# Is avoidance of hypoglycaemia a better target than HbA1C in frail older people with diabetes?

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**Alzheimer's Society**

**United Against Dementia**

## Outline

Why is this a major problem?

Clinical Case

Hypoglycaemia – unnoticed, but potentially deadly

Changing how we think about diabetes

Clinical implications for the future

# Growing burden of diabetes in older people

~425 million people living with diabetes, of whom approximately **123 million are aged between 65 to 99 years.**

**Proportion of older people with dementia who have co-existing diabetes is 13-20%.**

No standardised guidelines for older people who are having to juggle diabetes with multiple co-morbidities.

American Geriatrics Society 2015*: "increasing observational evidence … that clinicians often do not differentiate treatments for older patients who differ widely in health status"*

Numerous proposals for relaxed HbA1C targets e.g. >64 mmol (8.0%) in frail older.

# Specific Challenges in Frail Older People with Diabetes

Memory problems makes management even more difficult in patients:

- Forget to eat & drink.

- May not understand why/how to monitor glucose levels.

- May not recognize symptoms of hypoglycaemia.

- May not be able to communicate that they are feeling unwell

- Classical features of abnormal blood sugars may not be visible to carers

- Increased risk of Adverse Drug Reactions (renal and liver disease)

# Intensive diabetes drug use in frail older patients

Prevalence studies of high risk drug use:

- US Veterans >15k patients (diabetes and dementia) – insulin 35%; sulfonylurea 56%

- UK study (Norfolk age >70 years) – 36% on insulin and/or sulfonylurea; similar use

  even in groups with dementia or renal impairment.

Contrary to perceived wisdom, US study of 75-79 year olds:

- Greater success with insulin de-prescribing in healthy old (few or no comorbidities)

- Persistence of insulin use in those with dementia, and serious end-stage disease

## Our Patient Case

89-year old, male

- T2DM (Humalog Mix 25 12 Units BD, Metformin 500mg BD)

- Dementia (limited communication)

- Wife is sole carer – she does the glucose monitoring (BD) and insulin injections

- No hypoglycaemia awareness – subtle changes in behavior trigger wife to check glucose levels (finger-prick testing)

- Should we look at HbA1C and treat to (relaxed) target?

# HbA1C – genuinely useful or highly-over rated?

We treat what we can measure. We ignore difficult to measure parameters.

- HbA1C is easily measured –targets set and pursued.

- Hypoglycaemia – hard to capture, thus less of a priority

HbA1C – validity in frail older people?

- Can predict long-term complications 10-20 years

- Poor at predicting hypoglycaemia (both high and low HbA1C confers greater risk, probably due to fluctuations)

Immediate harm from hypo far greater priority in frail older people than prevention of retinopathy in 10 years' time?

What is the harm from hypoglycaemia in patients with diabetes and dementia?

# Pharmacoepidemiology study



DIABETES, OBESITY AND METABOLISM
A JOURNAL OF PHARMACOLOGY AND THERAPEUTICS

ORIGINAL ARTICLE | 🔓 Full Access

## The effects of hypoglycaemia and dementia on cardiovascular events, falls and fractures and all-cause mortality in older individuals: A retrospective cohort study

Katharina Mattishent MRCP ✉, Kathryn Richardson PhD, Ketan Dhatariya PhD, George M. Savva PhD, Chris Fox MD, Yoon K. Loke MD

# Pharmacoepidemiology study: Analysis

Not ethical to randomize to hypos / no hypos

- Have to look back at real-life GP data linked to NHS hospital records

- Records of patients with dementia and hypo documented by GP or hospital (n=1679)

- Able to track patients *after* hypo – check for fall, fractures, CV events, death.

- Use statistical adjustment to compare against control group "no hypos" (n=7183)

- Calculate adjusted Hazard Ratios (aHR)

# Pharmacoepidemiology study: Results

At **12 months follow-up**, significantly higher probability of adverse events in those with hypo:

- **Falls and fractures** - aHR 1.94 (95% CI 1.67 to 2.24)

- **Cardiovascular events** - aHR 2.00 (95% CI 1.61 to 2.48)

- **Mortality** - aHR 2.36 (95% CI 2.09 to 2.67)

## Mechanism of harm from hypoglycaemia

Cognitive impairment well-documented in laboratory data

Epidemiology – those with recurrent hypos are subsequently more likely to develop

dementia during follow-up

Hypoglycaemia associated with cardiac problems on ECG monitoring:

- Ventricular arrhythmias

- QT prolongation

All of above could lead to falls and heart attacks.

