Hypoglykemi

- hva er bakgrunnen ?

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Kasuistikk

Bevisstløs 4 åring. Puster greit. Foreldre får ikke liv i ham.

Tidligere frisk.

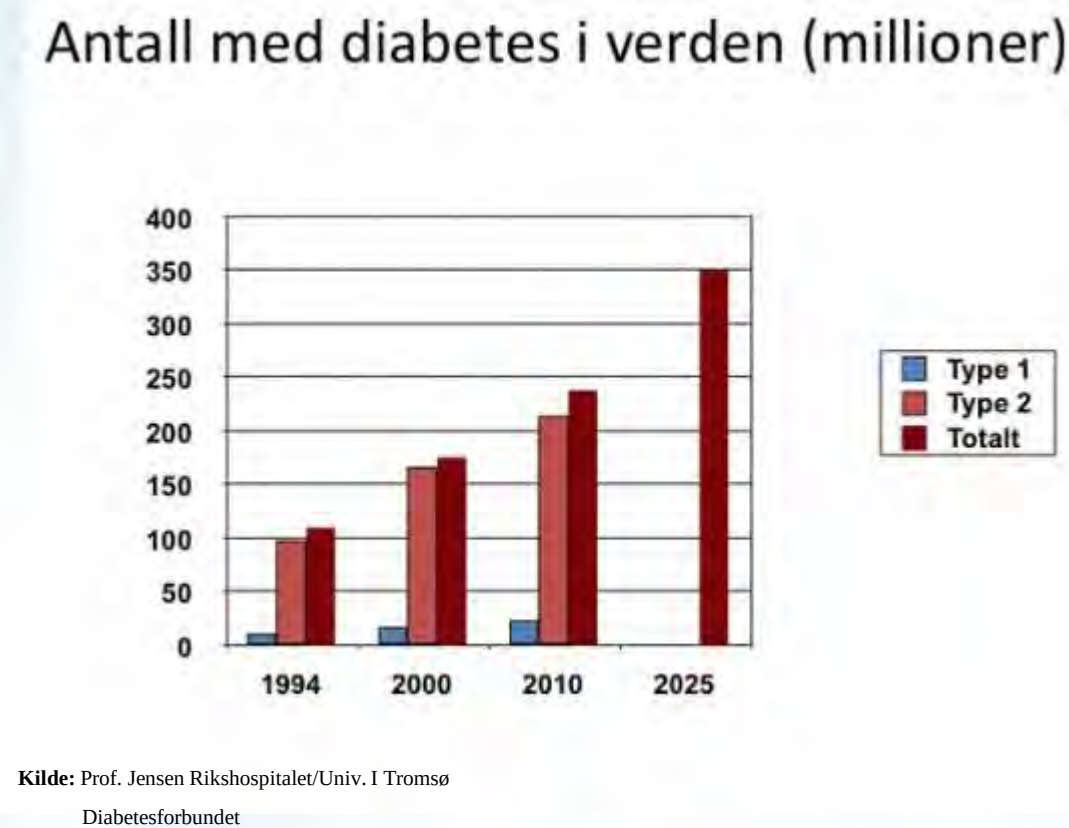
Ambulanse: Resp/sirk ua. Ingen funn. Starter transport retning sykehus.

LAT: Har dere sjekket blodsukker?

1.2 mmol/ml

Gir råd om Glukose adm. Våkner opp. Litt trøtt.

Omfang



Kilde: Prof. Jensen Rikshospitalet/Univ. I Tromsø

Diabetesforbundet

Diabetes i Norge – Type 1 diabetes

- Ca 25.000 personer
- 600 nyoppdagede hvert år
  (250 barn < 15 år)
- Mest vanlig hos unge barn og voksne
- Ingen egenproduksjon av insulin

Kilde: Prof. Jensen Rikshospitalet/Univ. i Tromsø
Diabetesforbundet (www.diabetes.no)

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Diabetes i Norge – Type 2 diabetes

- Ca 300.000 personer
- 50 % vet enda ikke at de har diabetes
- I hovedsak personer > 40 år
- Mellom 6000-7000 nyoppdagede hvert år
- Nedsatt insulinfølsomhet og nedsatt insulinproduksjon

