

# Hypoglycaemia – a 24-hour concern

More than just a health concern, hypoglycaemia impacts every aspect of life for people with diabetes. Reducing the risk of hypoglycaemia is a shared responsibility, with significant benefits for patients, families and society at large.

PHYLLISA DEROZE  
Phyllisa has type 2 diabetes  
United Arab Emirates

*“To not have hypoglycaemia would mean my world wouldn’t have to stop for diabetes, because that’s what happens with hypoglycaemia, my world completely stops, like nothing else matters. Whatever I’m doing, taking my daughter to school, cooking, normal things, when hypos kick in, my world must stop.”*

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“It’s the worst when I’m asleep. It doesn’t happen straight away – it’s usually at 2, 3, maybe even 4 o’clock. So they’re never this side of midnight. When I’m having a fit, when my sugar’s that low, I’m flailing my arms, kicking my legs, sweating quite a bit. Kate would try and calm me down, but to try and get someone to drink something when they’re fitting – I would imagine it’s extremely difficult, I would be terrified. If she can’t wake me up that’s when she might need extra assistance. Usually the first thing I remember is the lights are on, there’s three, four strangers in green jumpsuits trying to give me a sugary drink. You’re hearing things but you’re not really listening – that sense of not knowing what’s going on, it’s not a very nice feeling. No one wants to call the paramedics out, especially for what I think is a minor nuisance to them, whereas they could be helping someone else with life-threatening injuries. I always feel guilty; I think it’s something I could’ve prevented just by taking a bit more care. If my sugar goes much lower and I end up in a coma, then that’s my biggest worry.”

JONATHAN FERNANDES  
Jonathan has type 1 diabetes  
UK

## INFOBOX 1

### What is hypoglycaemia?

**Diabetes** is characterised by the absence or inadequate production of insulin and the inability of the body to respond fully to insulin.<sup>1</sup> Untreated, this condition leads to high blood sugar levels (hyperglycaemia), which is associated with an increased risk of diabetes-related complications such as kidney and cardiovascular diseases, stroke, amputations and blindness.<sup>1</sup> The most common forms of diabetes are types 1 and 2. Type 1 diabetes typically occurs in children and adolescents, and is a condition in which the body produces little or no insulin. Type 2 diabetes is seen primarily in adults and accounts for approximately 90% of all cases of diabetes.<sup>1</sup>

Keeping blood sugar at normal or near-normal levels is the target of diabetes treatment. To achieve good control of blood sugar, many people depend on insulin treatment. For people with type 1 diabetes, who produce very little or no insulin at all,<sup>1</sup> insulin is vital for survival. While strict blood sugar control is shown to reduce the risk of long-term complications, it may also increase the risk of hypoglycaemia.<sup>2</sup>

**Hypoglycaemia** is a state where there are low levels of glucose (sugar) in the blood. It may occur when a person with diabetes eats too little food, exercises without adequate nutrition or takes too much medicine. Insulin and sulfonylureas are among the common treatments associated with increased risk of hypoglycaemia.<sup>1,3</sup>

A person with hypoglycaemia may feel nervous, shaky, weak or sweaty, and may experience headache, blurred vision and/or hunger. Low sugar levels in the brain may result in confusion, concentration challenges, difficulty speaking and unusual behaviour.<sup>4</sup>

A hypoglycaemic event may be characterised as mild,<sup>A</sup> moderate<sup>B</sup> or severe.<sup>C,5</sup> Mild and moderate hypoglycaemic events (non-severe) usually do not require assistance from other people,<sup>6</sup> while severe hypoglycaemia is associated with serious cognitive impairment, requires assistance and may lead to seizure, coma, loss of consciousness or death.<sup>5</sup>

**A:** Mild hypoglycaemia or glucose alert value hypoglycaemia (BG  $\leq$  3.9 mmol/l ( $\leq$  70 mg/dl)).  
**B:** Moderate hypoglycaemia or clinically important hypoglycaemia (BG  $<$  3.0 mmol/l ( $<$  54 mg/dl)).  
**C:** Severe hypoglycaemia has no specific glucose threshold and requires external assistance for recovery.<sup>5</sup>

# EXECUTIVE SUMMARY:

Hypoglycaemia is common



**83%**

of people with type 1 diabetes experience at least one hypoglycaemic event per month<sup>7</sup>

**47%**

of people with type 2 diabetes experience at least one hypoglycaemic event per month<sup>7</sup>

Hypoglycaemia is costly



**GBP 468m**

is the annual direct cost of hypoglycaemia in the UK<sup>8</sup>

**GBP 399m**

is the annual indirect cost of hypoglycaemia in the UK<sup>8</sup>

## For patients and their families, hypoglycaemia is a 24-hour concern

Increased risk of cardiovascular disease, dementia, depression and death (p 14)

**2.7**

times increased risk of cardiovascular death with severe hypoglycaemia among people with type 2 diabetes<sup>9</sup>



Health

Learning and productivity at work are impaired (p 8)

**8.6 and 3.6**

productive days are lost by people with type 2 and people with type 1 diabetes respectively due to a severe hypoglycaemic event<sup>10</sup>



Study/work

Family life and recreation are challenged (p 12)

**61%**

of family members are worried about the risk of hypoglycaemia to their loved one<sup>11</sup>



Social life

Quality of sleep and next-day functioning are decreased (p 10)

**70%**

of people feel tired the day after a night-time event<sup>12</sup>



Sleep

Hypoglycaemia risk can be reduced without compromising long-term health through...



1. Enhanced support for patients, families and caregivers with direct family involvement in patient care.



2. The newest diabetes treatments and monitoring devices that enable good blood sugar control while minimising the risk of hypoglycaemia.



3. Establishing a shared understanding of the burden of hypoglycaemia and ensuring that it is properly taken into account in diabetes care.

# Hypoglycaemia is an underestimated complication of diabetes care

Hypoglycaemia is a well-known consequence of life-saving diabetes treatment. However, the actual extent of the problem and the burden on patients, families and society is poorly understood.

Today, 425 million people, double the number in 2005,<sup>1</sup> live with diabetes, and this figure is projected to grow to 629 million by 2045.<sup>1</sup>

## Few live without complications

The Rule of Halves<sup>13</sup> states that only half of those living with diabetes are aware of their condition. Of those who are diagnosed, only half receive care, and of those, half achieve recommended treatment targets. Just half of this group – approximately 6% of all people with diabetes – live without complications. Some diabetes-related complications are long term, such as kidney and cardiovascular diseases, stroke, amputations and blindness.<sup>1</sup> Other complications, such as hypoglycaemia, are a daily concern related to managing diabetes.



only 6%

of all people with diabetes live without complications<sup>13</sup>

## Hypoglycaemia occurs frequently

Hypoglycaemia (Infobox 1, p 2) is a condition in which the blood sugar falls to below-normal levels. It is a common consequence of diabetes treatment.<sup>1,3</sup> 88% of hypoglycaemic events are mild to moderate<sup>14</sup> and, generally, patients can manage these events on their own. During a severe event, patients require assistance. Severe events may lead to seizure and coma.<sup>4</sup> There is no common understanding of the scope of the problem. Across studies, hypoglycaemia incidence rates, of any severity, vary widely – from 18 to 138 events and ▶



“Hypoglycaemia is seen as a side effect of taking insulin. Like with other medication, you may experience this or the other. So, it's a normal side effect and you don't know that it's something that should be reported, so you don't. No one ever told me that I need to report my hypoglycaemia.”

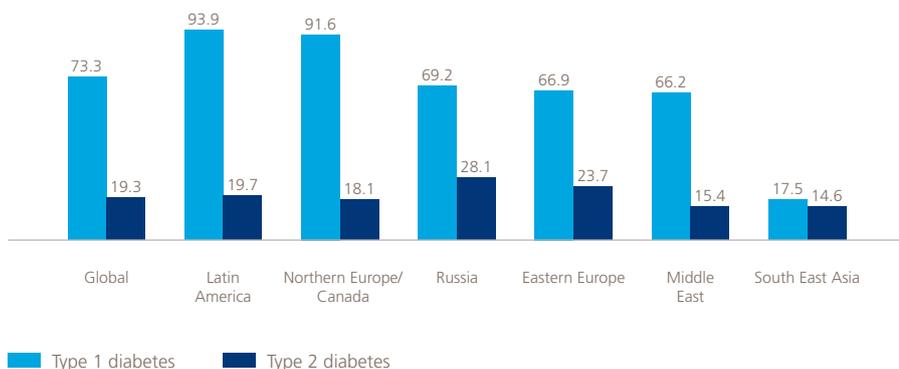
PHYLLISA DEROZE

Phyllisa has type 2 diabetes  
United Arab Emirates

FIGURE 1 – HYPOGLYCAEMIA RATES

## 73.3 and 19.3 hypoglycaemic events are experienced every year by people with type 1 and type 2 diabetes respectively<sup>7</sup>

Estimated annual hypoglycaemia rates



from one to 45 events per patient per year for people with type 1 and type 2 diabetes respectively.<sup>15</sup> Recently, a global study known as HAT concluded that, among people with type 1 and type 2 diabetes, 83% and 47% respectively experienced at least one hypoglycaemic event per month.<sup>7</sup> Patients experienced multiple events of varying severity per year (Figure 1).<sup>7</sup>

### Often unreported by patients

In the HAT study, patients reported fewer events than the number that actually occurred (Figure 2). This is consistent with evidence that patients do not notice most events,<sup>16</sup> which may lead to preventing people with diabetes to timely adjust their



83%

of hypoglycaemic events go unnoticed by the patient<sup>16</sup>

treatment, nutrition or exercise regimen in a timely manner, thereby ensuring good blood sugar control.

Furthermore, repeated events can cause the body to stop producing warning signs that blood sugar levels are falling.<sup>17</sup> When this happens, a person's risk of severe

events increases.<sup>19</sup> In one study, the frequency of severe events was 17-fold greater in people without symptoms compared with those with normal awareness of hypoglycaemia.<sup>19</sup>

Severe events tend to lead to even more severe events. Recurrent events may also impair the body's response to hypoglycaemia.<sup>20</sup>

Better awareness of hypoglycaemia may improve health outcomes, but many people do not discuss hypoglycaemia with their doctor<sup>21</sup> (see more on pp 11 and 16).

### Complications are costly

The negative effects of diabetes complications in general and hypoglycaemia in particular can be measured in both human and economic terms. Diabetes-related complications have a major negative impact on people's quality of life.<sup>22</sup> In fact, of the 425 million people with diabetes, 327 million are in their productive years – between the ages of 20 and 64<sup>1</sup> – posing challenges to health systems and economies worldwide. 71 million healthy life years are lost due to diabetes-related disability and death each year.<sup>23,A</sup> Furthermore, approximately 4 million people die from diabetes and its complications each year. Nearly half of these people are under the age of 60.<sup>1</sup> In 2016, diabetes ranked seventh in the top 10 global causes of death.<sup>24</sup>

FIGURE 2 – UNDERREPORTING

### Many cases of hypoglycaemia are not reported<sup>7,18</sup>

Estimated annual hypoglycaemia rates



A: DALY (disability adjusted life year) is a measure of overall disease burden, expressed as the cumulative number of years lost due to ill health, disability or early death.<sup>25</sup>

## Reducing hypoglycaemia may...

### ... save lives



185,000 life years

could be saved in the UK by people with type 2 diabetes maintaining good blood sugar control and avoiding hypoglycaemia using the newest treatments<sup>26</sup>