How can we improve detection of hypoglycaemic episodes in older people with diabetes and memory problems?

# Continuous glucose monitoring (CGM)



*24 hour coverage for 10-14 days*

# CGM in older people – Systematic review
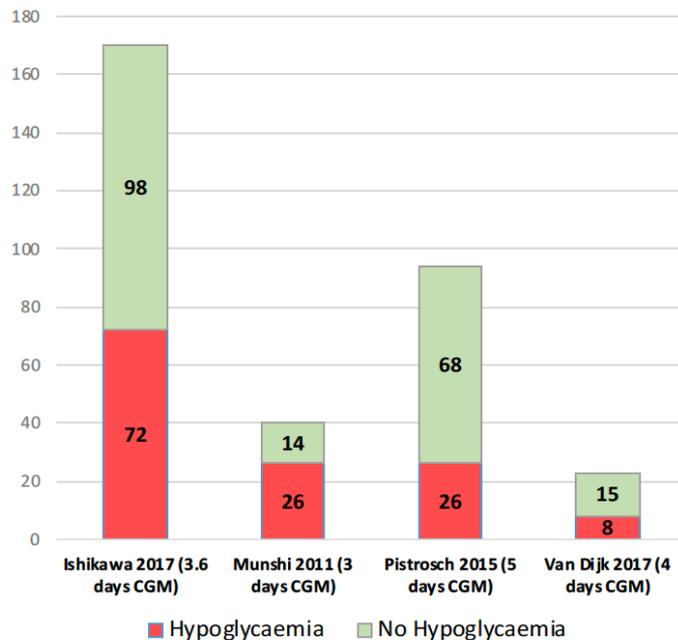
Journal of Diabetes and its Complications
Volume 32, Issue 8, August 2018, Pages 805-812

ELSEVIER

Detection of asymptomatic drug-induced hypoglycemia using continuous glucose monitoring in older people – Systematic review

K. Mattishent, Y.K. Loke

*Number of patients with and without hypoglycaemia*



- Some patients spent nearly 2hr/day in hypoglycaemic range.

- CGM picked up hypoglycaemic episodes in a sizeable proportion patients.

- In one study (van Dijk) 100% of the hypoglycaemic episodes were asymptomatic.

- None of the studies focused on patients with memory problems

# Our Data in Older Patients with Memory Problems
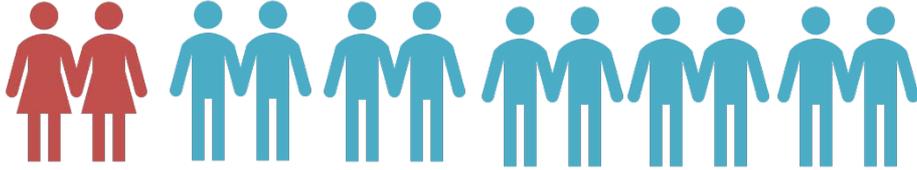
Mean age 85; all except one had type 2 diabetes; 9 on insulin.
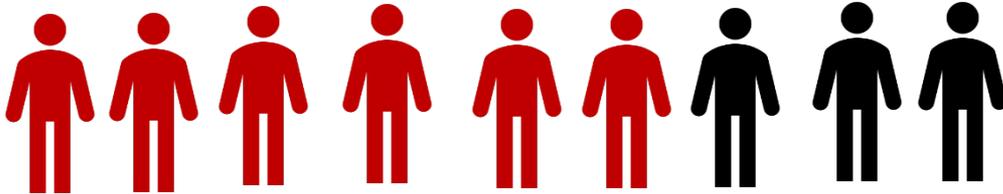
**6/9 insulin users** had recorded hypoglycaemic events (duration of the hypoglycaemia ranged between 106-437 minutes)
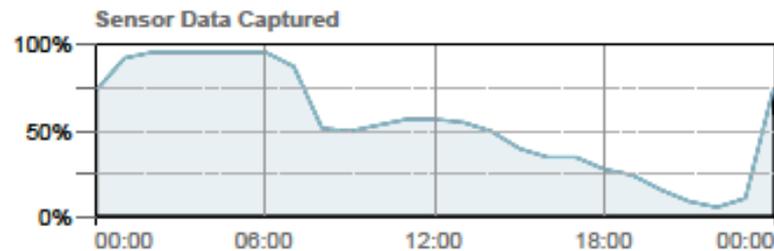
# CGM in our 89 y old insulin- treated patient

