Glucose profiles of older adults with type 1 diabetes using sensor-augmented pump therapy in Australia: pre-randomisation results from the ORACL study

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Summary

Background Older adults with type 1 diabetes are recommended modified glucose targets. However, data on the effects of diabetes technology in older age are scarce. We assessed older adults established on sensor-augmented insulin pump therapy during clinical trial run-in and compared their continuous glucose monitoring (CGM) profiles with consensus recommendations. We aimed to provide insight into the applicability of currently recommended CGM-based targets while accounting for current Diabetes UK guidelines.

Methods In this analysis, adults aged 60 years or older with type 1 diabetes with a duration of at least 10 years and entering the Older Adult Closed Loop (ORACL) trial were studied. The trial was done at two tertiary hospitals in Australia. Individuals who were independent with diabetes self-management, as well as those receiving caregiver assistance for their diabetes management, were eligible for inclusion. Participants underwent baseline clinical assessment, which included medical history and examination, testing for frailty, functional ability, cognitive functioning, psychosocial wellbeing, and subjective sleep quality; fasting venous blood samples were collected for C-peptide, glucose, and glycated haemoglobin A1c, measurement. Sensor-augmented pumps, carbohydrate-counting education, and diabetes education were provided to participants by diabetes nurse educators, dietitians, and endocrinologists experienced in type 1 diabetes clinical care. CGM data were subsequently collected for 2 weeks during sensor-augmented pump therapy. The ORACL trial is registered with the Australian New Zealand Clinical Trial Registry, ACTRN12619000515190.

Findings Our analysis included all 30 participants who completed the ORACL trial run-in—19 (63%) women and 11 (37%) men (mean age 67 years [SD 5], median diabetes duration 38 years [IQR 20–47], and insulin total daily dose 0·55 units [0·41–0·66] per kg bodyweight). Ten (33%) of 30 participants had impaired hypoglycaemia awareness and six (20%) were pre-frail; none were frail. The median CGM time in range 3·9–10·0 mmol/L was 71% (IQR 64–79). The time spent with glucose above 10·0 mmol/L was 27% (18–35) and above 13·9 mmol/L was 3% (2·4–10·2). The time with glucose below 3·9 mmol/L was 2·0% (1·2–3·1) and the time below 0·0 mmol/L was 0·2% (0·1–0·4). Only two (7%) of 30 participants met all CGM-based consensus recommendations modified for older adults. Time in hypoglycaemia was lower among the 16 participants with predictive low-glucose alerts enabled than among the 14 participants not using predictive low-glucose alerts (median difference −1·1 percentage points [95% CI −2·0 to −0·1]; p=0·038). This difference was even greater overnight (−2·3 percentage points [−3·2 to −1·0]; p=0·0018). One serious adverse event occurred (elective cardiac stent).

Interpretation Using sensor-augmented pumps after multidisciplinary education, this group of older adults without frailty achieved a time in range far exceeding minimum consensus recommendations. However, the current stringent hypoglycaemia recommendations for all older adults were not met. Predictive low alerts could reduce hypoglycaemia, particularly overnight. Investigation into the effectiveness of CGM-based targets that consider frailty, functional status, and diabetes therapies for older adults is warranted.

Funding JDRF and Diabetes Australia.

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recommendations (including less stringent glycated haemoglobin A$_1c$ [HbA$_1c$] targets) based upon frailty, cognitive impairment, and dependence for older adults with type 1 diabetes.$^7$ Continuous glucose monitoring (CGM), which measures interstitial fluid glucose via transeptane sensors, is increasingly becoming the standard of care for individuals with type 1 diabetes; yet, Diabetes UK treatment guidelines for older adults with type 1 diabetes place emphasis upon geriatric characteristics (such as cognition, functional independence, and frailty status) when recommending glucose targets and clinical management plans. However, the Diabetes UK guidelines do not include CGM-based glucose targets. Therefore, we did a further search on PubMed from database inception up to July 26, 2022, to identify studies that specifically targeted older adults with type 1 diabetes, using the search terms (elder[ti] OR “older adult”[ti] OR “older adults”[ti] OR “senior citizen”[ti] OR “senior citizens”[ti] OR retired[ti]) AND (“type 1 diabetes”), which yielded 220 papers, of which 68 were studies involving older adults with type 1 diabetes. Manual screening of these 68 papers indicated that only six papers derived from two studies (one from our research group) assessed participant frailty or functional ability.