### ... save money



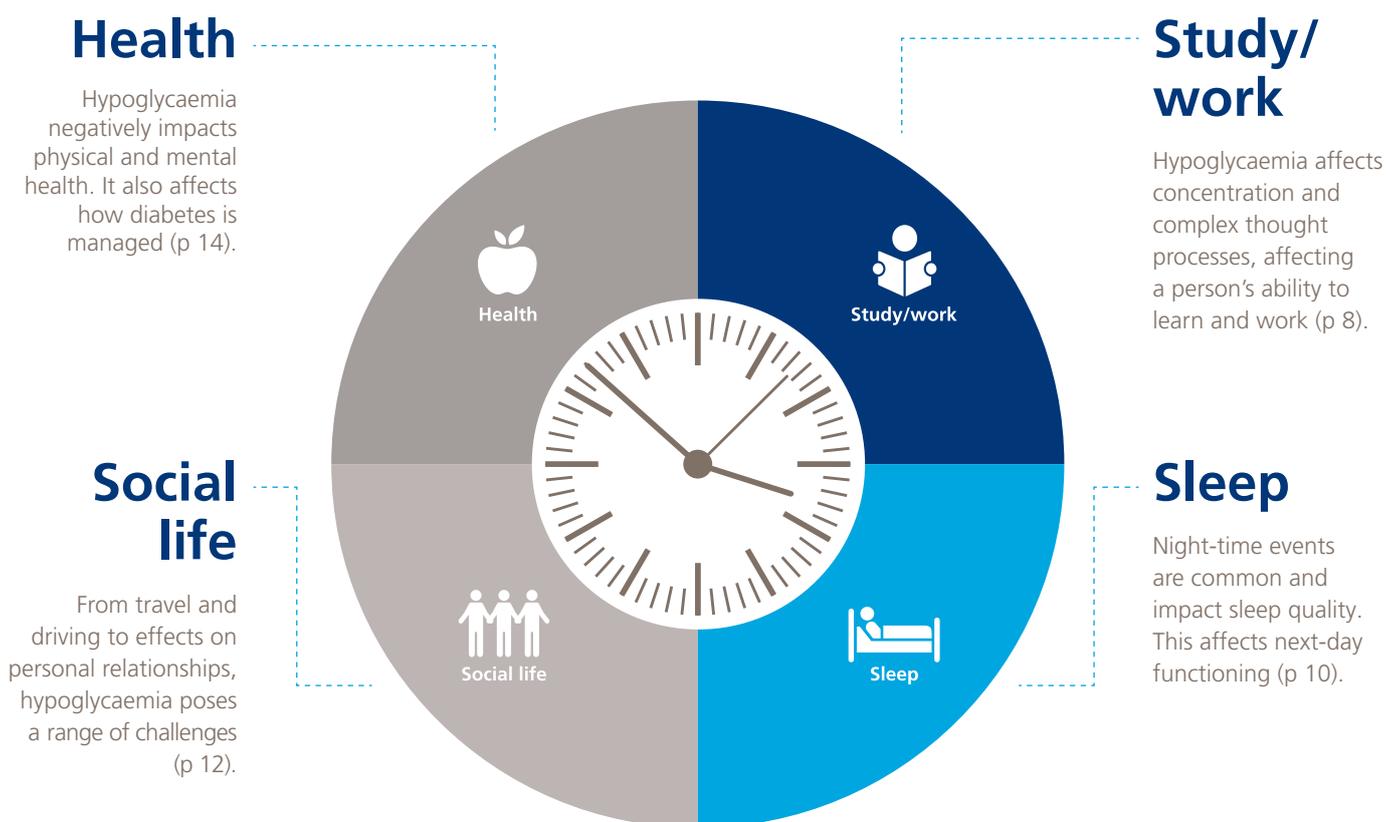
GBP 117m

could be saved annually if hypoglycaemia rates in the UK were reduced by 25%<sup>8</sup>

## ... alleviate the burden for patients, their families and society.

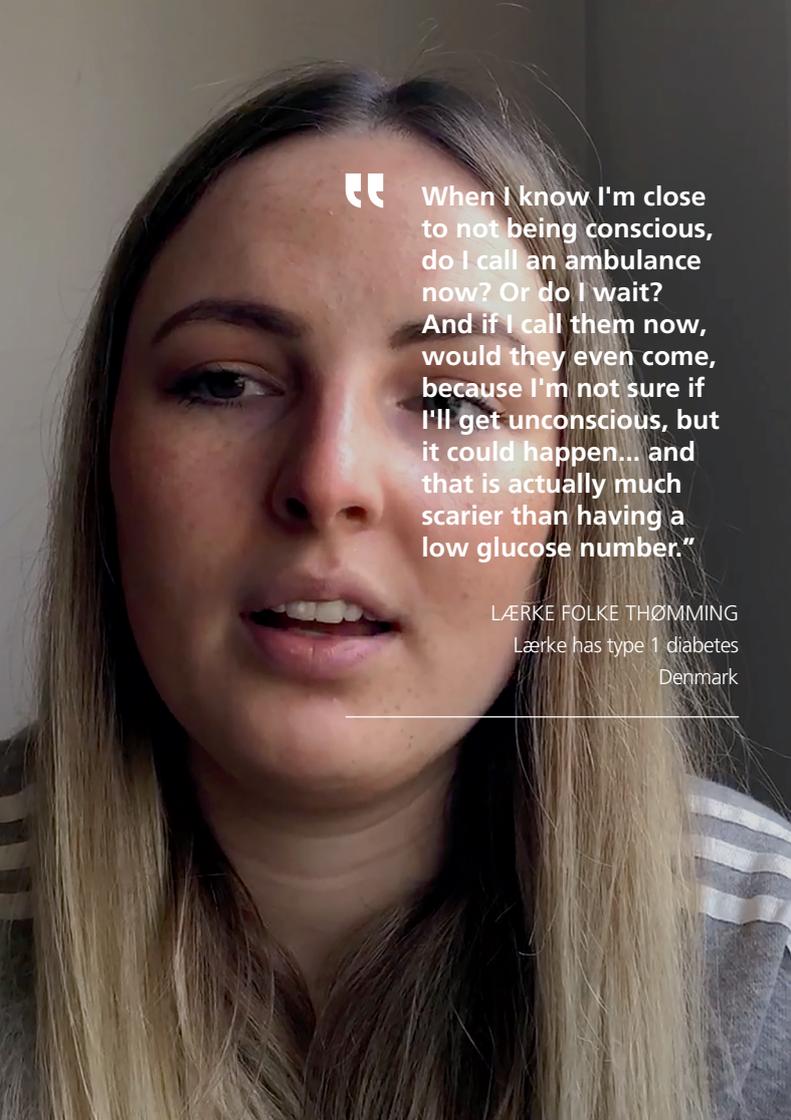
# Hypoglycaemia is a 24-hour concern that impacts all aspects of life

Hypoglycaemia can happen at any time of the day or night, affecting a person's physical, mental and social functioning. The health impact can be profound, and its cumulative effect on healthcare costs is substantial.



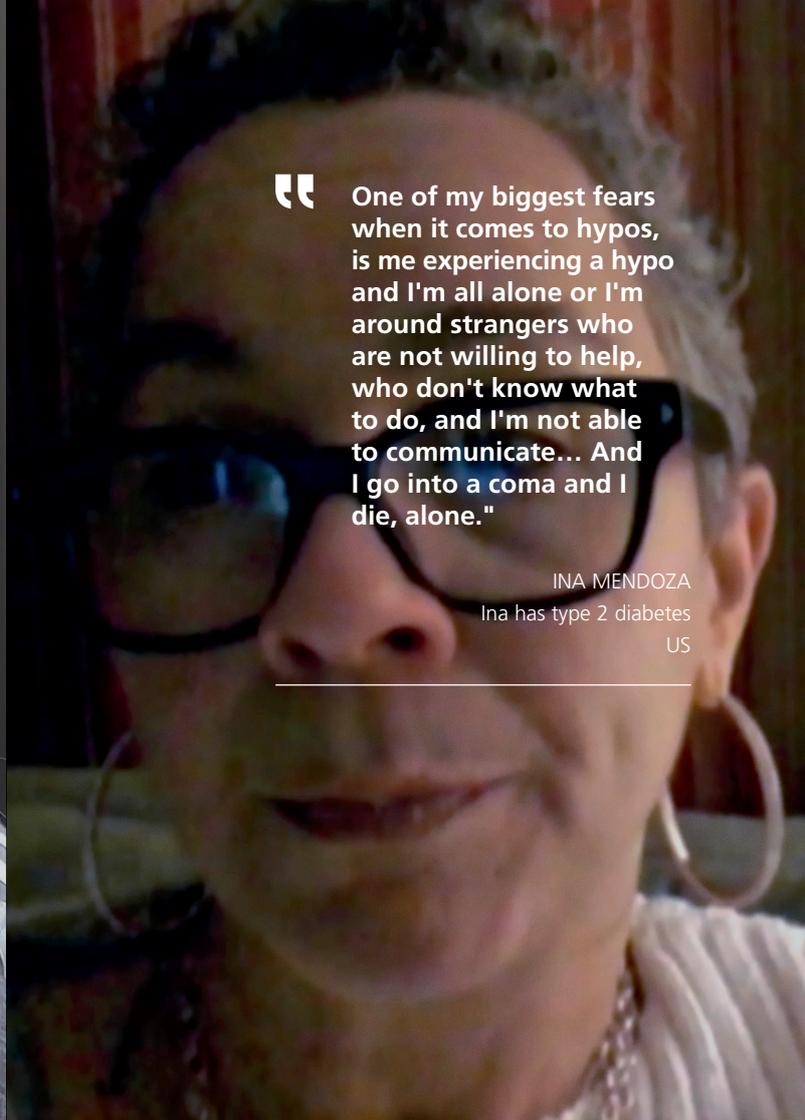
## COSTS

Hypoglycaemia poses a significant economic burden. Costs are incurred when healthcare resources are used to treat a hypoglycaemic event (direct costs) and also when absence from work results in lost productivity (indirect costs) (p 18).



“ When I know I'm close to not being conscious, do I call an ambulance now? Or do I wait? And if I call them now, would they even come, because I'm not sure if I'll get unconscious, but it could happen... and that is actually much scarier than having a low glucose number.”

LÆRKE FOLKE THØMMING  
Lærke has type 1 diabetes  
Denmark



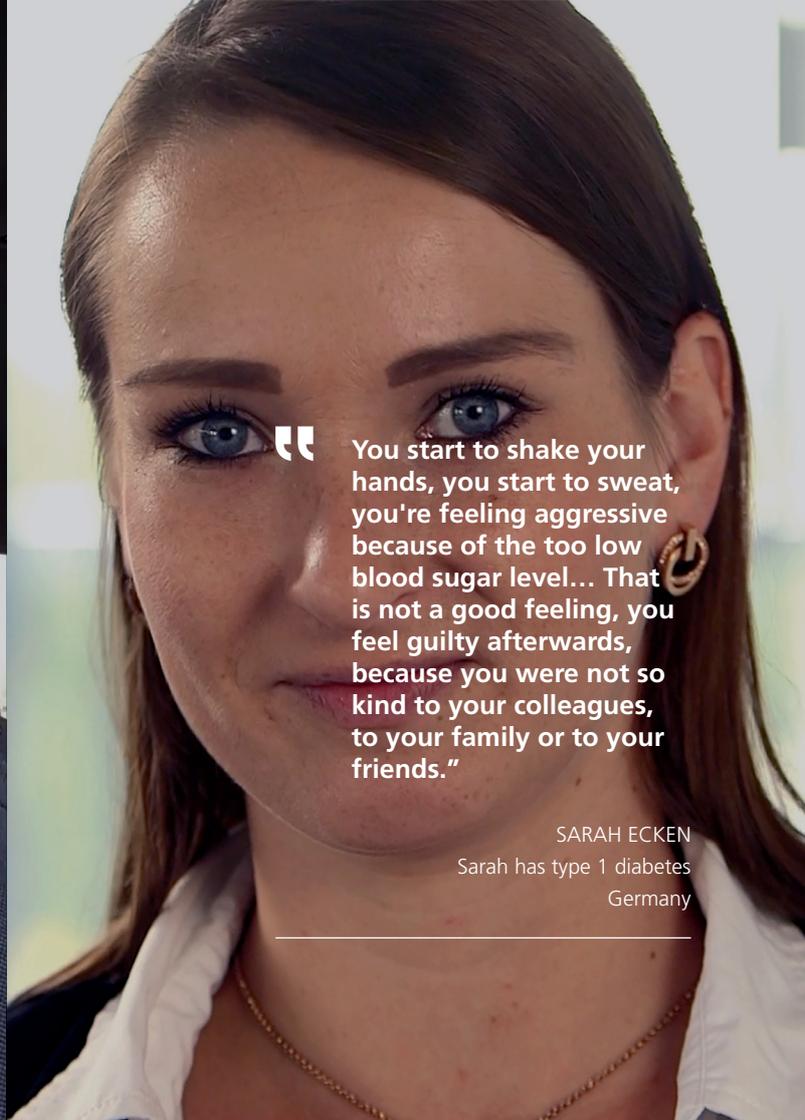
“ One of my biggest fears when it comes to hypos, is me experiencing a hypo and I'm all alone or I'm around strangers who are not willing to help, who don't know what to do, and I'm not able to communicate... And I go into a coma and I die, alone.”

INA MENDOZA  
Ina has type 2 diabetes  
US



“ It was a frightening experience, but one which made me monitor my blood glucose levels much more intensely, and made me take care of my diabetes even more.”

STEPHEN MATHERS  
Stephen has type 2 diabetes  
UK



“ You start to shake your hands, you start to sweat, you're feeling aggressive because of the too low blood sugar level... That is not a good feeling, you feel guilty afterwards, because you were not so kind to your colleagues, to your family or to your friends.”

SARAH ECKEN  
Sarah has type 1 diabetes  
Germany

# Learning and productivity are impaired by hypoglycaemia

Hypoglycaemia affects mental processes, such as the ability to focus and solve problems. Whether an event occurs during the daytime or at night, its impact on productivity is substantial.

Moderate and severe hypoglycaemia can affect brain functions that influence a person's ability to learn and work<sup>27</sup> (Infobox 2).