📱 **Glucose**

| | |
|---|---|
| **AVERAGE GLUCOSE** | **6.6** mmol/L |
| % above target | 13 % |
| % in target | 72 % |
| % below target | 15 % |

**Average Glucose**

**Low-Glucose Events**

| | |
|---|---|
| **LOW-GLUCOSE EVENTS** | **4** |
| Average duration | 437 Min |
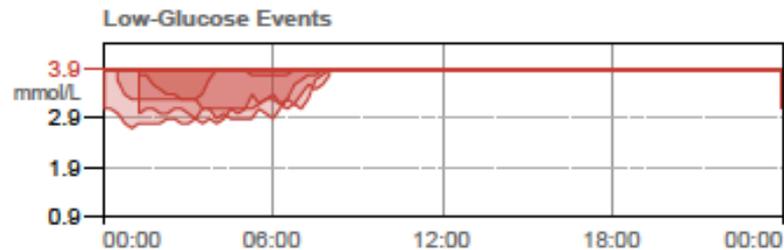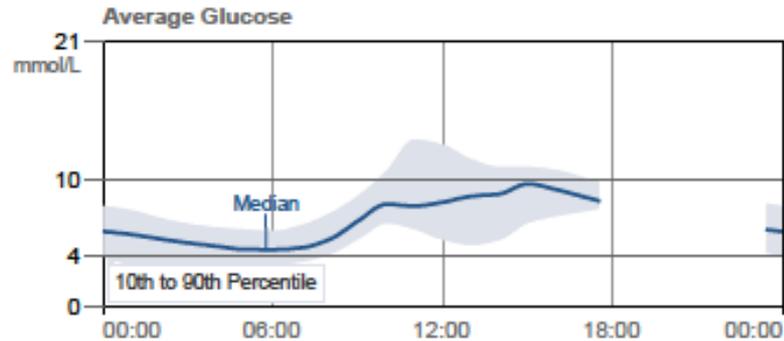
📶 **Sensor Usage**

| | |
|---|---|
| **SENSOR DATA CAPTURED** | **55** % |
| Daily scans | 3 |

**Sensor Data Captured**

# Consider time in range instead of HbA1C

A1C is currently key surrogate marker.
Reflects average glucose over the last 2–3 months.
**Limitations**: no data about acute changes and fluctuations; fails to identify magnitude and frequency of intra- and inter-day glucose.

CGM – can assess glycaemic control throughout several days
Quantify time below, within, and above the established glycaemic targets.

*Three patients with same HbA1C 7.0% but very different 24 hour glucose profiles*



Vigersky, R. J Diabetes. 2019 Jan;11(1):23-3
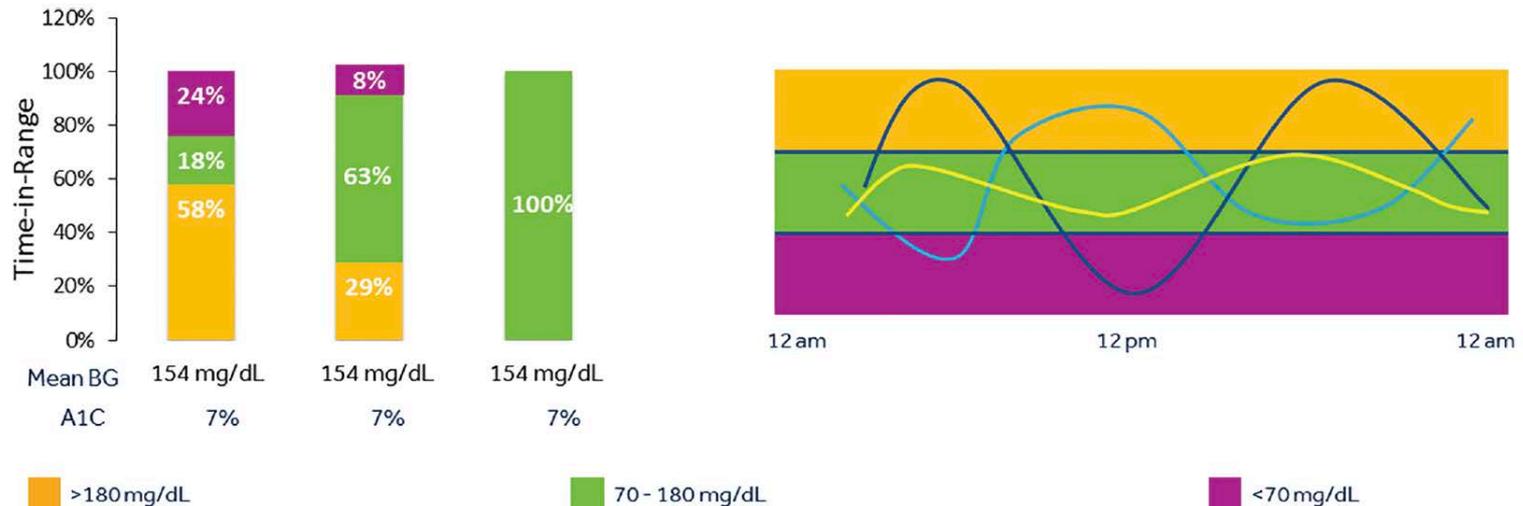
# Newly proposed targets for time in range