### Added value of this study

To our knowledge, our report is the first to consider older-adult type 1 diabetes consensus recommendations for CGM targets in a sample of older people with no frailty. In this study, older age and long-duration type 1 diabetes were not barriers to safely using sensor-augmented pump therapy and sustaining high CGM time in range. However, only a few participants met all the modified CGM-based targets recommended by Battelino and colleagues for older adults (with the stringent hypoglycaemia target met by less than a quarter of the group). Nevertheless, this group of older adults with no frailty met CGM-based consensus recommendations for younger adults; there were no clinically concerning events among functionally independent individuals. Less time spent in hypoglycaemia was observed among the participants who were using CGM predictive low-glucose alerts, particularly overnight.

### Implications of all the available evidence

Our findings support consideration of further individualisation of glucose targets for older adults with type 1 diabetes, including consideration of frailty and functional status, and the insulin delivery and glucose monitoring technology being used. Moreover, our findings encourage the use of CGM predictive low-alerts.

### Methods

#### Study design and participants

This is a post-hoc analysis of prospective data collected before random assignment in the Older Adult Closed Loop (ORACL) trial.$^9$ The trial was done at two tertiary hospitals in Australia. Adults aged 60 years or older with type 1 diabetes with a duration of at least 10 years and who were using an insulin pump (with or without CGM) were recruited to the study. Individuals who were independent with diabetes self-management, as well as those receiving caregiver assistance for their diabetes management, were eligible for inclusion. Exclusion criteria included use of non-insulin glucose-lowering agents, corticosteroids, or closed-loop automated insulin delivery within the past 3 months; visual or hearing agents, corticosteroids, or closed-loop automated insulin delivery within the past 3 months; visual or hearing impairment; or use of non-insulin glucose-lowering agents, corticosteroids, or closed-loop automated insulin delivery within the past 3 months. The trial was done in two phases: a clinical trial run-in, and to compare their glucose profiles with consensus CGM-based clinical target recommendations for older adults. By establishing the frailty status of these individuals, we aim to provide insight into the applicability of these currently recommended CGM-based targets while accounting for current Diabetes UK guidelines.

#### Research in context

**Evidence before this study**

We searched PubMed for continuous glucose monitoring (CGM)-based clinical targets for older adults with type 1 diabetes from database inception to July 26, 2022, using title search terms ("continuous glucose monitoring" OR "CGM") AND ("recommendation" OR "consensus" OR "clinical target"), with no language restrictions. The search yielded 15 papers, which we manually inspected to identify any CGM-based treatment target recommendations exclusively for older adults. Only one paper, by Battelino and colleagues (2019), specifically mentioned older adults. Battelino and colleagues recommended modified CGM-based targets for older adults, with a more stringent hypoglycaemia target accompanied by a lower time-in-range target compared with their recommendations for younger individuals; notably, these modified recommendations were for all older adults with diabetes, without reference to their frailty or functional status. This age-based generalisation is noteworthy, as Diabetes UK treatment guidelines for older adults with type 1 diabetes place emphasis upon geriatric characteristics (such as cognition, functional independence, and frailty status) when recommending glucose targets and clinical management plans. However, the Diabetes UK guidelines do not include CGM-based glucose targets. Therefore, we did a further search on PubMed from database inception up to July 26, 2022, to identify studies that specifically targeted older adults with type 1 diabetes, using the search terms (elder[ti] OR “older adult”[ti] OR “older adults”[ti] OR “senior citizen”[ti] OR “senior citizens”[ti] OR retired[ti]) AND (“type 1 diabetes”), which yielded 220 papers, of which 68 were studies involving older adults with type 1 diabetes. Manual screening of these 68 papers indicated that only six papers derived from two studies (one from our research group) assessed participant frailty or functional ability.

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impairment precluding the use of study devices; and a clinical diagnosis of moderate or severe dementia. Complete inclusion and exclusion criteria have been published previously.9

The protocol was approved by a central human research ethics committee (human research ethics committee 275/18) and governance was provided at each participating centre. All participants provided written informed consent.

Procedures

Participants underwent baseline clinical assessment, which included medical history and examination, testing for frailty,20–23 functional ability,10–13 cognitive functioning,16–19 psychosocial wellbeing,20–23 and subjective sleep quality;24 fasting venous blood samples were collected for C-peptide, glucose, and HbA1c measurement in a central laboratory. Diabetes education, carbohydrate-counting education, and insulin dosing advice were provided by diabetes nurse educators, dietitians, and endocrinologists experienced in type 1 diabetes clinical care. Participants were provided with standardised sensor-augmented pump therapy equipment (MiniMed 670G pump and Guardian 3 sensors; Medtronic, Northridge, CA, USA). Pumps were used exclusively in manual delivery mode with CGM set to “Alert on low”. Predictive low alerts (“Alert before low”) and pump suspension on low glucose were optional. Predictive low-glucose suspension was prohibited, to avoid any algorithm-based determination of insulin delivery during the trial run-in. Sensor-augmented pump therapy settings were clinically individualised based on study clinician assessment.