Kilde: Prof. Jensen Rikshospitalet/Univ. i Tromsø
Diabetesforbundet (www.diabetes.no)

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Diabetes i Norge – andre former

- Svangerskapsdiabetes
- MODY (Maturity-Onset Diabetes in the Young)
- LADA (Latent Autoimmune Diabetes in Adults)
- Sekundær diabetes (diabetes som følge av andre sykdommer)

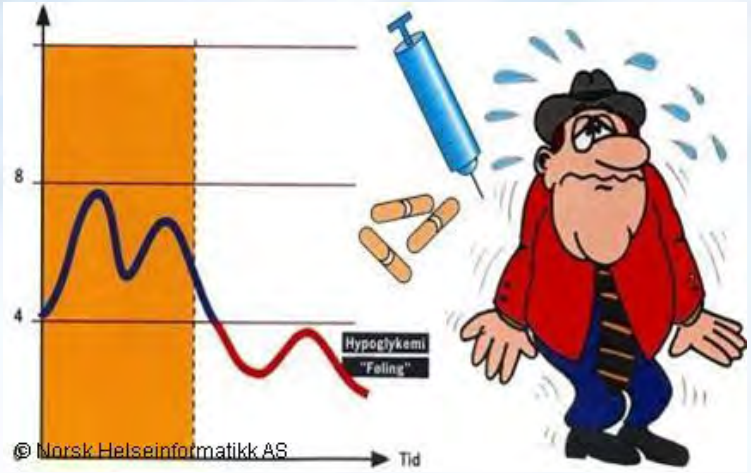
Kilde: Prof. Jensen Rikshospitalet/Univ. i Tromsø
Diabetesforbundet (www.diabetes.no)

Normale reguleringsmekanismer ved hypoglykemi

- Redusert utskillelse av insulin fra pankreatiske β-celler
- Økt sekresjon av glukagon fra pankreatiske α-celler
- Økt adrenalin utskillelse fra binyrene

Hypoglykemi

- Blodsukker
  - < 4mmol/l
  - < 2.5 mmol/l
  - ?



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Hypoglykemi

Diabetologia (2009) 52:1–3
DOI 10.1007/s00125-008-1205-5

FOR DEBATE

Preventing hypoglycaemia: what is the appropriate glucose alert value?

P. E. Cryer

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Keywords Glucose alert value · Glucose counter-regulation · Hypoglycaemia · Self-monitoring of plasma glucose

Abbreviation
ADA American Diabetes Association

[Everyone is entitled to their own opinion, but not their own facts

Daniel Patrick Moynihan]

Contrary to the assertions of Swinnen et al. [1], Frier [2] and Arnelo et al. [3], the American Diabetes Association (ADA) Workgroup on Hypoglycaemia [4] defined hypoglycaemia in diabetes as 'all episodes of an abnormally low plasma glucose concentration that expose the individual to potential harm'. It is not possible to state a single plasma glucose concentration that defines hypoglycaemia because the glycaemic thresholds for responses to falling glucose levels, including those for symptoms, are dynamic. The ADA Workgroup recommended that people with diabetes (implicitly those with insulin secretagogue- or insulin-treated diabetes) should become concerned about the possibility of developing hypoglycaemia at a self-monitored plasma glucose concentration of ≤3.9 mmol/l (70 mg/dl) [4]. Given the limited accuracy of monitoring devices [5], this conservative lower limit for individuals with diabetes approximates the lower limit of the postabsorptive plasma glucose concentration range (approximately 3.9–6.1 mmol/l [70–110 mg/dl]) [6]) and the glycaemic threshold for activation of glucose counter-regulatory systems (approximately 3.6–3.9 mmol/l [65–70 mg/dl] [6–9]), and is low enough to cause reduced glucose counter-regulatory responses to subsequent hypoglycaemia [10] in non-diabetic individuals. It is higher than the glucose levels required to produce symptoms in non-diabetic individuals (approximately 2.8–3.1 mmol/l [50–55 mg/dl] [6–9]) and substantially higher than those that do so in people with well-controlled diabetes [11], although individuals with poorly controlled diabetes sometimes have symptoms at higher glucose levels [11, 12]. Thus, the recommended glucose alert level of ≤3.9 mmol/l (70 mg/dl) is data-driven, generally gives the patient time to take action to prevent a clinical hypoglycaemic episode, and provides some margin for the limited accuracy of glucose monitoring devices at low plasma glucose concentrations [5]. The ADA Workgroup-recommended alert value does not, of course, mean that people with diabetes should always self-treat at an estimated plasma glucose concentration of ≤3.9 mmol/l (70 mg/dl). Rather, it suggests that they should consider actions ranging from repeating the measurement in the short term, through behavioural changes such as avoiding exercise or driving, to carbohydrate ingestion and adjustments of the treatment regimen.