### Reduced cognitive function

In particular, hypoglycaemia weakens a person's ability to remain alert and focused over a period of time. It has a negative impact on a person's capacity to respond rapidly, apply complex thought processes and multitask.<sup>27,28</sup>

Hypoglycaemia also affects memory. One concern is the impact on short-term and working memory, which govern a person's intellectual and problem-solving abilities.<sup>28</sup> Another concern is the effect on spatial long-term memory, which influences the ability to remember where something is located or to navigate from one place to another.<sup>29</sup>

### Learning disabilities may result

There is evidence that hypoglycaemia affects mental processes in children. One study showed that the time children needed to carry out mental arithmetic and make simple choices was significantly longer during an event.<sup>30</sup>



**17% fewer**

**young people with type 1 diabetes completed their 12th year of education compared with healthy individuals, according to a study from Australia<sup>32</sup>**

Further research suggests that the cognitive effects associated with severe hypoglycaemia during childhood may persist into adulthood.<sup>31</sup> In one study, adults who had type 1 diabetes as young children scored lower in tests that measured their ability to think abstractly, use logic, solve problems and manage time than adults whose type 1 diabetes developed later in life.<sup>33</sup> Another study found an association between repeated events of hypoglycaemia and a lasting negative impact on verbal and full-scale IQs.<sup>32,A</sup> Lower scores in tests of cognitive skills may also be an indicator of lower earning potential. The wages of adults who score lower in cognitive tests are, on average, 8.3% lower.<sup>34</sup>



“For me, [emotional challenges] are motivation to make a cognitive recognition that you're hypoglycaemic. Prior to making a decision, you need to wait 15 minutes to allow your blood sugar to rise. Like at work, if I'm seriously low, I can lose all motivation; I need to realise that I'm fine, it's all going to be good, just eat some smarties, candies or glucose tablets, and you'll be good to go.”

GARRETT JENSEN

Garrett has type 1 diabetes  
US

### INFOBOX 2

### Cognitive functions affected<sup>28,29,31</sup>



Attention



Memory



Complex thought processing



Spatial ability



Verbal function

A: IQ (intelligence quotient) is a score designed to assess human intelligence.<sup>35</sup>

# STUDY/WORK:

The disruption to daily activities caused by hypoglycaemia is measured not only in response time but also in recovery time. While it takes a couple of hours to recognise and respond to an event,<sup>6</sup> it takes 11 hours to recover from a mild or moderate daytime event. When the event occurs during sleep, recovery time is considerably longer – 16 hours.<sup>36</sup>

## Events reduce productivity

Figure 3 illustrates the impact of mild or moderate hypoglycaemia. For severe events, lost work time may be much greater.



**twice as many**

**people who reported symptoms of hypoglycaemia retired because of their health, according to a Swedish study<sup>37</sup>**

In a different study, respondents with type 1 diabetes said that after a severe event, they lost, on average, 3.6

productive days. For people with type 2 diabetes, the loss was 8.6 days.<sup>10</sup>

## Caregivers lose work hours

Productivity losses extend to caregivers as well. A person who provides assistance to someone who is having a hypoglycaemic event loses 1.76 productive hours per event on account of telephone calls, extra travel and missed work time.<sup>38</sup>

## Employment prohibitions

In certain occupations, for example operating heavy machinery or working at heights or underwater, hypoglycaemia may pose risks to both the person experiencing the event and those nearby.<sup>39</sup> This has led to employment prohibitions. While such risks are not acceptable in some types of employment, the overall incidence of severe hypoglycaemic events in the workplace is low. Consequently, blanket restrictions on the employment of people with insulin-treated diabetes may not be justified.<sup>39</sup>

Furthermore, lack of awareness about diabetes, including hypoglycaemia, in the workplace may lead to discrimination against people with diabetes. Therefore, it is common for people with diabetes not to disclose or talk about their condition at work.<sup>40</sup>



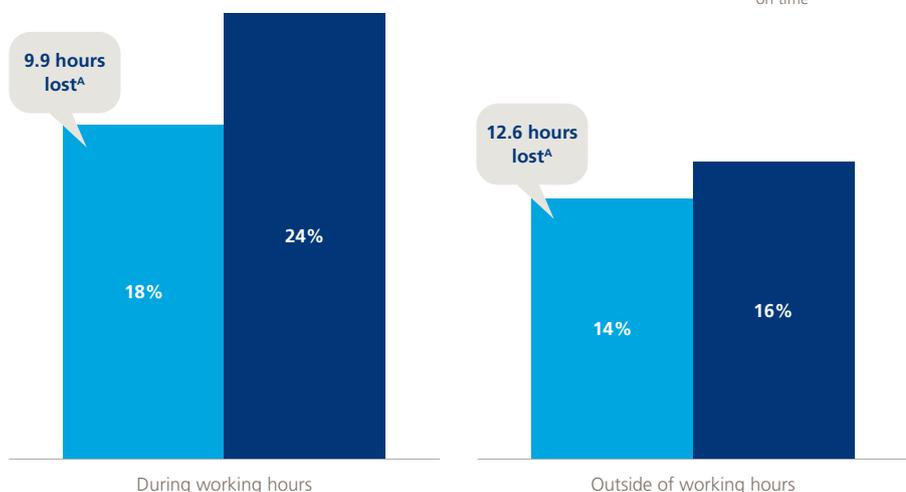
“My main concern around hypos is that I’m a private hired licence driver, and I need to maintain my blood glucose readings between two agreed levels whilst driving. My fears are that one day I wouldn’t be able to manage that.”

STEPHEN MATHERS  
Stephen has type 2 diabetes  
UK

FIGURE 3 – IMPACT OF MILD OR MODERATE HYPOGLYCAEMIA ON PRODUCTIVITY

## 12.6 hours of work lost after a hypoglycaemic event that occurs outside of working hours<sup>14</sup>

% of people reporting lost productivity after a mild or moderate event



A: Average missed working time among people with type 1 or type 2 diabetes.

## SLEEP:

# Hypoglycaemia at night is a common but silent danger

Sleep decreases a person's ability to recognise and respond to hypoglycaemia. Night-time events rob people of sleep and alter their ability to function the next day. Falls and injuries at night are an increasing concern.

A hypoglycaemic event can occur at any time of day or night. An event that occurs while sleeping at night is called nocturnal hypoglycaemia and carries its own unique set of health risks (Infobox 3).

### Hypoglycaemia at night is common

As with hypoglycaemia incidence in general, studies vary regarding the occurrence of night-time events.<sup>15</sup> In one study of more than 20,000 people in nine countries in Western Europe, the US and Canada, 10.4% of people with diabetes reported having a mild or moderate night-time event in the previous month.<sup>12</sup>

Among this group, events tended to occur frequently: 62% of people with type 1 diabetes and 54% of people with type 2 diabetes experienced night-time events at least several times a month.<sup>12</sup>

A larger study of patients in 24 countries on all six continents found that more than four out of 10 people with type 1 diabetes experience a night-time event of any severity at least once a month. The same is true for one in six people with type 2 diabetes.<sup>7</sup>

Night-time hypoglycaemia incidence in young children is almost 40%.<sup>41</sup> Children under the age of five may experience double the incidence of hypoglycaemia compared with older children.<sup>41</sup> Many of these events go undetected by their caregivers.<sup>41</sup>



**41% and 16%**

**of people with type 1 and type 2 diabetes respectively experience night-time hypoglycaemia at least once a month<sup>7</sup>**

### Night-time events impact sleep

Sleep plays a critical role in optimal functioning. Sleep deprivation is associated with impairment of cognitive function,<sup>42</sup> increases in body mass index and obesity, hypertension and cardiovascular disease. Not having enough sleep is also a risk factor for ▶



“My family and friends are really frightened because of hypoglycaemia. They've heard some stories like, 'she did not wake up in the morning, she died'. So, I have to text my parents and friends in the morning that I'm fine.”

SARAH ECKEN

Sarah has type 1 diabetes  
Germany

### INFOBOX 3

## Why are night-time events critical?

A person who is asleep is less able to treat a hypoglycaemic event. During sleep, organ function and brain activity decrease. Sleep also suppresses the body's natural response to an event.<sup>43</sup> Consequently, during sleep, a person is less likely to notice symptoms of hypoglycaemia.<sup>44</sup> In fact, the risk of severe events is higher during sleep because of the absence or diminished intensity of symptoms.<sup>39,44</sup>

In some cases – especially during deep sleep stages – people do not wake up to treat the night-time event.<sup>12</sup>

**50%**  
of severe events in people with type 1 diabetes occur at night<sup>27</sup>

**11%**  
of those who experienced mild or moderate hypoglycaemia during sleep did not wake up during the night<sup>12</sup>

# SLEEP:

diabetes and prediabetes,<sup>12</sup> a condition where blood sugar is higher than normal but not high enough to be called diabetes.

Mild or moderate night-time events can diminish the quality and duration of sleep (Figure 4).<sup>36</sup> People who woke up during a mild or moderate night-time event reported a moderate impact on their sleep. For most people, it took a while to fall back to sleep, and more than 10% of respondents did not get back to sleep at all.<sup>12</sup>

In some rare cases, younger people with type 1 diabetes who experienced night-time severe hypoglycaemia have been reported to die from a rare occurrence called dead-in-bed syndrome, which may be induced by hypoglycaemia.<sup>45,46</sup> One study concludes that around 6% of deaths among people with diabetes below the age of 40 may be attributable to dead-in-bed syndrome.<sup>47</sup>

## Day-after functioning is difficult

The day after a poor night's sleep, it can be hard for any person to function well.

This is also true for people who experience mild to moderate hypoglycaemia at night. For these people, next-day fatigue, reduced energy levels, daytime sleeping and difficulty concentrating are common.<sup>48</sup> Being tired also has a societal impact through productivity loss (Figure 5).<sup>14</sup> Night-time events create more fear and anxiety than events during the day and have been linked to greater productivity loss than many other events that occur in the workplace.<sup>12</sup>



## 70% of people

feel tired the day after a night-time event<sup>12</sup>

## Falls and injuries may result

It is becoming clear that falls and injuries at night may be related to hypoglycaemia.<sup>12</sup> Approximately 7% of those who had a mild or moderate event at night say they

tripped or fell during the event and, of these, 31% were injured. More than a quarter of these injuries required a visit to a doctor or healthcare professional.<sup>12</sup> This is of particular concern in the elderly, for whom falls are a risk of serious health issues or death.<sup>12</sup> See p 17 for more information about the association between hypoglycaemia and falls.

## Night-time events impact partners

The person who experiences a night-time event is not alone in losing sleep. Often, those who share a bed with the affected individual wake up because of their partner's restless sleep or are woken up for help (Figure 6).<sup>12</sup>

## Doctors do not always ask

Of those people who experience night-time events, 24.5% say their doctors do not ask about them during routine appointments. Approximately 17% say they receive advice on how to manage night-time hypoglycaemia that does not work for them.<sup>12</sup>

FIGURE 4 – QUALITY OF SLEEP

## 3 out of 10 people had a good night's sleep after a night event<sup>36</sup>

How much did this mild or moderate hypoglycaemia at night impact your sleep quality? Did you feel like you had a good night's sleep compared with a normal night?

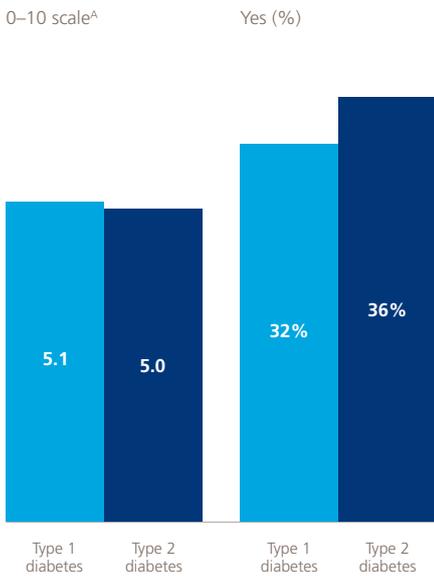


FIGURE 5 – IMPACT ON WORK

## 1 in 4 people missed work time after a night-time event<sup>14</sup>

Missing work time Missing a meeting/appointment or not finishing a project on time

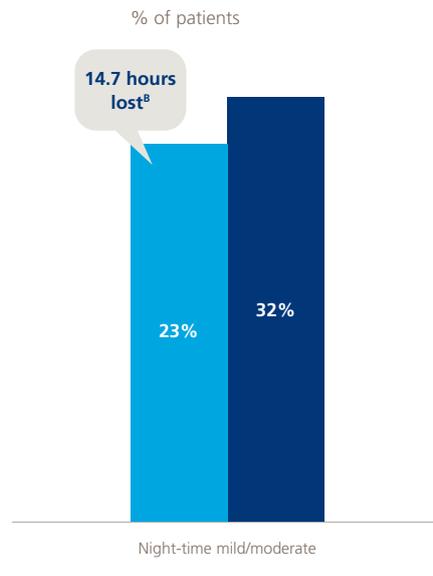
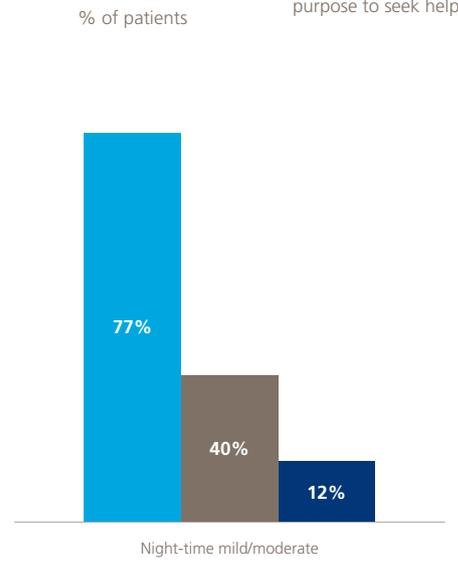


FIGURE 6 – IMPACT ON FAMILY

## 40% of people unintentionally woke others<sup>12</sup>

On the night of the event: Made an effort not to wake others Unintentionally woke others Woke others on purpose to seek help



A: 0 – The event did not affect my sleep quality at all. 10 – The event prevented me from getting back to sleep. B: On average, among those who missed work time.