## Older / High-Risk Individuals[1]

| Diabetes Group | Time in Range (TIR) | | Time Below Range (TBR) | | Time Above Range (TAR) | |
|---|---|---|---|---|---|---|
| | % of readings time/day | Target Range | % of readings time/day | Below Target Level | % of readings time/day | Above Target Level |
| Older/High-Risk Type 1/ Type 2 | >50% >12 hr | 70-180 mg/dL 3.9-10 mmol/L | <1% <15 min | <70 mg/dL <3.9 mmol/L | <10% <2 hr, 24 min | >250 mg/dL >13.9 mmol/L |
| *Each incremental 5% increase in TIR is associated with clinically significant benefits for Type 1 / Type 2* [2,3] | | | | | | |



Older/High-Risk:
Type 1 & Type 2
Diabetes

**Target**

>250 mg/dL (13.9 mmol/L)  —  <10%

>180 mg/dL (10.0 mmol/L)  —  <50%*

Target Range: 70–180 mg/dL (3.9–10.0 mmol/L)  —  >50%
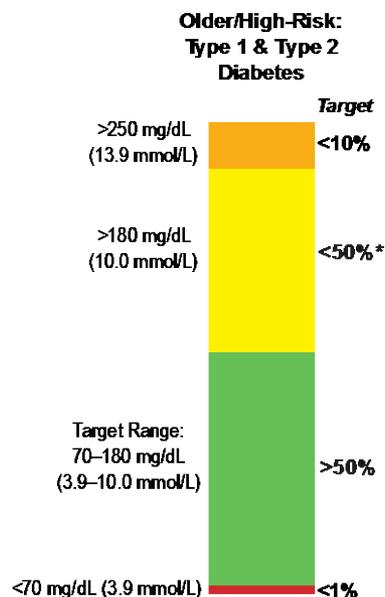
<70 mg/dL (3.9 mmol/L)  —  <1%

**Table 2—Standardized CGM metrics for clinical care: 2019**
1. Number of days CGM worn (recommend 14 days) (42,43)
2. Percentage of time CGM is active (recommend 70% of data from 14 days) (41,42)
3. Mean glucose
4. Glucose management indicator (GMI) (75)
5. Glycemic variability (%CV) target ≤36% (90)*
6. Time above range (TAR): % of readings and time >250 mg/dL (>13.9 mmol/L)
7. Time above range (TAR): % of readings and time 181–250 mg/dL (10.1–13.9 mmol/L)
8. Time in range (TIR): % of readings and time 70–180 mg/dL (3.9–10.0 mmol/L)
9. Time below range (TBR): % of readings and time 54–69 mg/dL (3.0–3.8 mmol/L)
10. Time below range (TBR): % of readings and time <54 mg/dL (<3.0 mmol/L)

*Use of Ambulatory Glucose Profile (AGP) for CGM report*

*1. Battelino T, et al Diabetes Care. 2019 Aug;42(8):1593-1603;  2. Beck RW, et al. J Diabetes Sci Technol. 2019 Jan 13:doi: 10.1177/1932296818822496;*
*3. Vigersky RA, et al. Diabetes Technol Ther. 2019;21(2):81-85.*