After completing the run-in period, CGM and safety outcomes were collected for 2 weeks during sensor-augmented pump therapy. CGM provided sensor glucose readings every 5 min. At least 10 days (midnight to midnight), each with at least 70% valid CGM readings, were required to be included in the analysis; these data were considered sufficient to represent an individual’s glucose levels.25

CGM metrics were calculated and reported according to CGM reporting recommendations, as follows: available CGM readings were used and time in range was calculated by dividing the number of readings within a range by the total number of valid readings. CGM profiles were assessed with reference to consensus CGM-based clinical target recommendations,9 examined separately for the overall (24 h a day), daytime (0600 h to 2359 h) and overnight (0000 h to 0559 h) periods. Counts of self-reported severe hypoglycaemia events, defined as hypoglycaemia requiring third-party assistance to resolve, were collected from participants at each study visit. Sensor hypoglycaemia episodes, at thresholds of below 3·9 mmol/L and below 3·0 mmol/L, were defined as having CGM readings below the threshold for at least 15 min (ie, at least four consecutive CGM readings) and ending when CGM readings were at or above the threshold for at least 15 min.25 The C-peptide assay limit of detection was 3 pmol/L (with reference interval <700 pmol/L for fasting samples in individuals without obesity and without diabetes during normoglycaemia).

Safety outcomes collected were serious adverse events, device-related adverse events, severe hypoglycaemia events, diabetic ketoacidosis, diabetes-related ambulance attendances, diabetes-related hospitalisations, falls, delirium, incident pressure sores, and incident infections.

Statistical analysis

The sample size for this study was based on the requirement for the primary outcome for the ORACL randomised, crossover trial, which was 30 participants (allowing for a 20% dropout rate).9 Descriptive statistics are presented as frequency (%) and median (IQR) or mean (SD). The distribution of continuous variables was examined visually using quantile–quantile plots. Since most outcomes followed a skewed distribution, and to keep analyses consistent, groups (predictive low alert vs alert on low only; impaired vs preserved hypoglycaemia awareness) were compared using Wilcoxon rank-sum tests. Associations between the concentration of C-peptide and CGM metrics were examined visually using scatterplots and using Pearson’s correlation coefficient (after visual inspection of homoscedasticity). No missing data were observed.

Analyses were done using Stata Statistical Software, version 16.1. The ORACL trial is registered with the Australian New Zealand Clinical Trial Registry, ACTRN12619000515190.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Our analysis included all 30 participants who completed the ORACL trial run-in—19 (63%) women and 11 (37%) men (median age 68 years [IQR 64–71], median diabetes duration 38 years [IQR 20–47], and insulin total daily dose 0·55 units [0·41–0·66] per kg bodyweight; table 1). Full baseline characteristics are presented in table 1. The assessment measures that we used in this study did not detect any clinically meaningful degree of frailty, malnutrition, depression, or cognitive impairment among the participants (table 1).

The period of education provision until the commencement of CGM data collection ranged from 9 days to 78 days, with a median of 35·5 days (IQR 28–49). 11 (37%) of 30 participants had a single education session, eight (27%) had two sessions, ten (33%) had three sessions, and one (3%) had four education sessions until deemed proficient in carbohydrate-counting and diabetes device management by the multidisciplinary study team. After education and sensor-augmented pump therapy
### Table 1: Participant characteristics