## SOCIAL LIFE:

# Quality of personal relationships and social life is affected

Hypoglycaemia can create tension in families and other relationships. Low blood sugar may also complicate driving, travelling and taking part in sport or other leisure activities.

As the frequency and severity of hypoglycaemia increases, so quality of life decreases (Figure 7).<sup>10</sup> One of the most emotionally trying aspects of this may be how events, whether actual or anticipated, create stress in families.

### A fragile home environment

Hypoglycaemia negatively impacts mood and motivation, promotes erratic behaviour and provokes anger.<sup>28</sup> Emotional fluctuations such as these often affect interpersonal relationships, work performance or social activities.<sup>28</sup>

The psychosocial consequences of hypoglycaemia on family life are uniquely individual and, from a scientific standpoint, not well understood.<sup>4</sup> Anecdotal evidence and personal stories, however, suggest that the stress of dealing with events of severe hypoglycaemia disrupts domestic life and can even lead to marital breakdown.<sup>4</sup> When a patient or caregiver feels helpless to prevent further events of hypoglycaemia, tension and anxiety may only increase. For women with diabetes and their families, having a child may

be challenging. Pregnancy may lead to an increased risk of hypoglycaemia and associated complications.<sup>4</sup> However, with modern treatment methods, healthy pregnancy is possible.<sup>4</sup>



## 61% of family

members are worried about the risk of hypoglycaemia to their loved one<sup>11</sup>

### The entire family is affected

Hypoglycaemia leads to family stress in other ways (Infobox 4). As with people with diabetes (see p 9), family members are often affected in economic terms because of reduced job productivity.<sup>38</sup> Many find themselves emotionally unprepared for the often inevitable changes in their loved one's behaviour and family life. Fatigue and burnout are common.<sup>49</sup>



“ I got the feeling of having somebody's life in my hand. She was completely helpless. [After the event] I was in a bad way. I had to go off by myself to get my head around what had happened. I felt really upset. I felt awful finding my partner on the floor like that. I thought she was going to die, I really did.”

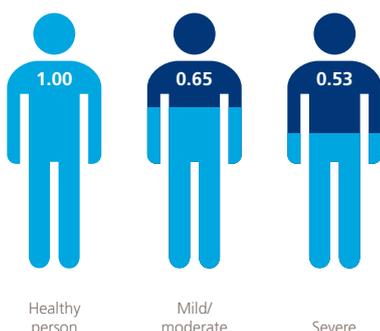
HENRIK CARSTENSEN

Henrik is married to Louise, who has type 1 diabetes  
Denmark

FIGURE 7 – QUALITY OF LIFE

### 47% decrease in quality of life after a severe event<sup>10</sup>

Mean EQ-5D index<sup>A</sup> by severity of hypoglycaemia



A: EQ-5D index is a measure of quality of life.<sup>10</sup>

INFOBOX 4

### Family members experience the burden of helping others<sup>49</sup>

-  Fear of being harmed physically
-  Feel anxious and worried
-  Neglect their own health and well-being
-  Give up recreational activities
-  Arrive late for work or turn down employment

# SOCIAL LIFE:

Hypoglycaemia interferes with balance, coordination, vision and consciousness.<sup>27</sup> For some people, this makes usual daily activities a challenge, and impacts their emotional well-being (Figure 8).<sup>50</sup>

## Driving may be dangerous

When blood sugar levels fall, driving skills can be compromised. Because of this, many countries impose licence restrictions on people with diabetes.<sup>27</sup>



**82% greater risk**

**of motor vehicle accidents if hypoglycaemia occurs while driving<sup>51</sup>**

Studies have shown that fewer than 25% of people who experienced an event behind the wheel were aware that their driving was impaired.<sup>39</sup> It is believed that around 30 serious accidents occur on

the road each month in the UK due to hypoglycaemia.<sup>39</sup>

## Recreation is restricted

Travelling can disrupt normal blood sugar control. Irregular meal times, difficulties following an insulin regimen and crossing time zones can all make hypoglycaemia more likely.<sup>39</sup>

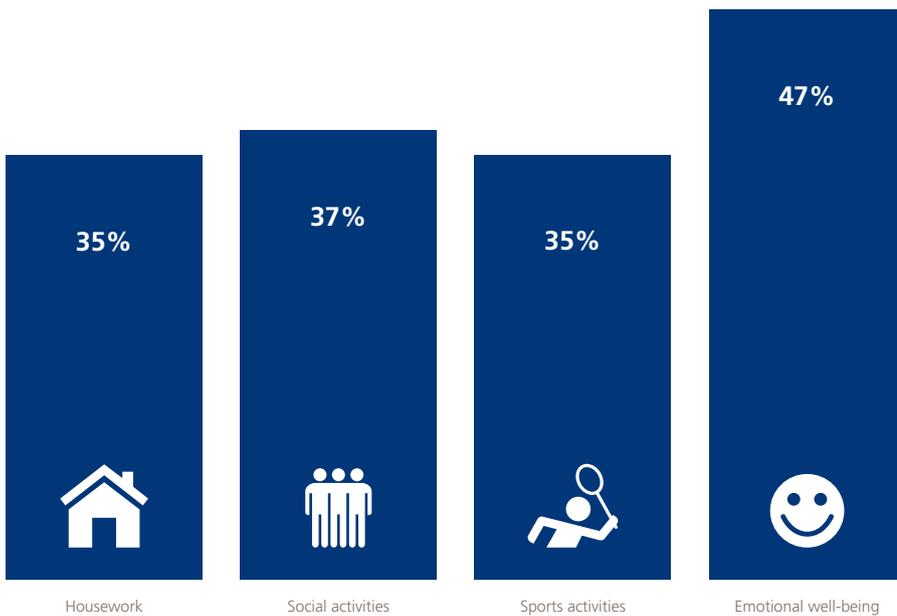
Furthermore, some sporting activities, such as those involving heights or water, may be inadvisable for people who are at risk of hypoglycaemia.<sup>4</sup> Similarly, recreational activities that involve physical activity, such as dancing<sup>4</sup> or children's summer camps,<sup>52</sup> can prompt worry.

With preparation, however, many people with diabetes can participate safely in sporting and recreational activities.<sup>4</sup> Social events that involve alcohol can be a concern, especially for young adults who move out of the home. Often, these individuals are managing their diabetes on their own for the first time at the same time as navigating a new culture in which alcohol and late-night socialising are common.<sup>39</sup>

FIGURE 8 – IMPACT ON DAY-TO-DAY ACTIVITIES

## 37% of people with type 2 diabetes reported that hypoglycaemia impacts their social activities<sup>50</sup>

% of people reporting that mild or moderate hypoglycaemia has an impact on ...



“Just the thought that I would be responsible for other people having to act for my behaviour, my poor health, means I certainly wouldn't do long-distance walking on my own, for the fear of having a hypo and having the emergency services called on my behalf.”

STEPHEN MATHERS  
Stephen has type 2 diabetes  
UK

# Fear and stigma cause treatment irregularities, with long-term costs

Reducing insulin doses is a common and risky strategy for mitigating hypoglycaemia. It may lead to poor blood sugar control, negatively impacting life expectancy, health and costs.

Worry about hypoglycaemia is a strong motivator of behaviour. In fact, 56% of people with diabetes are very worried about the risk of a hypoglycaemic event.<sup>53</sup> Furthermore, many feel guilt or embarrassment when they experience an event.

### Patients and doctors are troubled

Many people with diabetes live in fear of hypoglycaemia. According to surveys, hypoglycaemia causes the same level of worry as the risk of developing a serious diabetic complication, such as vision loss or renal failure.<sup>39</sup>

One consequence of this fear is chronic anxiety, the symptoms of which can mirror those of hypoglycaemia. A person who cannot make this distinction may not respond appropriately to an event.<sup>44</sup> Doctors, too, are concerned about hypoglycaemia, often resulting in them being less aggressive with treatment.<sup>54</sup>

### Fear changes treatment

Fear of hypoglycaemia promotes compensating behaviours that may affect blood sugar control and have long-term health consequences. After an event, patients often decrease or skip insulin doses (Figure 9).<sup>44,55</sup> In some cases, doctors advise patients to reduce their doses or to use a lower-than-recommended initial dose.<sup>56</sup>



**72% of doctors**

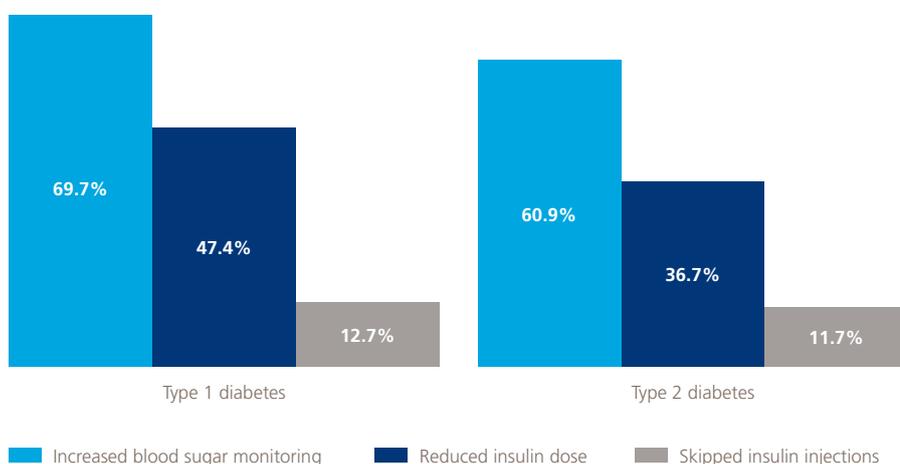
**say they would treat patients more aggressively if there was no concern about hypoglycaemia<sup>54</sup>**



FIGURE 9 – TREATMENT ADJUSTMENTS

## 47.4% of people living with type 1 diabetes reduce their insulin dose after a hypoglycaemic event<sup>55</sup>

% of patients



“When I’m going to an important meeting, I might take less insulin than what I know I need, because I just want to make sure that I’m not taking too much and getting too low in the middle of the important meeting. It’s just not that professional to be drinking out of a juice box when you’re talking to your boss or other important people.”

LÆRKE FOLKE THØMMING  
Lærke has type 1 diabetes  
Denmark

# HEALTH:

Fear of hypoglycaemia in children is a common parental concern. Parents sometimes maintain slightly higher-than-optimal blood sugar levels in their children to avoid an event.<sup>57</sup>

The effects of inadequate blood sugar control on life expectancy, health and costs are clear. The magnitude of these effects differs according to the type of diabetes.<sup>A</sup>

## Shorter life expectancy

A person with type 2 diabetes who allows blood sugar to remain high to avoid hypoglycaemia may expect to live 1.2 to 1.7 years less than someone who is treated with the newest treatment options designed to reduce the risk of hypoglycaemia.<sup>26,A</sup>

For people with type 1 diabetes, the effect is more pronounced, because diagnosis usually occurs at a younger age. The typical person in the UK with type 1 diabetes taking the newest diabetes medicines may live 5.3 years longer than someone who skips insulin doses to avoid hypoglycaemia. In Spain, the difference may be even greater – up to 6.6 years of life lost.<sup>26,A</sup>

## Years in good health are reduced

Poor blood sugar control also impacts the number of years a person may live in perfect health.<sup>B</sup>

Take, for example, people with type 2 diabetes. In the UK and Spain, patients who allow their blood sugar to remain high may live 16.3 and 12.6 years beyond diagnosis respectively. However, only 7.4 and 6.5 respectively of these years will be in perfect health after adjusting for quality of life (QALYs).<sup>B</sup> This is about 10% lower than in patients with good blood sugar control.<sup>26,A</sup>

In people with type 1 diabetes, the effects of blood sugar control on time spent in good health are greater. Poor control may yield a reduction of 18–19% in post-diagnosis QALYs.

