Type 1 diabetes in older adults: identifying the challenge

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I have received speaker honoraria, conference sponsorship, unrestricted educational grants and/or attended meetings (i.e. had free dinner) sponsored by:

- Astra Zeneca,
- Bayer,
- Boehringer Ingelheim,
- Bristol Myer Squib,
- Colgate Palmolive,
- Eli Lilly,
- Glaxo SmithKline,
- Janssen,
- Lundbeck,
- Menarini,
- Merck,
- Napp,
- Novartis,
- Novo Nordisk,
- Pfizer,
- Sanofi Aventis,
- Servier,
- Takeda

I currently hold research grants from

- Astra-Zeneca,
- Bayer,
- Colgate Palmolive,
- Novartis,
- Novo Nordisk & Takeda

Half of the honoraria I receive are diverted directly to [https://www.healthamplifier.org](https://www.healthamplifier.org) supporting medical services and education in one of the poorest communities in Tanzania.
I would never allow a scientist to partake in my government – Give them a new piece of information and they are liable to change their mind.

Abraham Lincoln
16th President of the United States
Diabetes is a growing problem

*Numbers expressed in millions
The number of older adults with diabetes is expected to double over the next 5 years\(^2\)

1 in 4 people in residential care have diabetes\(^2\)

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The (mis) perceptions

Type 2 diabetes is a disease of the elderly
Type 1 diabetes is a disease of the young
Up to 25% of people with type 1 diabetes are diagnosed as adults

Subdivisions within type

- Adult onset type 1 diabetes more likely to have detectable c-peptide\(^1\)

- As a result they usually have
  - Better clinical outcomes\(^2\)
  - Less hypoglycaemia\(^2\)

- Shorter burden of disease

So what? They’re just a bit older...

- Little person gets bigger
- It’s just about size!

- Fundamental changes in physiology
- Kidneys, liver, heart, brain, autonomic nervous system, endocrine system, all start to fail
Mortality and weight in older adults

In younger patients, higher body weight is a poor prognostic indicator. In older patients, the converse is true.

In hospital mortality vs. BMI in young elderly vs. very elderly

HbA\textsubscript{1c} differs for older adults

Possible explanation

Older vs younger adults

- **Lower red blood cell (RBC) count\textsuperscript{1}**

- **Decreased secretion of EPO due to decline in renal function\textsuperscript{1}**

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What is Old...

- Chronological vs physiological vs functional age
- Office of National Statistics in the UK – 65yrs
- WHO – someone whose age has passed the median life expectancy at birth

- UK – 81.2yrs
- In Africa – 50-55yrs
- Latin America – 60yrs
Age vs. Frailty...

Both of these actors are the same age.
Mortality of 75+ year old those who survive 6 months stratified by Frailty status

Data on File of Mazoli, J, Strain, WD et al from CPRD database
The frail, elderly patient with diabetes

Older persons with diabetes are at higher risk than those without diabetes of:
- Usual complications of diabetes...

Ageing and Diabetes

CV disease, cancer and all cause morbidity/mortality

The frail, elderly patient with diabetes

Older persons with diabetes are at higher risk than those without diabetes of:

- Usual complications of diabetes...

  But Also

- Functional disability
- Geriatric syndromes: depression

The frail, elderly patient with diabetes

Older persons with diabetes are at higher risk than those without diabetes of:
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  - But Also
- Functional disability
- Geriatric syndromes: depression
- Geriatric syndromes: cognitive impairment

The frail, elderly patient with diabetes

Older persons with diabetes are at higher risk than those without diabetes of:

- Usual complications of diabetes...
- **But Also**
  - Functional disability
  - Geriatric syndromes: depression
  - **Geriatric syndromes: cognitive impairment**

Cognitive dysfunction should be added to the list of the complications of diabetes, along with retinopathy, neuropathy, nephropathy and cardiovascular disease.
Pathophysiology – diabetes and dementia

- Insulin resistance
- Absence of ApoE4 allele
- Cerebrovascular ischemic event
- Hypoglycaemia
- Reduced C-peptide
- Hyperglycaemic microvascular injury

Cognitive dysfunction

Hypoglycaemia and dementia

A longitudinal cohort study from 1980–2007 of 16,667 patients with a mean age of 65 years and type 2 diabetes who were members of an integrated health care delivery system in northern California