| Patients (n=30) | Patients (n=30) |
|----------------|----------------|
| **Age, years** | 67 (5)         |
| **Sex**        |                |
| Female         | 19 (63%)       |
| Male           | 11 (37%)       |
| **BMI, kg/m²** | 27.6 (26.4–31.0) |
| **Duration of type 1 diabetes, years** | 38 (20–47) |
| **Duration of insulin pump therapy, years** | 9 (4–13) |
| **Insulin total daily dose** |                |
| Units          | 42 (33–60)     |
| Units per kg bodyweight | 0.55 (0.41–0.66) |
| **Current carbohydrate counting** | 25 (83%) |
| **Current use of continuous glucose monitoring** | 12 (40%) |
| **HbA₁c**      |                |
| HbA₁c, mmol/mol | 59 (9)         |
| HbA₁c, %       | 7.6 (0.9)      |
| HbA₁c ≤7%      | 9 (30%)        |
| **Fasting C-peptide** |            |
| C-peptide, pmol/L | 7 (3–21)     |
| Detectable C-peptide | 23 (77%)     |
| **History of microvascular complications** | 16 (53%) |
| **History of macrovascular complications** | 6 (20%) |
| **Severe hypoglycaemia* events in the past 12 months** |            |
| 0              | 21 (70%)       |
| 1              | 5 (17%)        |
| ≥2             | 4 (13%)        |
| **FRAIL scale categories** |              |
| Non-frail      | 24 (80%)       |
| Pre-frail      | 6 (20%)        |
| Frail          | 0              |
| **Mini Nutritional Assessment** |          |
| Mini Nutritional Assessment score | 14 (13–14) |
| Normal nutritional status | 26 (87%) |
| At risk of malnutrition | 4 (13%) |
| Malnourished   | 0              |
| **Sarcopenia** |                |
| Sarcopenia SARC-F score | 0 (0–1)     |
| Sarcopenia present | 0           |
| **Walking speed** |              |
| Walking speed, m/s | 1.4 (1.2–1.6) |
| Normal walking speed | 30 (100%) |
| **Normal grip strength** | 29 (97%) |
| **Physical activity relative to others own age** |            |
| More active    | 19 (63%)       |
| About as active| 9 (30%)        |
| Less active    | 2 (7%)         |
| **Katz Index of Independence in Activities of Daily Living score** | 6 (6–6)   |
| **Lawton-Brody Activities of Daily Living score** | 8 (8–8) |
| **Caregiver assistance required for diabetes management** | 1 (3%) |
| **Mini Mental State Examination** | 30 (29–30) |

(Continued from previous column)

| MoCA |                |
| MoCA score | 27 (26–28)    |
| MoCA score range | 24–30 |
| Normal cognitive function (MoCA score ≥26) | 24 (80%) |
| Mild cognitive impairment (MoCA score 18–25) | 6 (20%) |
| Moderate or severe cognitive impairment (MoCA score <17) | 0 |
| **Verbal Intelligence Quotient** |                |
| NART score | 37 (32–44)    |
| NART ≥1.5 SD below normative data | 0 |
| **Executive functioning** |                   |
| Trails Making Task B, s | 85.5 (60.6–110.3) |
| Trails Making Task B ≥1.5 SD below normative data | 3 (10%) |
| **Psychomotor speed** |                  |
| Symbol Digit Modalities Test (number correct) | 41 (34–46) |
| Symbol Digit Modalities Test ≥1.5 SD below normative data | 0 |
| Trails Making Task A, s | 29.5 (24.8–40.5) |
| Trails Making Task A ≥1.5 SD below normative data | 2 (7%) |
| Grooved pegboard (dominant), s | 82 (75–100) |
| Grooved pegboard (non-dominant), s | 102 (80–117) |
| Pegboard (non-dominant) ≥1.5 SD below normative data | 3 (10%) |
| **Fear of hypoglycaemia, Hypoglycaemia Fear Survey-version II short form** |             |
| Total scale | 9 (6–14)       |
| Behaviour subscale | 3.5 (2–5)   |
| Worry subscale | 5 (3–10)      |
| **Hypoglycaemia awareness** |              |
| Gold score | 3 (2–4)       |
| Impaired awareness (Gold score 4 or more) | 10 (33%) |
| Clarke score | 2 (1–4)       |
| Impaired awareness (Clarke score 4 or more) | 9 (30%) |
| **PAID-5** |                  |
| PAID-5 score | 4.5 (2–7)     |
| Possible diabetes-related emotional distress (PAID-5 ≥8) | 6 (20%) |
| **Geriatric Depression Scale short form** |               |
| Geriatric Depression Scale score | 1 (0–2)       |
| Likely depression | 0           |
| **DIDP** |                |
| DIDP composite raw score | 4.5 (4.3–4.9) |
| DIDP converted scale score | 6.18 (61.2–69.4) |
| **PSQI** |                  |
| PSQI score | 5 (3–8)       |
| Inadequate sleep quality (PSQI >5) | 14 (47%) |

Data are mean (SD), n (%), or median (IQR), unless otherwise indicated. Data were collected at the first study visit (baseline). DIDP=Diabetes Attitudes, Wishes and Needs Impact of Diabetes Profile. FRAIL=Fatigue, resistance, ambulation, illness, loss of weight. HbA₁c=glycated haemoglobin A₁c. MoCA=Montreal Cognitive Assessment. NART=National Adult Reading Test. PAID-5=Problem Areas in Diabetes short form. PSQI=Pittsburgh Sleep Quality Index. SARC-F=strength, assistance with walking, rising from a chair, climbing stairs, and falls. *Severe hypoglycaemia event defined as hypoglycaemia needing assistance from another person for recovery.