## Cost of complications

The goal of diabetes treatment is to avoid complications. Time to emergence

of complications differs considerably between patients treated with the newest treatment options and those who receive older treatment options and deliberately keep their blood sugar high to avoid hypoglycaemia.

Across diabetes types in the UK and Spain, the onset of any complication may occur between 2.5 and 4.3 years sooner in patients with poor control. In people with type 1 diabetes, better control may result in a difference of a decade or more before vision and kidney problems set in.



**9.8–16.5 years**

**expected delay in the onset of eye disease among people with type 1 diabetes in the UK and Spain with good blood sugar control and who receive the newest treatments<sup>26,A</sup>**

When poor blood sugar control results in complications, the cost implications are substantial. In the UK, total costs for patients who manage their risk of hypoglycaemia through higher blood sugar levels may be 39–58% higher, depending on which type of diabetes the person has. In Spain, total costs may be 48% higher in this group, regardless of diabetes type.<sup>26</sup>



**58%**

**increase in lifetime costs for a person with type 1 diabetes in the UK who deliberately keeps blood sugar high to avoid hypoglycaemia<sup>26,A</sup>**



“ My doctors wanted me off the insulin because of the risk of hypos. They would rather have me run higher blood sugar than lower blood sugar because of the risk of hypos. But the long-term complications of high blood sugar are extremely damaging. Each time I have a hyper, one of my organs gets damaged. It is proven that each time my blood sugar goes beyond 140, an organ gets hurt. Yet my doctor is comfortable having me run my blood sugar around 180. I'm not. I want to live a full and healthy life.”

JULIE PUDLOWSKI

Julie has maturity onset diabetes of the young (MODY), a rare form of diabetes that is different from both type 1 and type 2  
Costa Rica

A: The estimates<sup>26</sup> provided here (see Methodology, p 26) are modelled on the basis of profiles of male patients with either type 1 or type 2 diabetes from Spain and the UK.

B: QALY is a measure of health adjusted to the quality of life. 1 QALY is equal to one year of life in perfect health.<sup>58</sup>

# Events elevate the risk of cardiovascular and mental health problems

Hypoglycaemia increases the risk of stroke, heart attack, dementia and depression. Each severe event also increases a person’s risk of death. Yet, hypoglycaemia is often not discussed with the doctor.

As with night-time events (p 11), many people do not talk about hypoglycaemia with their doctor (Figure 10), and many hypoglycaemic events are not reported.<sup>7,18</sup> Those conversations could be valuable, given that hypoglycaemia can lead to potentially serious health problems and in severe cases even death.

## Cardiovascular risks

Hypoglycaemia is strongly associated with a range of poor cardiovascular outcomes.<sup>9</sup> Severe hypoglycaemia increases the risk of heart attack and stroke (macrovascular<sup>A</sup> events). It also raises a person’s risk of kidney or eye damage (microvascular<sup>B</sup> complications) (Figure 11).<sup>9</sup> Patients with severe hypoglycaemia are also at higher risk of cardiovascular-related death (Figure 11).<sup>9</sup>



9%

increase in risk of death after 10 severe hypoglycaemic events<sup>59</sup>

## Mortality risk may be higher

Hypoglycaemic events, regardless of severity, may increase the risk of death. This risk is cumulative, meaning that the more events a person has, the greater the risk of death. Each confirmed hypoglycaemic event increases the risk of all-cause death by approximately 1%. Ten events of confirmed events increases all-cause death by 9%.<sup>59</sup>

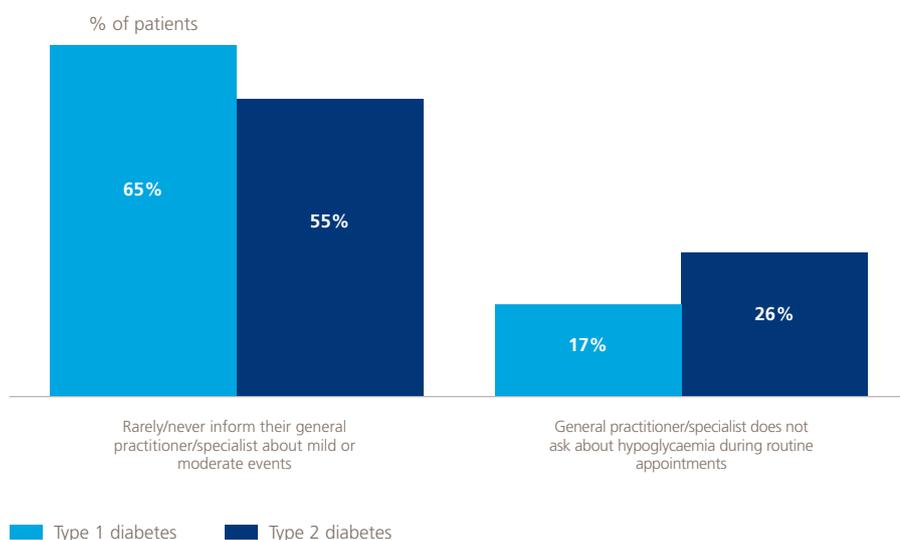


Although [reporting] is an individual responsibility, perhaps general practitioners could also be more proactive in that area and ask specifically about hypos and how they affect you. That should almost be the first or the second question in a consultation.”

STEPHEN MATHERS  
Stephen has type 2 diabetes  
UK

FIGURE 10 – CONSULTING A DOCTOR

65% of people with type 1 diabetes rarely or never inform their doctor about the event<sup>21</sup>



A: Macrovascular – a disease of any large blood vessels, for example stroke and heart attack.<sup>62</sup>  
B: Microvascular – a disease of the smaller blood vessels, for example eye disease that may lead to blindness.<sup>62</sup>

FIGURE 11 – CARDIOVASCULAR RISK

Severe hypoglycaemia was associated with a significant increase in...<sup>9</sup>

2.9x  
major macrovascular events

2.7x  
death from a cardiovascular cause

1.8x  
major microvascular events

# HEALTH:

## Alcohol is a risk factor

The connection between alcohol and blood sugar levels has been known for many years. In and of itself, occasional and moderate social use of alcohol is not a serious threat to health in people with diabetes.<sup>60</sup> However, one study reported that the risk of hypoglycaemia doubles after consumption of alcohol.<sup>61</sup>

For people who experience hypoglycaemia, alcohol consumption can pose a mortality risk.<sup>60</sup> Alcohol can sharply reduce blood sugar levels. In people who are not adequately nourished, this can be life-threatening.<sup>60</sup> Drinking may also reduce a person's awareness that their blood sugar levels are low and impair the body's response to an event.<sup>63</sup>

## Higher risk of dementia

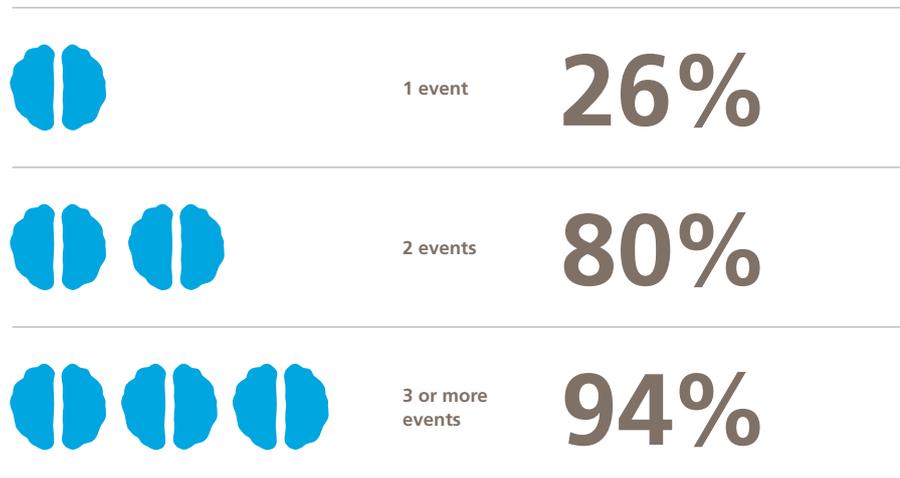
Scientists have known for many years that people with diabetes have a higher risk of developing dementia. More recent evidence suggests that severe hypoglycaemia plays a role in this (Figure 12).<sup>64</sup>

Repeated events of severe hypoglycaemia can cause permanent neurological damage that may accelerate the process of dementia (Figure 12).<sup>64</sup>

FIGURE 12 – RISK OF DEMENTIA

## Severe hypoglycaemia is associated with an increased risk of dementia in elderly people<sup>64</sup>

% risk increase in people with type 2 diabetes



Note: Older people with type 2 diabetes followed up for 27 years.<sup>64</sup>

Furthermore, lower quality of life, as defined by survey measures, may lead to anxiety and depression among people who experience hypoglycaemia.<sup>65</sup>



## 7 out of 10

express moderate or severe anxiety and depression due to hypoglycaemia<sup>65</sup>

Depression-related hospitalisation rates are higher in people with hypoglycaemia.<sup>66</sup>

## Injuries and fractures

Because hypoglycaemia interferes with balance, coordination and vision, it can also lead to falls (see p 11) that result in fractures, joint dislocations and head injuries.<sup>27</sup>

The chance of having a fall-related fracture is up to 70% higher in patients who experience a hypoglycaemic event than in patients who do not.<sup>67</sup> Fracture-related hospitalisation rates are also higher in patients with hypoglycaemia.<sup>66</sup>



“ During my lunchtime, I was walking in the city when I suddenly fell and broke my ankle. I had to take time off work for 10 months to take care of my ankle. Since then, I've had to change the way I used to work because now I get more tired when I'm standing up.”

SHEILA VASCONCELLOS  
Sheila has type 1 diabetes  
Brazil

## COST:

# Direct medical expenses are costly to payers and patients

The cost of diabetes complications is often framed in terms of long-term risks. Yet hypoglycaemia, which is an immediate complication, is itself a substantial contributor to the cost of treating diabetes.

In general, the use of healthcare resources increases after a hypoglycaemic event. This effect contributes to the direct medical costs of hypoglycaemia (Infobox 5).

### Comparing European costs

In the UK, for instance, the cost of treating moderate and severe hypoglycaemia exceeded 72 million British pounds in 2010–2011. In people with type 1 diabetes, these events accounted for 5% of the cost of treating all diabetes complications.<sup>68</sup> A different study from the UK suggests that the total annual direct cost of hypoglycaemia can be as high as 468 million pounds.<sup>8</sup> Across people with type 1 and type 2 diabetes, the cost of treating hypoglycaemia was higher than that of treating eye disease or hyperglycaemia.<sup>68</sup> In Germany, a 2002 study calculated healthcare service utilisation costs associated with severe hypoglycaemia. For people with type 2 diabetes, costs averaged 44,338 US dollars per 100,000 residents; for people with type 1 diabetes, costs averaged 8,129 dollars per 100,000 residents.<sup>69</sup>

In Sweden, hypoglycaemia of any severity among people with type 2 diabetes was



**GBP 39m**

**is the total cost of hypoglycaemia in the UK for people living with type 2 diabetes<sup>68</sup>**

estimated to cost 4.25 million euros per year. This 2006 study included lost work productivity in its calculations.<sup>70</sup>

### Need for help drives direct costs

Most of the direct costs of hypoglycaemia stem from the need for medical assistance. Figures 13, 14 and 15 illustrate the percentage of people who have sought various types of healthcare service after a severe event.<sup>71</sup>

Most of the time, a patient who experiences a mild or moderate event does not require medical assistance. In these cases, use of medical supplies represents another source of direct costs. For instance, any occurrence of hypoglycaemia prompts patients to test their

blood sugar more frequently.<sup>72</sup> 70% of people with type 1 diabetes say they test their sugar more often, using eight additional test strips per event. ▶

### INFOBOX 5

## Direct and indirect costs of hypoglycaemia

Direct costs refer to the use of healthcare services and products, for example a hospital stay, an ambulance journey, a visit to the emergency department or a doctor, or the supplies used to measure blood sugar. Indirect costs (see p 20) include lost productivity through absenteeism or presenteeism, disability costs and hypoglycaemia-related accidents such as vehicle crashes or falls.<sup>72</sup> Published cost estimates vary according to country and study methods.