The data reported by Swinnen et al. [1] nicely document that a higher plasma glucose cut-off value increases the percentage of affected patients and increases the proportion of patients who are asymptomatic; but those are predictable findings. Their data also indicate that a higher cut-off value

This invited for debate article reflects the views of the author, not necessarily those of the American Diabetes Association (ADA) or the ADA Workgroup on Hypoglycaemia.

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FOR DEBATE

Defining hypoglycaemia: what level has clinical relevance?

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Keywords Blood glucose · Counter-regulation · Diabetes · Glycaemic threshold · Hypoglycaemia · Impaired hypoglycaemia awareness · Insulin

Abbreviation
ADA American Diabetes Association

Never let the facts get in the way of a carefully thought-out bad decision.

John Marshall (1755–1835)

Because hypoglycaemia is so common in insulin-treated diabetes and remains the greatest impediment to strict glycaemic control, its evaluation is mandatory as an outcome measure of studies assessing new therapies for diabetes and those comparing insulin regimens or management strategies. Regrettably, the lack of consensus as to how hypoglycaemia should be defined has permitted, if not actively encouraged, a plethora of eccentric, vague and clinically irrelevant definitions to be applied in many therapeutic trials. The practical definition (from a clinical viewpoint) of severe (requiring external help for recovery) and mild (self-treated) hypoglycaemia, as described in the DCCT [1], has been widely adopted for epidemiological and clinical use, but its reliance on ascertaining the ability to self-treat hypoglycaemia does not capture events that do not generate symptoms—so-called asymptomatic 'biochemical' hypoglycaemia. This is a common problem in people with impaired awareness of hypoglycaemia, but is recognised to occur in all people treated with insulin, either because the glycaemic thresholds that trigger symptomatic and physiological responses are not breached, or warning symptoms are not subjectively perceived. The frequency with which biochemical hypoglycaemia appears to occur is dependent on how often it is measured. Estimates based on continuous glucose monitoring systems cannot be included because the sensors measure interstitial tissue glucose, and the inter-relationship between this and blood glucose is unclear.

Rationale for the American Diabetes Association definition of biochemical hypoglycaemia

A wide range of glucose concentrations could therefore represent biochemical hypoglycaemia; the difficulty arises in determining at what level it starts. To address this and other problems of defining hypoglycaemia, a Workgroup of the American Diabetes Association (ADA) published an insulin report in 2005 [2] in which the methods of identifying and measuring hypoglycaemia were reviewed and a classification of hypoglycaemia was proposed. Much of the report and recommendations are sound, sensible and justifiable, based on available evidence. The one contentious issue is their proposal that any blood glucose value equal to, or below, 3.9 mmol/l (70 mg/dl) should represent hypoglycaemia, whether or not symptoms are present. Many clinicians would regard a blood glucose of this concentration in a non-diabetic adult as being within the normal fasting range, and would not consider it to indicate significant hypoglycaemia. This is an important consideration as it is evident that the glucose level that is selected to define hypoglycaemia can influence estimates of the frequency of this therapeutic side effect—a choice that could have important clinical and commercial implications. To illustrate this, Swinnen et al. [3] applied a range of different glucose levels defining hypoglycaemia to the blood glucose data from two large prospective trials of people with type 2 diabetes who had commenced treatment with insulin. As reported in this issue of *Diabetologia*, they unequivocally demonstrate how changing the glucose cut-off