Table 1 continues in next column.
Figure 1: CGM metrics

(A) Sensor glucose levels, presented as median (IQR) of participants' sensor glucose values at each 5-min interval. The dashed horizontal lines denote the limit of the target range. (B–E) The proportion of time in glucose ranges by hour of the day. Dots denote individual participant results, lines denote median, and bars show the IQR. The dashed lines denote consensus CGM-based clinical target recommendation limits. (B) Proportion of time in range 3.9–10.0 mmol/L. (C) Proportion of time at >10.0 mmol/L. (D) Proportion of time at >13.9 mmol/L. (E) Proportion of time at <3.9 mmol/L. Diagrams to the right of the graphs show the number of individual participants who met the corresponding consensus CGM-based clinical target—a dark grey person indicates the target was met by a participant and a light grey person indicates the target was not met by a participant. Data in these diagrams are the proportion (95% CI) of participants meeting each target. CGM = continuous glucose monitoring.
Table 2: CGM metrics by time period, and by low-glucose alert setting

| CGM by time period (n=30) | CGM by low-glucose alert setting |
|---------------------------|----------------------------------|
| 24 h a day (0000 h to 0000 h) | Daytime (0600 h to 2359 h) | Overnight (0000 h to 0559 h) |
| Predictive low alert (n=16) | Alert on low only (n=14) | Percentage point difference (95% CI) | p value | Predictive low alert (n=16) | Alert on low only (n=14) | Percentage point difference (95% CI) | p value |
| Time with glucose | | | | | | | |
| ≥3.9–10.0 mmol/L | 71% (64 to 79) | 68% (60 to 77) | 82% (70 to 86) | 66% (55 to 78) | 72% (65 to 79) | −4.9 (−13.8 to 3.4) | 0.30 | 80% (60 to 87) | 83% (74 to 85) | −2.2 (−13.4 to 7.4) | 0.62 |
| >10.0 mmol/L | 27% (18 to 35) | 30% (21 to 38) | 18% (11 to 29) | 32% (19 to 44) | 23% (18 to 33) | 5.6 (−2.4 to 15.5) | 0.30 | 19% (13 to 40) | 14% (11 to 25) | 4.8 (−9.5 to 16.5) | 0.34 |
| >13.9 mmol/L | 3.9% (2.4 to 10.2) | 4.7% (3.3 to 10.9) | 2.5% (0.0 to 4.4) | 7.7% (1.7 to 11.4) | 3.4% (2.7 to 8.1) | 2.8 (−1.6 to 7.8) | 0.16 | 3.3% (0.0 to 8.6) | 1.4% (0.0 to 2.7) | 1.0 (−0.3 to 4.4) | 0.24 |
| <3.9 mmol/L | 2.0% (1.2 to 3.1) | 2.3% (1.1 to 2.8) | 1.4% (0.2 to 2.8) | 1.5% (0.6 to 2.1) | 2.7% (1.8 to 3.3) | −1.1 (−2.0 to −0.1) | 0.038 | 0.4% (0.1 to 1.1) | 2.9% (1.5 to 4.9) | −2.3 (−3.2 to −1.0) | 0.0018 |
| <3.0 mmol/L | 0.2% (0.1 to 0.4) | 0.2% (0.0 to 0.4) | 0.0% (0.0 to 0.3) | 0.2% (0.0 to 0.4) | 0.2% (0.0 to 0.4) | −0.0 (−0.2 to 0.1) | 0.53 | 0.0% (0.0 to 0.0) | 0.1% (0.0 to 0.0) | 0.00 (−0.6 to 0.0) | 0.031 |
| Mean glucose, mmol/L | 8.5 (7.1 to 9.3) | 8.7 (7.9 to 9.4) | 7.9 (7.3 to 8.8) | 8.9 (7.9 to 10.0) | 8.1 (7.7 to 8.9) | 0.6 (−0.2 to 1.4) | 0.37 | 8.2 (7.6 to 9.5) | 7.8 (7.1 to 8.8) | 0.6 (−0.3 to 1.4) | 0.23 |
| Glucose SD, mmol/L | 2.9 (2.4 to 3.4) | 3.0 (2.6 to 3.4) | 2.5 (2.0 to 2.7) | 3.0 (2.5 to 3.4) | 2.8 (2.4 to 3.3) | 0.2 (−0.2 to 0.6) | 0.30 | 2.6 (1.9 to 2.9) | 2.4 (2.2 to 2.5) | 0.2 (−0.3 to 0.6) | 0.28 |
| Glucose coefficient of variation | 34% (31 to 37) | 35% (30 to 37) | 30% (27 to 34) | 34% (31 to 37) | 34% (30 to 37) | −0.0 (−2.8 to 2.7) | >0.99 | 30% (25 to 34) | 30% (28 to 33) | −0.4 (−4.3 to 3.2) | 0.93 |

Results are median (IQR); between-group differences are presented using generalised Hodges-Lehman median difference with robust 95% CIs, analysed using Wilcoxon rank-sum test. Sensor low-alert settings were individualised based upon clinical assessment during run-in, before this CGM data collection. CGM=continuous glucose monitoring.