FIGURE 13 – HOSPITALISATION

### 17–86% require hospitalisation<sup>71</sup>

% of people who require hospitalisation, ambulance attendance or a follow-up appointment with a general practitioner after a severe event, by country

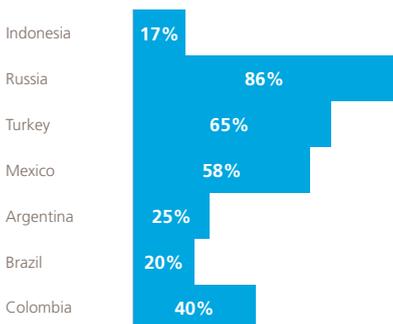


FIGURE 14 – AMBULANCE

### 44–97% require an ambulance<sup>71</sup>

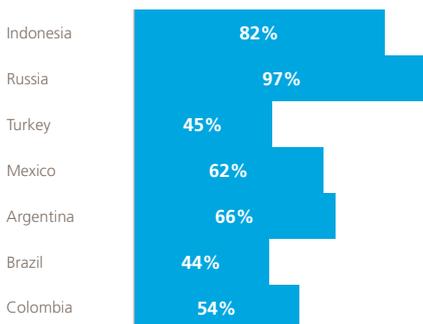
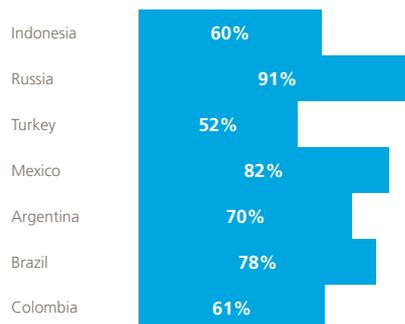


FIGURE 15 – DOCTOR VISIT

### 52–91% require a doctor visit<sup>71</sup>



**Note:** Physician-estimated resource use associated with a severe hypoglycaemic event in their country.

# COST:

The trend is similar in people with type 2 diabetes, 61% of whom test more often and use, on average, nearly six more test strips per event.<sup>72</sup>

## Severe events are costliest

Severe events account for the majority of the direct treatment costs associated with hypoglycaemia. In the UK, 63% of the direct cost of managing hypoglycaemia is attributable to severe events. Approximately half of this share is for hospitalisation (Figure 16).<sup>8</sup> In Sweden, the direct costs associated with hypoglycaemia may be up to 2,807 euros for one severe event.<sup>70</sup>

Depending on how the cost of severe events is viewed, there may be wide disparities from one country to the next (Figure 17).<sup>73</sup> In Brazil, for example, the cost of a severe event with hospitalisation may be up to 281 euros, which is about 50% of the country's average monthly income per capita.<sup>74,A</sup>

National differences also exist between the cost of a severe and a mild or moderate event. In Sweden, for instance, the average direct cost of a severe event is more than eight times that of a moderate event.<sup>70</sup> In the UK, the cost of a severe event is 14 times higher than a mild or moderate event in people with type 1 diabetes, and 31 times higher in people with type 2 diabetes.<sup>8</sup>

## Non-severe events add up

Severe events, while costly, are not the only driver of direct medical costs. According to some measures, mild and moderate

hypoglycaemia may incur significant total costs because they are more frequent.<sup>8,14,70</sup>

Direct costs associated with mild and moderate events are primarily caused by the need for additional doctor's appointments and various out-of-pocket expenses. In a survey of patients in the US, the UK, Germany and France, 25% of those who experienced a mild or moderate event said that they contacted a healthcare professional after the event.<sup>14</sup>

For patients, the out-of-pocket expenses can be considerable. The expense of managing mild or moderate events accounts for approximately 13% of patients' out-of-pocket, diabetes-related spending.<sup>75</sup>

Such expenses may include having to buy additional food to keep nearby in case of an event, travel to medical appointments and testing supplies. These types of expense add to the direct costs of hypoglycaemia. In 2010, they ranged, on average, from 203 dollars in the UK to 299 dollars in France.<sup>14</sup>

FIGURE 16 – DIRECT COST OF SEVERE EVENTS

## 53% of the cost of severe events in the UK was for hospitalisation<sup>8</sup>

GBP per average hypoglycaemic event

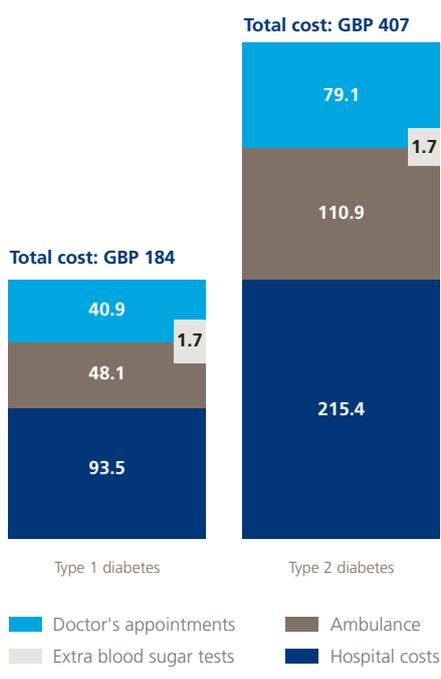
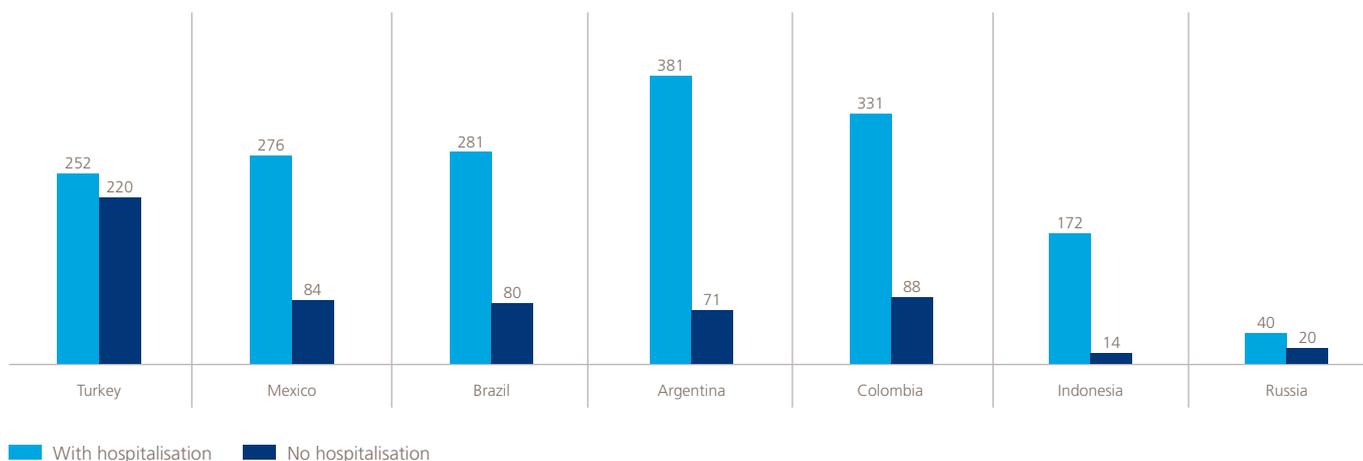


FIGURE 17 – DIRECT COST OF SEVERE HYPOGLYCAEMIA

## In many upper-middle-income<sup>B</sup> countries, the cost of hospitalisation is more than 200 euros<sup>73</sup>

EUR per event



A: Novo Nordisk standard currency exchange rate 2018 applied: 1 Brazilian real = 2.0 Danish kroner. 1 Danish krone = 7.45 euros.<sup>76</sup>

B: As defined by the World Bank.<sup>77</sup>

# COST:

## Hypoglycaemia is a shared economic burden

Indirect costs (Infobox 5, p 18), make up a sizeable proportion of the total economic burden of hypoglycaemia. Costs are incurred at individual, family and societal levels, and sometimes across levels.

For mild or moderate events of hypoglycaemia, indirect costs are a major contributor to the total cost of an event. A study in the UK calculated that, in addition to 468 million pounds in direct costs, the indirect costs associated with hypoglycaemia may amount to 399 million pounds, accounting for 46% of the total cost of hypoglycaemia in the UK.<sup>8</sup> In a Swedish study, indirect costs accounted for 59% of the costs associated with mild events.<sup>70</sup>

In monetary terms, the indirect costs associated with a mild or moderate event are relatively low (28 pounds in the UK,<sup>8</sup> 37–45 euros in Sweden<sup>70</sup>). When you consider, however, that a patient may have dozens of events per year<sup>7</sup> (see p 4), the total cost can be substantial.<sup>8</sup>

The impact of severe events adds to this total. The 2005 Swedish study estimated that for each severe event costing 3,917 euros, the indirect cost was 1,111

euros.<sup>70</sup> Much of this cost was attributed to lost work time while the person was hospitalised.<sup>70</sup>

### Productivity loss

A mild or moderate event may result in 10–15 hours of lost work time<sup>14</sup> (also see pp 9 and 11). For a severe event, the impact may be greater: in one study, the number of productive days lost after a severe event was up to three times greater than for a mild or moderate event (p 9).<sup>10</sup>

A number of studies have shown that patients take more time off from work after a night-time event than after an event that occurs during the day (Figure 18).<sup>14</sup> See more on p 11.

The need to take time off (Figure 19),<sup>71</sup> and the incidence of hypoglycaemia, shows that it can have a significant impact on a person's income.

Based on average daily wages in some European countries in 2017, a three-day

absence from work can cost a patient between 365 and 548 euros, depending on the country, adding to the indirect costs.<sup>76</sup> Sick leave represents another aspect of the indirect costs associated with hypoglycaemia. Among people with diabetes, those who experience hypoglycaemia have 77% more short-term sick leave days per year than those who do not experience hypoglycaemia.<sup>78</sup>

### Accidents also add to the cost

As described on pp 11 and 17, falls are a common consequence of low blood sugar. They also contribute to the indirect costs of hypoglycaemia. In one Belgian study of hospitalised patients with hypoglycaemia, per-admission costs were 65% higher among those who had suffered a fall.<sup>66</sup> Fracture-related admissions and traumatic fractures were more common in people who had experienced hypoglycaemia than those who had not.<sup>66</sup>

FIGURE 18 – PRODUCTIVITY LOSS

### 1.5–2 times greater productivity loss when events occur during sleep<sup>14</sup>

Loss per mild or moderate event (USD)

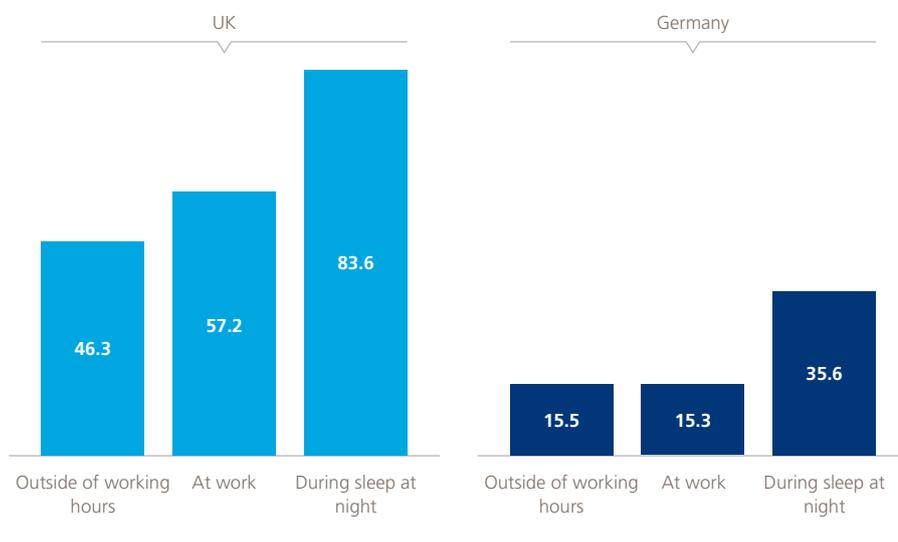
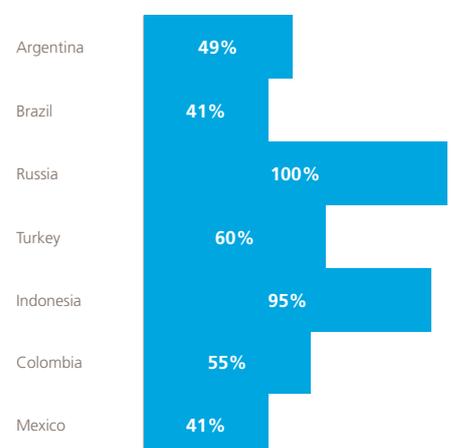


FIGURE 19 – TIME OFF WORK/STUDY

### Most people need time off work after a severe event<sup>71</sup>

% of people who need time off work/school after a severe event



**Note:** Physician-estimated need for time off work/school after a severe event in their country.

# COST:

Using France, Italy and Brazil as examples (see Methodology, p 26), Figures 20, 21 and 22 illustrate how costs are a shared burden. Some hypoglycaemia costs fall to individuals, some to family and caregivers, some to society and some to a combination of the above.