**Hypoglycaemia and risk of incident dementia cases**

<table>
<thead>
<tr>
<th>No. of hypoglycaemic episodes(^b) (n)</th>
<th>No. of dementia cases</th>
<th>Adjusted for Age (as time scale) BMI, Race/Ethnicity, education, sex, and duration of diabetes</th>
<th>Additionally adjusted for comorbidities(^c)</th>
<th>Additionally, adjusted for 7-year HbA(_{1c}) level, diabetes treatment and years of insulin use</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 or more</td>
<td>250</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>150</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>57</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 of more</td>
<td>43</td>
<td></td>
<td></td>
<td></td>
</tr>
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</table>

\(^{a}\) Analyses combined using Cox proportional hazard models; \(^{b}\)The 1 or more group was compared with 0 and 1, 2 and 3 or more groups were simultaneously compared to 0; \(^{c}\) Adjustment made using a comorbidity composite scale. BMI=body mass index; CI=confidence interval; HbA\(_{1c}\)=haemoglobin A\(_{1c}\)

Whitmer et al. JAMA 2009; 301:1565–572
Risk of incident dementia associated with average glucose level over the preceding 5 years among participants without diabetes

<table>
<thead>
<tr>
<th>Average Glucose Level</th>
<th>Hazard Ratio for Dementia (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>Participants without diabetes</td>
<td></td>
</tr>
<tr>
<td>95 mg/dl</td>
<td>0.86 (0.77-0.97)</td>
</tr>
<tr>
<td>100 mg/dl</td>
<td>1.00</td>
</tr>
<tr>
<td>105 mg/dl</td>
<td>1.10 (1.03-1.17)</td>
</tr>
<tr>
<td>110 mg/dl</td>
<td>1.15 (1.05-1.27)</td>
</tr>
<tr>
<td>115 mg/dl</td>
<td>1.18 (1.04-1.33)</td>
</tr>
<tr>
<td><em>p</em> value</td>
<td>0.01</td>
</tr>
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Relationship between glucose and risk of dementia

### Relationship between glucose and risk of dementia

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<tr>
<td>150 mg/dl</td>
<td>1.10 (0.92-1.30)</td>
</tr>
<tr>
<td>160 mg/dl</td>
<td>1.00</td>
</tr>
<tr>
<td>170 mg/dl</td>
<td>1.01 (0.92-1.12)</td>
</tr>
<tr>
<td>180 mg/dl</td>
<td>1.15 (0.98-1.34)</td>
</tr>
<tr>
<td>190 mg/dl</td>
<td>1.40 (1.12-1.76)</td>
</tr>
<tr>
<td><strong>p value</strong></td>
<td><strong>0.002</strong></td>
</tr>
</tbody>
</table>

CI, confidence interval
The physiology of hypos – older patients

Normal glucose suppresses insulin at 4.6 mmol/L

Normal physiological homeostasis

Glucose falls

↑Glucagon (3.8±0.3 mmol/L)

↑Adrenaline (epinephrine) (2.8±0.3 mmol/L)

↑BRAIN GLUCOSE UPTAKE (3.4 mmol/L)

↑Growth hormone (3.1 mmol/L)

↑Cortisol (3.0 mmol/L)

↑Neurotransmitters (2.4 mmol/L)

Glucose rises

↓COGNITION (2.8 mmol/L)

↓BRAIN GLUCOSE UPTAKE (3.4 mmol/L)

↓COGNITION (2.8 mmol/L)

Zammitt NN, Frier BM. Diabetes Care 2005;28:2948–61
Symptoms of hypoglycaemia are non-specific in older people

**Autonomic:**
- Palpitations
- Sweating
- Anxiety

**Neuroglycopenic:**
- Fatigue
- Confusion
- Drowsiness

- Irritability
- Dizziness
- Coma

**Particularly in older people:**
- Unsteadiness
- Light-headedness

All these are also common in older people without diabetes

Managing elderly patients is complicated by
- Multiple co-morbidities,
- Increased risk from the complications of treatment
- Reduced life expectancy, therefore reduced return

Treatment should focus on reducing risk of side effects and improving symptoms
Thank you for your attention