Table 2: CGM metrics by time period, and by low-glucose alert setting

establishment, 16 (53%) of 30 participants had CGM predictive low alerts enabled and 24 (80%) had pump suspension on low enabled (appendix p 2). 26 (87%) of 30 participants had at least 13 days with sufficient CGM data (ie, days with at least 70% valid CGM readings) and all participants had at least ten days with sufficient CGM.

Participants spent a median of 71% (IQR 64–79%) with glucose in range. The time spent with glucose above 10.0 mmol/L was 27% (18–35%) and above 3.9 mmol/L was 3.9% (2.4–10.2%). The time with glucose below 3.9 mmol/L was 2.0% (1.2–3.1%) and the time below 3.0 mmol/L was 0.2% (0.1–0.4%). Glucose time in range was highest, and time above and below range were lowest, overnight (figure 1; table 2). When comparing individual participant results with the consensus CGM-based recommendation for all older adults with diabetes, over 70% of participants met each glucose time-in-range and time-above-range consensus target (figure 1B–D). However, only seven (23%) people met the glucose time-below-range target had the predictive low-glucose alert enabled. With predictive low-glucose alerts enabled, the differences we observed were in the order of 5 percentage points higher time above range and lower time in range, plus higher mean glucose, albeit with wide confidence intervals (table 2). Participants with impaired versus preserved hypoglycaemia awareness had equivalent CGM metrics. C-peptide levels correlated only weakly with CGM metrics (Pearson’s correlation coefficients between 0.21 and 0.34; 0.22 for time below 3.9 mmol/L; appendix p 3).

There were 272 sensor hypoglycaemia episodes below 3.9 mmol/L that occurred in 29 participants, and 42 episodes below 3.0 mmol/L that occurred in 18 participants, respectively. The median incidence of sensor hypoglycaemia episodes per week was 4.7 (IQR 2.8–6.1) and 1.0 (IQR 0.0–2.0) for thresholds of below 3.9 mmol/L and below 3.0 mmol/L, respectively. Sensor hypoglycaemia episodes below 3.9 mmol/L were most frequent during the afternoon, although long episodes (≥60 min) occurred most frequently overnight (figure 2B).
insulin bolus delivered within the preceding 4 h, 165 (82%) of 201 episodes followed a bolus for food and 36 (18%) followed a correction-only bolus (appendix p 4).

Adverse events during the 2-week period of analysis comprised three severe hypoglycaemia events in one participant (a reduction from six events per fortnight reported in the 12 months before the study without CGM—this individual was dependent upon caregiver assistance for diabetes management; in the study, this participant had both predictive low-glucose alert and insulin pump suspension on low glucose enabled; appendix p 2, participant number 8), three intercurrent infections among two participants, and one serious adverse event (elective cardiac stent) in one participant.

Discussion

In this study, older adults with long-duration type 1 diabetes and no frailty had high glucose time in range when using sensor-augmented pumps after multidisciplinary education. However, this group did not meet the consensus CGM-based hypoglycaemia target currently recommended for all older adults. Although the glucose time in range for the population in this study far exceeded the consensus minimum target of 50% for older adults, and no hypoglycaemia-related clinical events occurred among the functionally independent participants, 77% of participants did not meet the currently recommended older-adult CGM-based target for time below range. The median glucose time below range was equivalent to 29 min per day, whereas the consensus-recommended older adult glucose time-below-range target is less than 14 min per day. As the use of CGM predictive low alerts was associated with a lower median glucose time below range by almost half, and by seven times overnight, such predictive alerts are likely to be important for minimising hypoglycaemia. Most hypoglycaemia episodes occurred within 4 h of prandial insulin bolus doses. Therefore, hypoglycaemia could be lessened among these individuals by examining their hypoglycaemia patterns and exploring their insulin bolus delivery timing in relation to meals. Consideration could be given to weakening insulin-to-carbohydrate ratios, and to further education focusing on the timing of meal-time insulin bolus dose delivery.