# Our CGM data - results (time in range %)
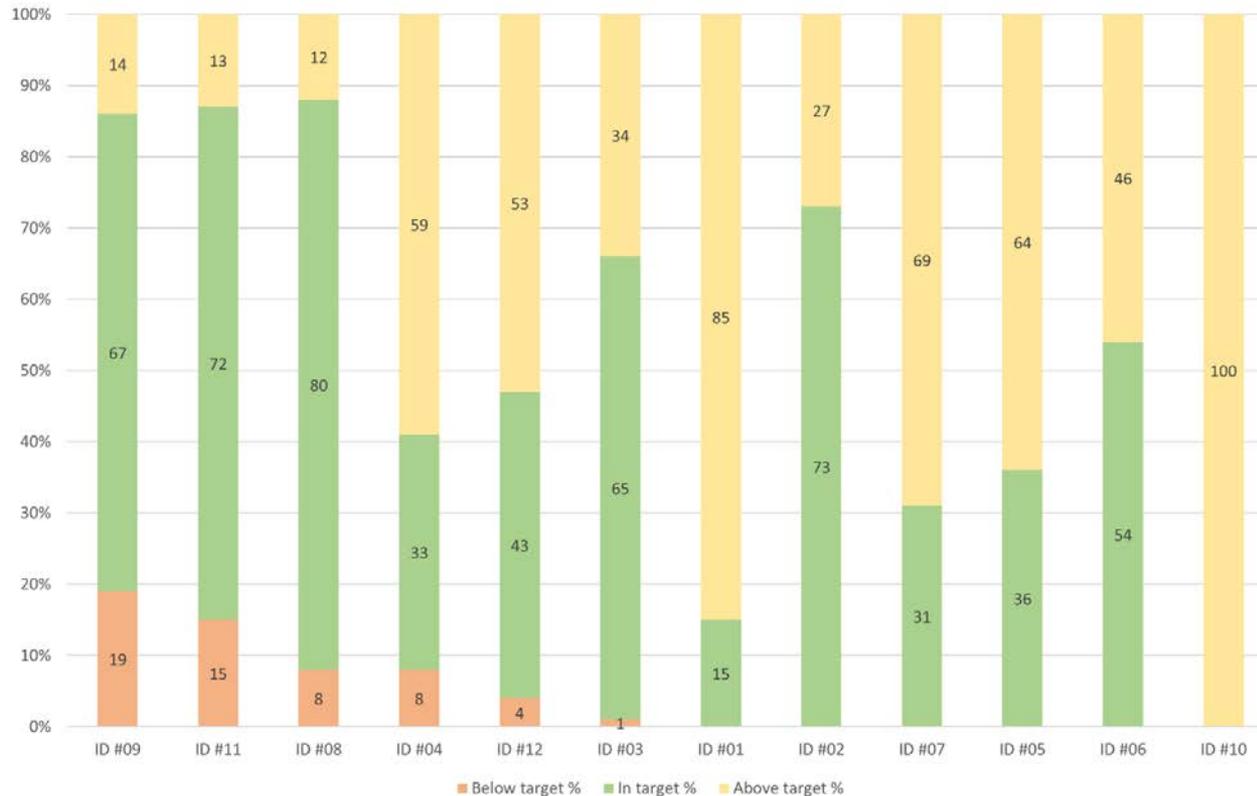


- 4/12 had 70% or more data capture.
  - 6/12 had >50% TIR
  - 6/12 had <1% TBR

# Are older people comfortable with CGM?

**Expectations**

"You've got to work with science and progress"; opportunity to "join the 21st century"

**Effectiveness**

"Well it's better than pricking your finger cos my fingers got like sore"

**Consequences**

Carers found the device particularly useful as it made them feel reassured and safer being able to check glucose levels.

**Overall opinion of the device**

"We both think it's progress and it's going to help people in the future".

# De-prescribing in Older People

Systematic review suggests this is feasible with low risk of harm

However, we do not know best method of achieving de-intensification:

- US Veterans: pop-up alert for relevant named patients on electronic record

- Only 9.6% of 2830 patients had their diabetes drugs reduced

- Prescribers significantly more likely to change drugs if symptomatic hypos found

- Study of national initiative: led to fewer over-treated patients but also more under-treated patients

# Clinical implications

Management of diabetes in later life should focus on **avoidance of hypoglycaemia, and not targeted HbA1C**.

Significant mind shift needed towards using **CGM** at least intermittently in older people, especially those with memory problems – **only way to reliably capture hypoglycaemia**.

- Conduct one set of baseline CGM
- Look at Time in Range and % Hypo
- Check for high risk drugs (e.g. insulin and sulfonylureas)
- Switch patients to drugs that have low Hypo Risk.
- Re-evaluate with further spell of CGM

# Acknowledgments

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# Thank you for listening