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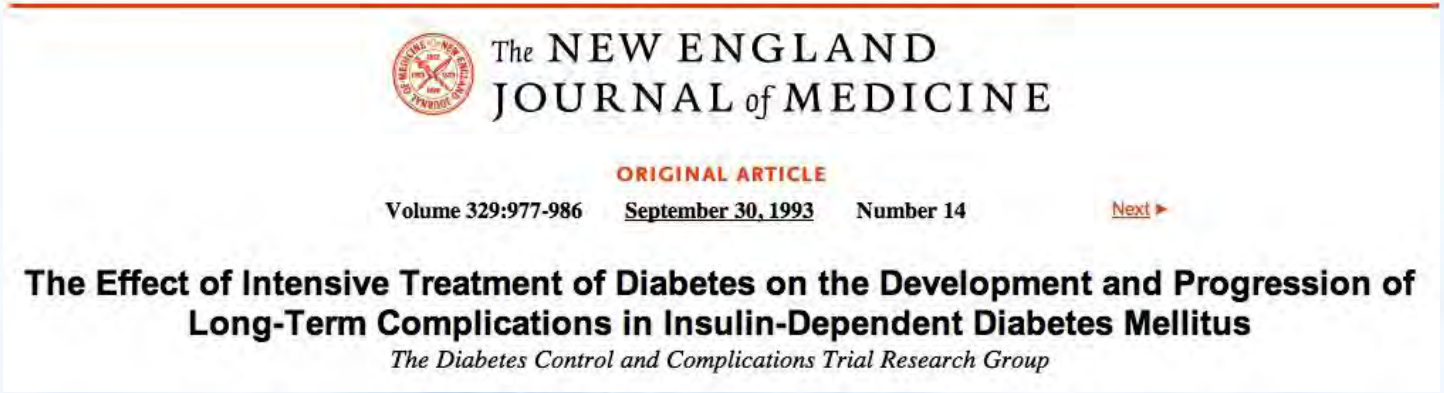
Hypoglykemi



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Volume 329:977-986 September 30, 1993 Number 14 Next ▸

The Effect of Intensive Treatment of Diabetes on the Development and Progression of Long-Term Complications in Insulin-Dependent Diabetes Mellitus

The Diabetes Control and Complications Trial Research Group

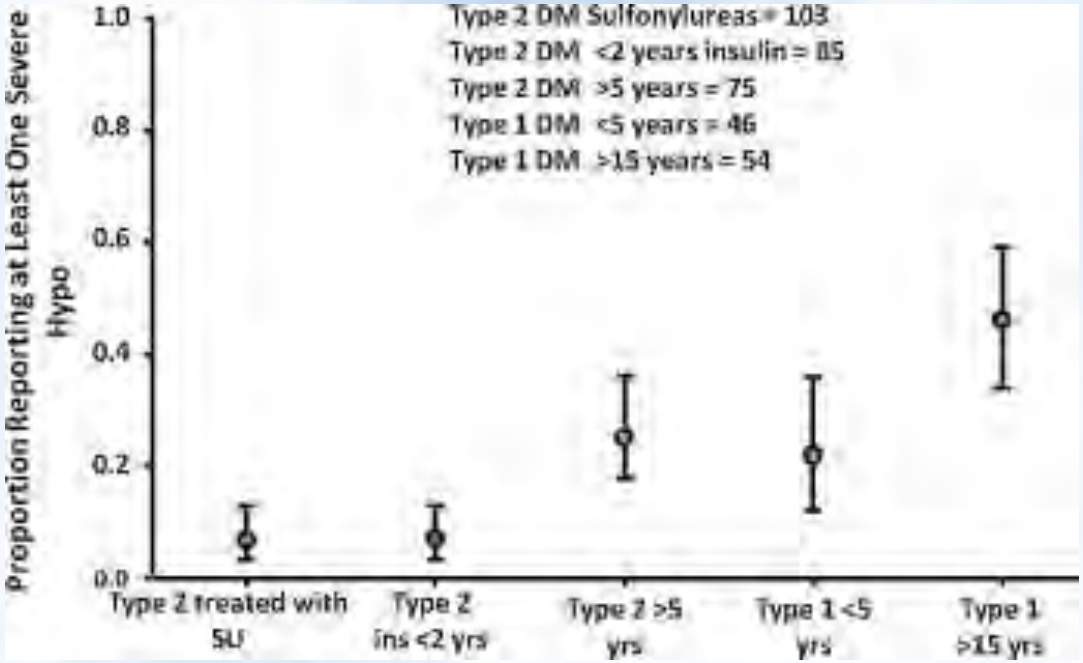
- Klinisk og praktisk vurdering
  - Mild: evne til å selvkorrigere
  - Alvorlig (engelsk; severe): behov for ekstern bistand