## Direct costs are substantial

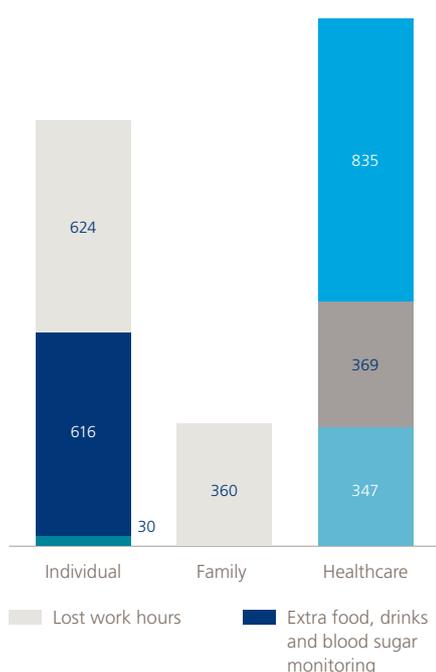
Direct medical expenditure drives the overall cost of hypoglycaemia. In France and Brazil, direct costs account for 70% of hypoglycaemia expenditure, and for 75% in Italy. The largest items of expenditure are hospitalisation, including ambulance journeys, accounting for almost 40% of all direct costs. In Brazil, medication to treat a hypoglycaemic event constitutes a significant share of direct costs as well.<sup>79</sup>

How the costs of hypoglycaemia are shared depends on a country's healthcare system and labour laws. In France, less than 7% of all direct medical costs are paid out of pocket. In Italy, the proportion of out-of-pocket expenses is 23%.<sup>80</sup>

FIGURE 20 – FRANCE

## EUR 3,180 in hypoglycaemia costs per person or EUR 11.8bn in total<sup>79</sup>

Annual cost per person with diabetes who receives care (EUR)



**Note:** The number of people with diabetes who receive care in France is 3.7 million.<sup>81</sup>

## Indirect costs are spread wide

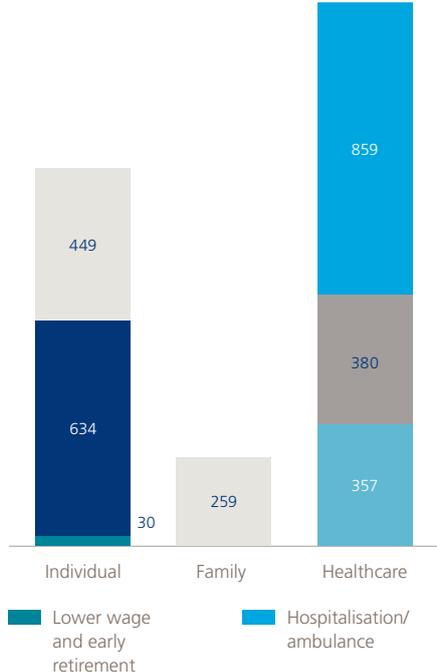
The shared burden of hypoglycaemia is even more evident when you look at indirect costs. Most indirect costs are in the form of lost work days. Work absence due to hypoglycaemia is a cost to the individual, but families also absorb costs by taking time off from work to care for the person experiencing an event.

Hypoglycaemia affects earning potential. Adults with lower cognitive scores, a potential consequence of hypoglycaemia in childhood, earn 8.3% less on average (p 8).<sup>34</sup> This corresponds to an average annual wage loss of 3,080, 2,440 and 590 euros in France, Italy and Brazil respectively.<sup>79</sup> The effect on earnings is similar to that of having three fewer years of schooling. Employers, too, share this burden through lost productivity. Average annual individual and family work days lost to hypoglycaemia range from 6.3 in France to 5.8 in Italy and 9.3 in Brazil. This translates to a substantial loss of full-time employees (Figure 23).

FIGURE 21 – ITALY

## EUR 2,968 in hypoglycaemia costs per person or EUR 4.85bn in total<sup>79</sup>

Annual cost per person with diabetes who receives care (EUR)

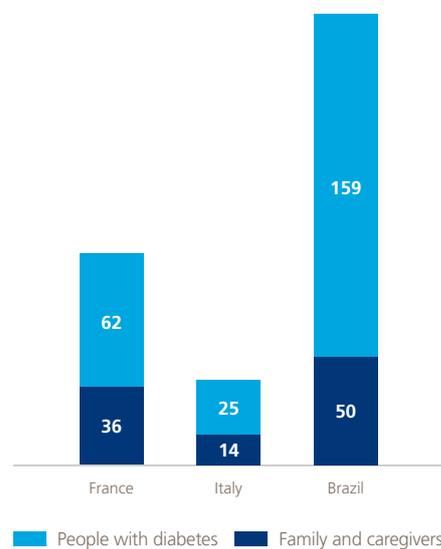


**Note:** The number of people with diabetes who receive care in Italy is 1.64 million.<sup>76</sup>

FIGURE 23 – FULL-TIME EMPLOYEES LOST

## 346,000 FTEs<sup>A</sup> lost annually across France, Italy and Brazil<sup>79</sup>

Total number of full-time employees lost ('000)

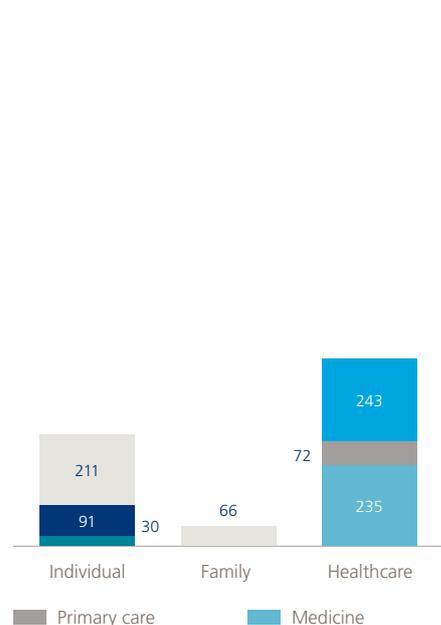


**A:** Full-time employees.

FIGURE 22 – BRAZIL

## EUR 948 in hypoglycaemia costs per person or EUR 5.12bn in total<sup>79</sup>

Annual cost per person with diabetes who receives care (EUR)



**Note:** The number of people with diabetes who receive care in Brazil is 5.4 million.<sup>1,82</sup>

## REDUCING HYPOGLYCAEMIA:

# If hypoglycaemia could be mitigated, what would the gains be?

Reducing hypoglycaemia without compromising long-term health outcomes may have a number of positive effects on health, quality of life, healthcare and household budgets.

Given the burden of hypoglycaemia described in the previous pages, it is evident that reducing fear, stigma and the incidence of hypoglycaemic events is likely to bring about significant improvements in the daily lives of individuals and families living with diabetes – at emotional, social as well as economic levels.

However, for patients dependent on insulin, it is critical that hypoglycaemia is reduced without compromising blood sugar control and long-term health outcomes, avoiding treatment and dosing irregularities.

Although hypoglycaemia cannot be fully eradicated,<sup>8</sup> solutions and treatment options are available (see more on pp 24–25) that can help save both lives and money in the long term by reducing the risk of hypoglycaemia while ensuring good blood sugar control.

### Saving lives

Better treatment and blood sugar control among people with diabetes may significantly increase life expectancy.

For every 10 severe events a person experiences, their risk of death increases by 9%.<sup>59</sup> Modelling based on British and Spanish studies, as described on p 15, suggests that lowering blood sugar levels with the newest treatment options rather than keeping blood sugar too high could, over the lifetimes of people currently diagnosed with type 2 diabetes, save 300,000 life years in Spain and 185,000 life years in the UK.<sup>A,26</sup>

Quality-adjusted life expectancy<sup>B</sup> may improve as well, potentially adding 180,000 and 96,000 life years in Spain and the UK respectively for people living with type 2 diabetes.<sup>A,26</sup>

### Reducing complications

Better blood sugar control may reduce the incidence of heart attack, stroke, and kidney and eye damage – all of which are risks associated not only with diabetes but also with severe hypoglycaemia.<sup>9</sup>



## 185,000 life years

could be saved in the UK among people with type 2 diabetes who maintain blood sugar control and avoid hypoglycaemia using the newest treatments<sup>26</sup>

The newest treatments, that reduce the risk of hypoglycaemia while ensuring good blood sugar control, may help delay the onset of diabetes-related complications, thereby saving associated costs. Lifetime cost savings from avoiding diabetes complications among people with type 2 diabetes, could add up to 467 million pounds in the UK and 3.6 billion euros in Spain.<sup>A,26</sup> ▶



“If I have fewer hypos, it will give me better quality of life, better chance of a long lifespan. Every hypo shortens our lifespan. Every day I have a severe hypo, I actually face the risk of dying. Every mistake in dosage can be fatal. Preventing hypos is to remove diabetes.”

JULIE PUDLOWSKI

Julie has maturity onset diabetes of the young (MODY), a rare form of diabetes different from both type 1 and type 2  
Costa Rica

A: Results are based on male patients with diabetes only. Assuming similar health outcomes for female patients with diabetes, results may be much higher.<sup>26</sup>  
Read more about this simulation on p 26.

B: QALY is a measure of health adjusted to the quality of life. 1 QALY is equal to one year of life in perfect health.<sup>58</sup>

# REDUCING HYPOGLYCAEMIA:

## Reducing the financial burden

Overall, hypoglycaemia is costly (see more on pp 18–21), but even small steps could result in cost savings in some countries. In others, particularly where diabetes prevalence is growing fast, greater reductions are needed to reverse cost trends.



**EUR 3.6bn**

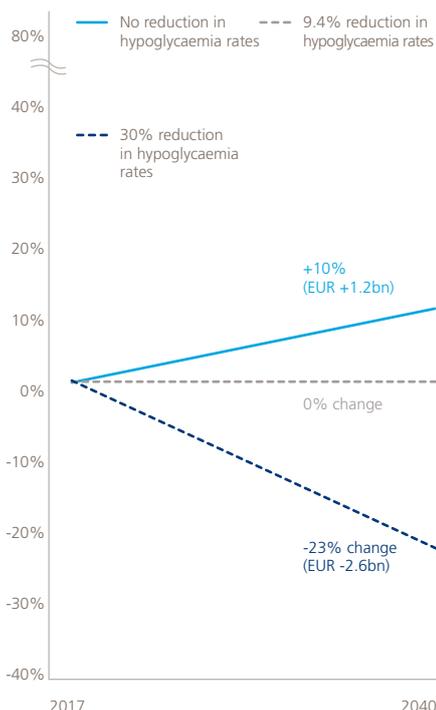
**could be saved in Spain among people with type 2 diabetes who maintain blood sugar control and avoid hypoglycaemia using the newest treatments<sup>26</sup>**

In a UK-based simulation, for instance, a 25% overall reduction in hypoglycaemia rates resulted in cost savings of 182,500

FIGURE 24 – FRANCE

## 2.6bn euros could be saved if hypoglycaemia rates were decreased by 30% by 2040<sup>79</sup>

% cost change by 2040 related to % reduction in hypoglycaemia rates



pounds per 100,000 residents,<sup>8</sup> or 117 million pounds nationally per year.<sup>8</sup>

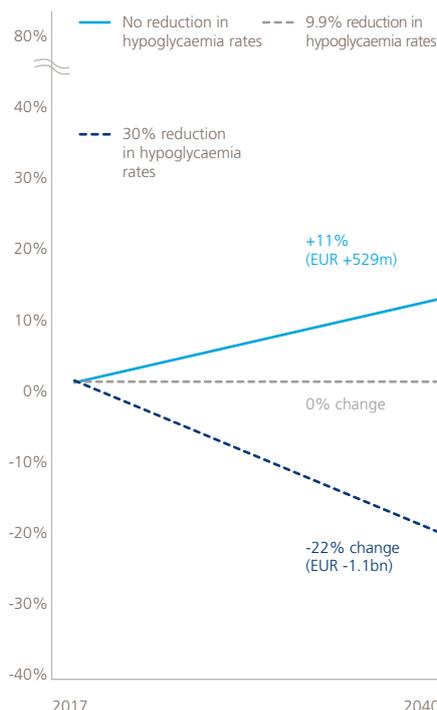
In France, diabetes prevalence is expected to climb 14% by 2040, while in Italy, the rise is projected to be 17%. Total hypoglycaemia costs are expected to rise more slowly – by about 10% in both countries – because of an ageing population. With a smaller percentage of residents in the workforce, productivity loss will decline over time. This combination of trends means that even small steps can lead to big gains. In both countries, a mere 9% reduction in incidence rates by 2040 would ensure that total hypoglycaemia costs remain the same between now and then.<sup>79</sup>

Stepping up to a 30% drop in hypoglycaemia rates may result in substantial cost savings of 720 and 660 euros per person with diabetes who receives care in France and Italy respectively. The total potential cost savings are shown in Figures 24 and 25 (see Methodology, p 26).