The consensus-recommended glucose time-below-range target of less than 1% for older adults does not distinguish between individuals by frailty or functional status. Notably, participants in our study did not show any clinically significant degree of frailty on the assessments we used in this study. Moreover, participants who were functionally independent did not have any acute hypoglycaemia-related clinical events during the assessment period while using sensor-augmented pump therapy. The individual who experienced severe hypoglycaemia (requiring caregiver assistance to treat) was dependent on caregiver assistance for diabetes management and other activities of daily living. The observed rate of severe hypoglycaemia in the study period for the above individual was half that before study enrolment. We suggest that alternative CGM-based targets might be appropriate for relatively healthy, robust, and independent older individuals, such as most of the individuals in this study, and that access to diabetes therapeutic technology should be considered when determining CGM-based targets. Sinclair and colleagues recommend that risk stratification should play an important part in type 1 diabetes clinical care, and should include assessment of functional status and self-management to individualise treatment and clinical targets, with specific emphasis placed on frailty status being considered routinely in diabetes care. Such assessments were done in the present study, thereby enabling our results to be considered in the context of participants' relatively independent functional status and absence of frailty. Our results show that current CGM-based targets recommended for all older adults, without consideration of frailty status, are not suitable for cognitively healthy and functionally independent individuals without frailty. Based on these data, we suggest...
that older adults with type 1 diabetes should not be advised to follow the modified CGM targets for high-risk diabetes populations solely on the basis of their chronological age. Target CGM goal setting, unless otherwise indicated by functional or frailty status of an individual older adult, should follow the general consensus clinical targets for adults. The conflation of chronological age with clinical risk highlights the need for an expert consensus statement regarding CGM-based targets for older adults that considers the treatment guidelines for older adults presented by Diabetes UK.\(^3\)

For cognitively healthy and independent older adults with type 1 diabetes, Diabetes UK recommends HbA\(_\text{1c}\) levels of 48–53 mmol/mol (6.5–7.0%) for adults aged up to 70 years and HbA\(_\text{1c}\) levels below 58 mmol/mol (7.5%) for those aged 70 years and older (unless associated with an unacceptable hypoglycaemia risk). However, these guidelines do not include any CGM-based clinical targets.\(^3\) More than 90% of participants in the present study achieved glucose time in range above 70%, equivalent to HbA\(_\text{1c}\) under 50 mmol/mol (6.7%).\(^26\) Whereas, if the time-in-range target were lowered to more than 50%, as suggested by Battelino and colleagues,\(^8\) this would be equivalent to an HbA\(_\text{1c}\) target of less than 58 mmol/mol (8.3%). Such a target is consistent with the HbA\(_\text{1c}\) recommended for more frail older adults,\(^7\) and we suggest this is too lax a glycaemic target for the independent individuals without frailty who enrolled in this study. Moreover, clinical guidelines outline the specific needs of older adults with diabetes and frailty during inpatient care, highlighting their vulnerability and different needs compared with older adults without frailty.\(^1\) Our findings raise the important issue of distinguishing older adults by frailty and functional status when determining individual glucose goals. When determining insulin dosing and CGM settings, hypoglycaemia avoidance could be a focus for the individuals at the highest risk of major sequelae, such as those with impaired hypoglycaemia awareness, high fracture risk from falling, frailty, and poor functional status, and those who are ocean swimmers or commercial drivers. By contrast, hyperglycaemia minimisation might be more of a therapeutic priority for those with proliferative retinopathy, to prevent disease progression. Access to diabetes therapeutic technology, including CGM, pumps, and automated insulin delivery systems, is another important factor in determining individual targets.

Meta-analyses have shown the difficulty of achieving time below range under 1% among people with type 1 diabetes using modern therapies, even when insulin delivery is automated via closed-loop systems.\(^28\)\(^-\)\(^30\) Our glucose time-below-range findings are consistent with the Wireless Innovations for Seniors with Diabetes Mellitus (WISDM) study,\(^6\) a large trial of adults aged 60 years and older with type 1 diabetes, who had similar clinical characteristics to the participants studied herein, although they were using either insulin pumps or multiple daily injections and were monitoring glucose without real-time CGM at enrolment. In the WISDM trial, time below range reduced by almost half among all participants randomly assigned to real-time CGM intervention. A subgroup of 55 participants using insulin pumps who were randomly assigned to the study intervention had a median time below range of 2.1% (IQR 1.3–3.6) with real-time CGM, whereas our cohort had a median time below range of 2.0% (1.2–3.1) once established on sensor-augmented pumps. Although residual C-peptide is associated with residual functional \(\beta\) cells in very long-duration type 1 diabetes,\(^11\) and might protect against hypoglycaemia,\(^10\) C-peptide was not associated with reduced hypoglycaemia in our analysis. This finding might relate to the protection from hypoglycaemia afforded by real-time CGM with alerts. Likewise, the absence of a difference in CGM metrics observed between the groups with impaired versus preserved hypoglycaemia awareness in our study, particularly relating to hypoglycaemia time, might reflect the impact of CGM low-glucose alerts. Similarly, in WISDM, no significant interaction was found between impaired hypoglycaemia awareness and the effect of real-time CGM.\(^6\)