Hyppighet

- T1DM - 2 episoder mild hypoglykemi pr uke[1,2]
- T1DM – 30-40% har alvorlig hypoglykemi (i snitt 1-2 episoder) pr år[3]
- T1DM > 15 år har mer enn 3 alvorlige episoder/år[4]

- T2DM ([m]/ insulin) mindre vanlig med alvorlige episoder enn T1DM, MEN 7-25% har minst 1 alvorlig episode/år[4,5,6]
- Hyppig (7%) ved bruk av sulfonylurea medisiner[4]
  (Glibenklamid (Euglucon®, Glibenclamid®), Glipizid (Mindiab®), Glimepirid (Amaryl®, Glimepirid®).

Andel med alvorlig hypoglykemi pr år



UK Hypoglycemia Study Group. Risk of hypoglycemia in types 1 and 2 diabetes: effects of treatment modalities and their duration. *Diabetologica 50* (2007): 1140-1147

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Risiko faktorer

- Tidligere hendelse med alvorlig hypoglykemi
- Økende alder
- Lengde av sykdomsforhold
- Streng glykemisk kontroll
- Søvn

Årsaker

- For store insulindoser (feil timing, feil type)
- For små mengder med karbohydrater
- Nedsatt endogen sekresjon (eks. ved alkohol)
- Økt sukkerforbruk (ved fysiske anstrengelser)
- Nedsatt immunfølsomhet
- Nyresvikt (nedsatt insulin clearance)
- Infeksjon (feber)

Klinikk - hypoglykemi

- **Start** innen få minutter (føling)
- **Hud**
  - Kaldsvett
- **Respirasjon**
  - Normal / normal ånde / keton
- **Sirkulasjon**
  - Puls normal eller økt
  - Blodtrykk normal eller høyt

- **Kramper**
  - Vanlig
- **Dehydrering**
  - ingen / normal diurese
- **Mental status**
  - Uklar tale
  - Uro / angst / aggressiv
  - Desorientert
  - Bevissthetsnedsettelse
- **Pupiller**
  - Normale
- **Recovery innen få minutter**

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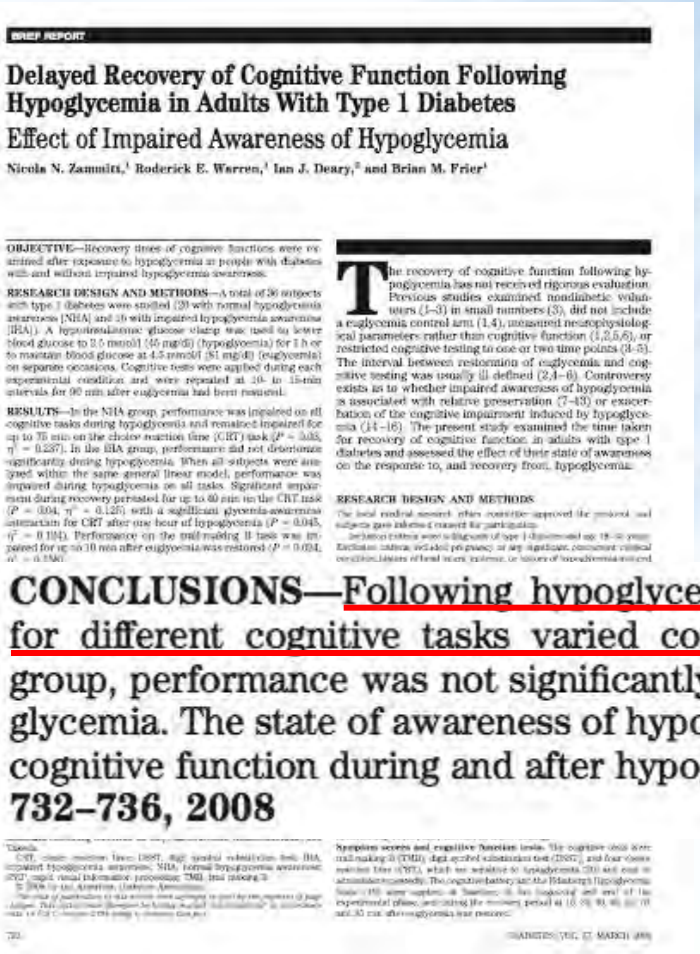
Alltid recovery innen få minutter…..?