FIGURE 25 – ITALY

## 1.1bn euros could be saved if hypoglycaemia rates were decreased by 30% by 2040<sup>79</sup>

% cost saving by 2040 related to % reduction in hypoglycaemia rates



In Brazil, the situation is quite different. The total cost of hypoglycaemia is expected to rise by 82% by 2040, to 9.3 billion euros, primarily because of a projected increase in diabetes prevalence of 87% between now and then (Figure 26).

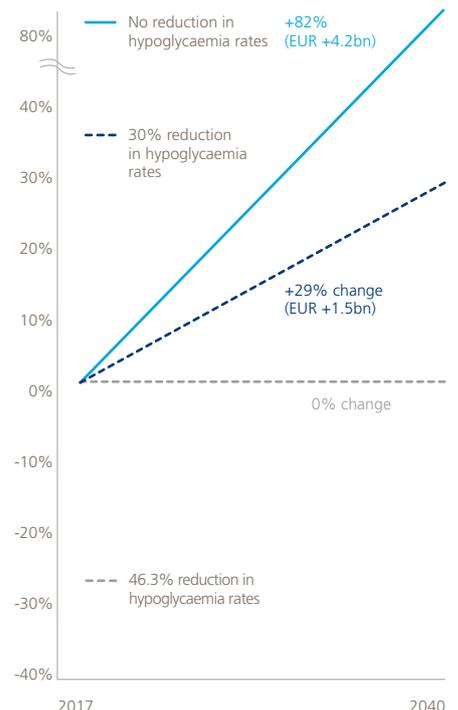
Incremental gains are a first step, but progress in Brazil must be swift and sustained to save costs. It would take a 46% reduction in incidence rates for hypoglycaemia costs to be the same in 2040 as they are today.

People in Brazil with type 1 diabetes experience 10.8 severe events per year. For people with type 2 diabetes, the rate is 3.7 severe events per year.<sup>7</sup> Reducing incidence rates to the level found in Europe – 3.4 and 1.3 events in people with type 1 and type 2 diabetes<sup>7</sup> respectively – could yield savings of 2.5 billion euros per year. This translates to 468 euros per person with diabetes who receives care.<sup>79</sup>

FIGURE 26 – BRAZIL

## 46.3% reduction in hypoglycaemia rates must be achieved to maintain costs at their current level<sup>79</sup>

% cost saving by 2040 related to % reduction in hypoglycaemia rates



## CALL TO ACTION:

# How can we reduce the risk of hypoglycaemia?

Realising the potential benefits of reducing hypoglycaemia requires action at multiple levels. Novo Nordisk is committed to driving a cross-sector dialogue to find solutions in order to reduce the risk of hypoglycaemia.

As with any complex problem, solutions will require strategies across multiple levels (Infobox 6).

### 1. Increase hypoglycaemia support for patients, families and caregivers

Programmes that empower patients and improve patient awareness and self-management skills, such as peer-to-peer online support groups, have proven their value in reducing the incidence of severe hypoglycaemia.<sup>27,44</sup>

Given that fear of hypoglycaemia is a barrier to blood sugar control, it is also important for patients and their doctors to create an open and constructive dialogue, free from judgement, about hypoglycaemia, how often it occurs and patients' concerns about it.<sup>21</sup> Involving family members in patient consultations more is another recommendation. Involving the caregiver could benefit both the patient and the caregiver.<sup>49</sup> Furthermore, peer-support groups, interactive websites and other

forums offer opportunities to help families and caregivers understand that they are not alone.

Because hypoglycaemia affects learning,<sup>4</sup> young people in schools and universities need extra support and flexible learning environments. The use of a so-called care ambassador has been shown to reduce the rate of hypoglycaemia in children with diabetes.<sup>44</sup> Equipping teachers with the skills to help young people may also be beneficial.

Discrimination against people with hypoglycaemia should also be avoided. The incidence of severe hypoglycaemia in the workplace is low, yet employment discrimination against people with type 1 diabetes still occurs.<sup>39</sup> The UK's 2010 Equality Act<sup>83</sup> is an example of how laws may be applied to prevent discrimination against people with insulin-treated diabetes. Beyond legal actions, more general awareness about hypoglycaemia could help people feel safer and better understood at work.



“ I believe that people close to a person with diabetes, including doctors, need to understand more about how hypoglycaemia affects our body and mind. We [people with diabetes] need to talk more about how we feel and when we need some support. Let them understand that we often can't control diabetes, and that we do the best we can.”

SHEILA VASCONCELLOS  
Sheila has type 1 diabetes  
Brazil

#### INFOBOX 6

### Multi-level strategies for limiting hypoglycaemic events



# CALL TO ACTION:

## 2. Improve access to better treatment and monitoring

Not only is insulin vital for millions of people with diabetes in ensuring good health, it is also life-saving, particularly for those living with type 1 diabetes. Skipping insulin or reducing doses to avoid hypoglycaemia is not a sustainable solution for good health. Instead, the key is to reduce the frequency and severity of hypoglycaemia while maintaining optimal blood sugar control.

New-generation insulin analogues work in a way that slowly releases medication into the blood stream over time, rather than all at once. Steady release reduces the risk of triggering a hypoglycaemic event, without compromising blood sugar control.

Continuous glucose monitoring (CGM) devices provide a level of safety, making patients aware that blood sugar levels are falling before they can feel it. CGM

devices have been shown to prevent severe events,<sup>27</sup> and the data they provide can help patients better understand the effects of medicine, nutrition and exercise on blood sugar.<sup>16</sup> Improved access to medicine and monitoring devices for people with type 1 or type 2 diabetes may promote good diabetes management and early prevention of complications.

## 3. Focus on best-practice hypoglycaemia management in diabetes care

Recently, we have come to understand the importance of a holistic approach to measuring health outcomes that accounts not only for tight blood sugar control but also for humanistic factors, such as quality of life and incidence and severity of hypoglycaemic events.<sup>84</sup>

Therefore, patient-reported outcomes may have to be given greater attention as well. The International Consortium for Health

Outcomes Measurement (ICHOM) is working with physician leaders, outcomes researchers and patient advocates to develop outcomes measures that matter to patients.

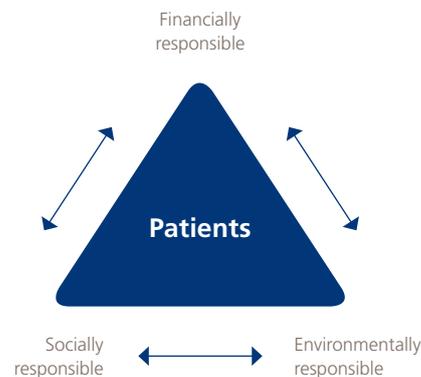
Robust and accepted clinical and economic evidence is essential for decision-making that results in the best possible patient care. Hypo-RESOLVE is a European research project designed to provide clinicians with actionable data about hypoglycaemia.<sup>85</sup> It is hoped that this and other research may settle conflicting methods and evidence about the definition, incidence and effects of hypoglycaemia, among other things.

Overall, more research on the topic of hypoglycaemia may be of immense value, especially with regard to new technologies that may improve diabetes management and research into why people may not report hypoglycaemic events.

# Our commitment to helping people with diabetes

Novo Nordisk is a global healthcare company with more than 95 years of innovation and leadership in diabetes care. Our purpose is to drive change to defeat diabetes and other serious chronic diseases. Our way of doing business is governed by the Triple Bottom Line (TBL) principle, which ensures that we consider the financial, environmental and social impacts of our business decisions while always keeping the patient's best interests in mind.

With our Changing Diabetes® commitment, we aim to bend the diabetes curve and address the biggest unmet needs for people with diabetes. The risk of hypoglycaemia is a key diabetes-related challenge. It is our responsibility to help address the issue. We invest in:



### Innovative treatments

Our key contribution is to discover and develop innovative biological medicines, including insulins that aim to reduce or even eliminate the risk of hypoglycaemia.<sup>86</sup> However, it takes more than medicine to address the challenges of hypoglycaemia.



### Cross-sector partnerships

Novo Nordisk is participating in a new research project, Hypo-RESOLVE. Twenty-three leading international players from academia, industry and civil society have joined forces to find better solutions to alleviate the burden and consequences of hypoglycaemia in diabetes.<sup>85</sup> Read more about Hypo-RESOLVE at [www.hypo-resolve.eu](http://www.hypo-resolve.eu).



### Advocacy for better health

We aim to lead a cross-sector dialogue on the topic of hypoglycaemia through this Blueprint for Change and other advocacy work. We encourage all manufacturers and healthcare partners to join us in helping increase understanding about the challenges and opportunities, to reduce the risk of hypoglycaemia.

# Methodology

## Literature review

A review of existing literature, including databases, scientific papers and publications, was conducted to collect existing evidence and literature on the topic of hypoglycaemia. The Scopus database was used, which is the largest abstract and citation database of peer-reviewed literature in the world.<sup>87</sup>

Underlying search topics included the incidence of hypoglycaemia, the direct and indirect costs of hypoglycaemia, awareness and fear of hypoglycaemia, quality of life-related aspects, treatment and care considerations, the health-related consequences of hypoglycaemia, and the impacts of hypoglycaemia on families and communities at large.

The search was not limited to any geographical area and included both type 1 and type 2 diabetes. Only studies published in English were included.

The literature search was conducted in February 2018.

## Economic analysis in France, Italy and Brazil

The economic analysis on p 21 is based on existing literature and data related to the direct and indirect costs of hypoglycaemia.

The analysis is based on the hypoglycaemia incidence data from an international survey on hypoglycaemia among insulin-treated patients with diabetes (HAT study).<sup>7</sup>

Total cost values are based on the number of people with diabetes who receive care (people who receive medicine and are cared for by a healthcare professional). In France, this number is equal to 3.7 million people according to the national health insurance.<sup>81</sup>

In Brazil, the number of people with diabetes who receive care is estimated at 5.4 million people.<sup>1,82</sup> In Italy, it is estimated to correspond to 1.64 million people.<sup>76</sup> All cost estimates are presented

in 2017 prices in euros, using OECD consumer price indices.<sup>88</sup>

The cost projections presented on p 23 are based on IDF 2040 diabetes prevalence projections<sup>1</sup> and United World Population Prospects for age-specific population in 2040.<sup>89</sup> Costs per event and hypoglycaemia prevalence rates are assumed to be unchanged, which may lead to the results being underestimated.

The full methodology is available on request.

## Health-economic analysis

Through the IMS CORE Diabetes Model,<sup>90</sup> we simulated patient journeys to quantify the long-term clinical and cost burden associated with hypoglycaemia in people with type 1 and type 2 diabetes in the UK and Spain.

In one scenario, the patient is assumed to have good blood sugar control and receive the newest treatment for diabetes focused on minimising the risk of hypoglycaemia. People with type 2 diabetes are assumed to start their treatment using oral antidiabetic medications at the time of diagnosis, switching to injectable antidiabetic therapy, and then switching to new-generation insulin later in their journey. People with type 1 diabetes are assumed to receive new-generation insulin.

The patient in the other scenario is assumed to keep blood sugar high to avoid the risk of hypoglycaemia, thereby reducing the risk to the level of the patient in the first scenario. At the same time, this patient receives traditional or older therapy, with the respective risk of hypoglycaemia. People with type 2 diabetes are assumed to start their treatment using oral antidiabetic medications at the time of diagnosis, switching to insulin analogues later in their journey. People with type 1 diabetes are assumed to receive insulin analogues.

Both simulations are based on male patients.

All cohort characteristics for the scenarios are taken from published literature sources.

The time horizons for the simulations are 40 years for people with type 2 diabetes and 50 years for people with type 1 diabetes. The simulations do not take into account the cost of intervention.

The full methodology is available on request.

## Review process

This report has been reviewed by five people who live with diabetes and who are members of the Novo Nordisk DEEP panel (Disease Experience Expert Panel). DEEPs consist of patients or relatives who live with a chronic disease and can provide disease-specific insights and advice.

Novo Nordisk collaborates with DEEPs following the methodology of the European Patients' Academy on Therapeutic Innovation (EUPATI) and the Patient Partner project funded by the 7th Framework Programme of the European Commission.

DEEP members are reimbursed for the services they provide to Novo Nordisk.

Read more about the DEEPs at [novonordisk.com/patients/DEEP](http://novonordisk.com/patients/DEEP).

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### ABOUT NOVO NORDISK

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Novo Nordisk is a global healthcare company with 95 years of innovation and leadership in diabetes care. This heritage has given us experience and capabilities that also enable us to help people defeat obesity, haemophilia, growth disorders and other serious chronic diseases. Headquartered in Denmark, Novo Nordisk employs approximately 43,100 people in 79 countries and markets its products in more than 170 countries. Novo Nordisk's B shares are listed on Nasdaq Copenhagen (Novo-B). Its ADRs are listed on the New York Stock Exchange (NVO). For more information, visit [novonordisk.com](http://novonordisk.com), Facebook, Twitter, LinkedIn and YouTube.

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