 adults (67%) attending specialist T1D services.

Graphs showing HbA1c levels and % with complications for men and women with and without partners.
Adverse effects of hypoglycaemia on relatives

N=2057 relatives; 25% T1D.

% of family members who report that diabetes is a moderate to heavy burden on the family

Proportion of family members (%, 95% CI)

N=2057 relatives; 25% T1D.
Ci, confidence interval; UK, United Kingdom; USA, United States of America.
Not just type 1 diabetes...

% of responding family members who express worry about hypoglycaemia*

2057 relatives, 25% T1D.
**“I am mainly or very worried about the risk of hypoglycaemic events in the individual with diabetes”. UK, United Kingdom; USA, United States of America.
The worry relates to the hypoglycaemia

- 23 wives, 38 husbands
- Those whose partners had experienced recent severe hypoglycaemia showed:

**NO difference in**
- Depression
- Anxiety
- Marital conflict

**MORE**
- Fear of hypoglycaemia
- Marital conflict about diabetes management
- Sleep disturbances caused by hypoglycaemia

Four types of distress:

- Management
- Role
- Emotional
- Hypoglycaemia
Scale for measuring diabetes distress in relatives of adults with T1D

Four types of distress:

- Management
- Role
- Emotional
- Hypoglycaemia

% of 317 relatives with high distress score for this item

Greater partner diabetes distress was linked with:

- Younger age
- Female gender
- Involvement in the PWD management
- Lower relationship satisfaction
- Less trust in the PWD’s physician
- Higher HbA$_{1c}$
- More frequent hypoglycaemia

PWD, person with diabetes.
Hypoglycaemia and the family

- Effect of hypoglycaemia on spouses
- Effect on other family members/caregivers
- Fear of hypoglycaemia and the family
- Strategies to mitigate deleterious effects
- Technology impact in families
Impact of hypoglycaemia on diabetes burden

DAWN2 in the Netherlands
N = 412 PWD, N = 86 family members
NSH, non-severe hypoglycaemia; PWD, persons with diabetes; SH, severe hypoglycaemia.

Odds ratios for reporting diabetes burden

- Insulin use
- NSH
- SH
- Occasional worry

PWD

Family members
The relatives report more SH......

<table>
<thead>
<tr>
<th></th>
<th>PWD</th>
<th>Partner</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of SH in last year</td>
<td>1.6</td>
<td>2.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HA</td>
<td>37%</td>
<td>35%</td>
<td></td>
</tr>
<tr>
<td>IAH</td>
<td>63%</td>
<td>65%</td>
<td></td>
</tr>
</tbody>
</table>

HA, hypoglycaemia awareness; IAH, impaired awareness of hypoglycaemia; SH, severe hypoglycaemia.
Relatives of people with problematic hypoglycaemia

- Fear and worry about safety
- Physical and emotional impact of caring for a person with HU
  - Exhaustion
    - Disrupted sleep
  - Neglecting one’s own health and social needs
  - Resentment and ambivalence
    - Used as a safety net
- Education, information, and support needs

Being very careful not to let... grab me. ... strength is huge at that point... I do get physically afraid. I won’t let... hold my hand
Relatives of people with problematic hypoglycaemia

- Fear and worry about safety
- Physical and emotional impact of caring for a person with HU
  - Exhaustion
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    - Used as a safety net
- Education, information, and support needs

I just don’t have a social life

HU, hypoglycaemia unawareness.
Relatives of people with problematic hypoglycaemia

- Fear and worry about safety
- Physical and emotional impact of caring for a person with HU
  - Exhaustion
    - Disrupted sleep
  - Neglecting one’s own health and social needs
  - Resentment and ambivalence
    - Used as a safety net
- Education, information, and support needs

As soon as we get home and... relaxes,... nearly always has a hypo....
Children of adults with diabetes

- 51 adults with diabetes, 22% T1D
- 15.7% reported child carers, age range 5 – 18 years
  - planning meals
  - drawing up or administering medications,
  - testing blood glucose
  - interpreting results
  - transporting
Children of adults with diabetes

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- 15.7% reported child carers, age range 5 – 18 years
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  - interpreting results
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<table>
<thead>
<tr>
<th>Activity</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Provide juice or food if hypoglycaemic</td>
<td>12</td>
<td>23</td>
<td>35</td>
<td>68.6</td>
</tr>
<tr>
<td>Meal planning or preparation</td>
<td>8</td>
<td>19</td>
<td>27</td>
<td>52.9</td>
</tr>
<tr>
<td>Stay with adult at night or when ill</td>
<td>8</td>
<td>16</td>
<td>24</td>
<td>47.1</td>
</tr>
<tr>
<td>Promote activity</td>
<td>8</td>
<td>14</td>
<td>22</td>
<td>43.1</td>
</tr>
<tr>
<td>Draw up insulin, lay out medication</td>
<td>3</td>
<td>11</td>
<td>14</td>
<td>29.4</td>
</tr>
<tr>
<td>Check feet</td>
<td>7</td>
<td>8</td>
<td>15</td>
<td>27.5</td>
</tr>
<tr>
<td>Call to check on adult</td>
<td>5</td>
<td>8</td>
<td>13</td>
<td>25.5</td>
</tr>
<tr>
<td>Perform glucose testing</td>
<td>3</td>
<td>7</td>
<td>10</td>
<td>19.6</td>
</tr>
<tr>
<td>Provide transportation</td>
<td>6</td>
<td>3</td>
<td>9</td>
<td>17.6</td>
</tr>
<tr>
<td>Serve as interpreter (English/Spanish)</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td>11.8</td>
</tr>
<tr>
<td>Give insulin injections</td>
<td>1</td>
<td>4</td>
<td>5</td>
<td>9.8</td>
</tr>
</tbody>
</table>
When the teenager has diabetes