BRIEF REPORT

Delayed Recovery of Cognitive Function Following Hypoglycemia in Adults With Type 1 Diabetes

Effect of Impaired Awareness of Hypoglycemia

Nicola N. Zammitt,[1] Roderick E. Warren,[1] Ian J. Deary,[2] and Brian M. Frier[1]

OBJECTIVE—Recovery times of cognitive functions were examined after exposure to hypoglycemia in people with diabetes with and without impaired hypoglycemia awareness.

RESEARCH DESIGN AND METHODS—A total of 36 subjects with type 1 diabetes were studied (20 with normal hypoglycemia awareness [NHA] and 16 with impaired hypoglycemia awareness [IHA]). A hyperinsulinemic glucose clamp was used to lower blood glucose to 2.5 mmol/l (45 mg/dl) (hypoglycemia) for 1 h or to maintain blood glucose at 4.5 mmol/l (81 mg/dl) (euglycemia) on separate occasions. Cognitive tests were applied during each experimental condition and were repeated at 10- to 15-min intervals for 90 min after euglycemia had been restored.

RESULTS—In the NHA group, performance was impaired on all cognitive tasks during hypoglycemia and remained impaired for up to 75 min on the choice reaction time (CRT) task ($P = 0.03$, $\eta^2 = 0.237$). In the IHA group, performance did not deteriorate significantly during hypoglycemia. When all subjects were analyzed within the same general linear model, performance was impaired during hypoglycemia on all tasks. Significant impairment during recovery persisted for up to 60 min on the CRT task ($P = 0.04$, $\eta^2 = 0.126$) with a significant glycemia-awareness interaction for CRT after one hour of hypoglycemia ($P = 0.045$, $\eta^2 = 0.104$). Performance on the trail-making B task was impaired for up to 10 min after euglycemia was restored ($P = 0.024$, $\eta^2 = 0.180$).

The recovery of cognitive function following hypoglycemia has not received rigorous evaluation. Previous studies examined nondiabetic volunteers (1–3) in small numbers (3), did not include a euglycemia control arm (1,4), measured neurophysiological parameters rather than cognitive function (1,2,5,6), or restricted cognitive testing to one or two time points (3–5). The interval between restoration of euglycemia and cognitive testing was usually ill defined (2,4–6). Controversy exists as to whether impaired awareness of hypoglycemia is associated with relative preservation (7–13) or exacerbation of the cognitive impairment induced by hypoglycemia (14–16). The present study examined the time taken for recovery of cognitive function in adults with type 1 diabetes and assessed the effect of their state of awareness on the response to, and recovery from, hypoglycemia.

RESEARCH DESIGN AND METHODS

CONCLUSIONS—Following hypoglycemia, the recovery time for different cognitive tasks varied considerably. In the IHA group, performance was not significantly impaired during hypoglycemia. The state of awareness of hypoglycemia may influence cognitive function during and after hypoglycemia. ***Diabetes* 57: 732–736, 2008**

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IHA – Impaired awareness of hypoglycemia

- Assosiert med langvarig insulin bruk
- Nedsatt intensitet på varsel symptomer
- Klinikk: hovedsakelig adferdsforandringer
- Økt fare for alvorlig hypoglykemi
- Årlig risikoøkning for alvorlig hypoglykemi
- T1DM – 50% ved diabetes > 25 år[5]
- T2DM (m/insulinbruk) – forekomst < 10 %

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Diabetes - Konklusjon

- Økende utfordring
- Lett å diagnostisere
- Hovedsakelig enkel behandling

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