- Personal distress*
- Teen management distress*
- Parent/teen relationship
- Healthcare team-related

*associated with hypoglycaemia.
Impact of Fear of Hypoglycaemia in parents of young children:

- Experience of severe hypoglycaemia increases monitoring and fear
- Hypoglycaemia at night and in social situations more distressing
- Maternal depression and anxiety related to fear of hypoglycaemia

- Nocturnal monitoring
- Accepting or driving higher blood glucose
Hypoglycaemia and the family

- Effect of hypoglycaemia on spouses
- Effect on other family members/caregivers
- Fear of hypoglycaemia and the family
- Strategies to mitigate deleterious effects
- Technology impact in families
Helping the family with hypoglycaemia

- The hypoglycaemia treatment pathway for the PWD
- Elimination of contributory health factors
- Structured education in flexible insulin therapy
- Technology
  - Pumps
  - CGM
  - Automated insulin adjustment algorithms
- Transplantation

Reassess every 3–6 months

Advance therapy if not to target
(No SH in past 3–6 months and HbA$_1c$ ≤8% and Clarke Score <4)

Consider first line
- Structured education for MDI with SMBG
  or
- Hypoglycaemia-specific education

Consider second line
- CSII with SMBG
  or
- MDI with RT-CGM

Consider third line
- SAP without LGS
- SAP with LGS
  or
- Very frequent contact (weekly for 3–4 months)

Consider fourth line
- Islet transplant
  or
- Pancreas transplant

Level 1–2 evidence

Level 3–4 evidence

CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion; LGS, low glucose suspend; MDI, multiple daily injection; PWD, persons with diabetes; RT-CGM, real-time continuous glucose monitoring; SAP, sensor-augmented pump; SH, severe hypoglycaemia; SMBG, self-measured blood glucose.

Psychological barriers to hypoglycaemia avoidance

SH risk
Low

IAH, impaired awareness of hypoglycaemia; SH, severe hypoglycaemia.
Psychological barriers to hypoglycaemia avoidance

Psychological barriers to hypoglycaemia avoidance

<table>
<thead>
<tr>
<th>SH risk</th>
<th>Concern</th>
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<tbody>
<tr>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>High</td>
<td>Low</td>
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Psychological barriers to hypoglycaemia avoidance

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<th>Attitudes to awareness</th>
<th>HA</th>
<th>IAH</th>
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<tr>
<td>Asymptomatic hypoglycaemia normalised</td>
<td>2 (0.25–3)</td>
<td>1 (0–3)</td>
</tr>
<tr>
<td>Hypoglycaemia concern minimized</td>
<td>2 (1–4)</td>
<td>4 (2–6)*</td>
</tr>
<tr>
<td>Hyperglycaemia avoidance prioritized</td>
<td>4 (3–5.75)</td>
<td>6 (4–7)*</td>
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Hypoglycaemia and the family

- Effect of hypoglycaemia on spouses
- Effect on other family members/caregivers
- Fear of hypoglycaemia and the family
- Strategies to mitigate deleterious effects
- Technology impact in families
Impact of technology for partner on spouse

问答研究，74名伴侣
CGM，连续血糖监测；SAP，传感器增强泵；SMBG，自我测量血糖。
“Providers should consider an assessment of symptoms of diabetes distress, depression... including caregivers and family members in this assessment.”
“Providers should consider an assessment of symptoms of diabetes distress, depression... including caregivers and family members in this assessment.”

Providers should consider including caregivers and family members
Concluding remarks

Simon Heller, BA, MB, Bchir, DM, FRCP
Professor of Clinical Diabetes
University of Sheffield
Director of Research and Development and
Honorary Consultant Physician
Sheffield Teaching Hospitals NHS Foundation Trust
Sheffield, United Kingdom
Please remember to complete your evaluation form

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- Module II – Patient Education Goals
- Module III – Impaired Awareness
- Module IV – CVD
- Spanish, French, Hindi, Mandarin and Arabic

Today’s symposium will also be available on our website
Follow us on Twitter and LinkedIn to stay up to date on the latest updates from the IHSG
Summary and adjournment
Hypoglycaemia: a problem with many faces

A Symposium on the occasion of the 54th Annual Meeting of the European Association for the Study of Diabetes

3 October 2018
Berlin, Germany

Brought to you by members of the International Hypoglycaemia Study Group