The strengths of our study include the robust, prospective collection of data from community-dwelling older adults with long-duration type 1 diabetes, the detailed baseline assessments to characterise the group, and the comprehensive education approach plus provision of standardised commercially available sensor-augmented pump therapy to all participants. Use of assessment tools for clinically relevant frailty, dependency, and cognitive testing placed emphasis on individual characteristics, which facilitated the discussion of CGM targets. The small sample size is a limitation of our study; small differences might not have been detected. The study results are also subject to confounding, which cannot be adjusted for given the small sample size. This study used a standardised CGM product, with an integrated algorithm for hypoglycaemia prediction alerts. The effect of predictive alerts might not be consistent across all CGM products when being used by older adults. Other limitations include the relatively short period of observation during a trial run-in, the absence of a comparator group, and the absence of a spectrum of frailty status among our study participants. Therefore, our findings might not be generalisable to broader groups of older adults with type 1 diabetes outside a trial setting, particularly those with higher frailty or dependence. The Diabetes UK guidelines for cognitively healthy and independent older adults with type 1 diabetes (ie, individuals meeting the guidelines’ Functional category I) might be most applicable to older adults without frailty, as studied here (albeit without CGM-based targets included in the guidelines). The application of our findings to older individuals with type 1 diabetes and increased frailty remains to be determined. Longer observation of these study participants and formal
comparison of sensor-augmented pump versus closed-loop automated insulin delivery were assessed in the two-stage randomised crossover ORACL trial.\(^7\)

In conclusion, the novelty of our study is in its characterisation of older adults and their glucose profiles while using sensor-augmented pump therapy, with reference to CGM targets recommended for all older adults. These findings add to the current inadequate evidence base on older-adult CGM metrics and, to our knowledge, are the first to relate these outcomes to current consensus CGM-based clinical target recommendations while accounting for frailty and functional status. We propose that international consensus recommendations to use modified CGM-based targets for all older adults are not suitable for robust, independently living older adults. We showed glucose time in range and hypoglycaemia readings that are achievable with sensor-augmented pump therapy for older adults without frailty over a short period, with more favourable CGM profiles than reported in previous studies of older adults using less advanced technology. Predictive low alerts might support older adults meeting consensus CGM-based targets by reducing hypoglycaemia, particularly overnight. Further evidence is needed regarding the effectiveness of individualised, risk-stratified CGM targets and advanced diabetes technology among older adults across the spectrum of frailty.

**Contributors**

SAM conceptualised and led the study. SAM, ST, GMW, PGC, MHL, RJM, DNO, NAO, and VS co-designed the study and acquired financial support for the project. ST, SJ, and CAG contributed to refining the protocol. PGC, ST, and SAM were responsible for participant screening and enrolment, informed consent, and providing medical care. CAG coordinated the research project. SV curated the data. ST, GMW, SJ, and ST, and SAM contributed to data analysis. ST and SAM drafted the manuscript. All authors critically reviewed the report, had access to the study data, and accept responsibility for the decision to submit for publication. ST, SJ, and SAM are the guarantors of this work and, as such, take responsibility for the integrity of the data and the accuracy of the data analysis.

**Declaration of interests**

ST reports a research grant from Insulet Corporation. SF reports honoraria for lectures from AstraZeneca, Boehringer Ingelheim, Eli Lilly, Novo Nordisk, and Sanofi; serving on advisory boards for Medtronic, Mylan, Pfizer, Sanofi, and Viatris; and chairing the Australian Diabetes Society Living Evidence Guidelines for Diabetes Medical Device Technologies. MHL reports speaker honoraria from Medtronic. RJM reports research grants from Medtronic; receiving honoraria for lectures from Eli Lilly Australia and Novo Nordisk Pharmaceuticals; travel support from Novo Nordisk Pharmaceuticals; serving on advisory boards for Novo Nordisk Pharmaceuticals and Eli Lilly Australia; and serving as a voluntary board member for the Australian Diabetes Society. DNO reports serving on advisory boards for Abbott, Medtronic, MSD, Novo, Roche, and Sanofi; receiving research support from Medtronic, Novo, Roche, Lilly, and Sanofi; and receiving travel support from Novo and MSD. SAM reports support for research from Medtronic; receiving speaker honoraria from Eli Lilly Australia, Roche Diabetes Care Australia, and Sanofi-Aventis Australia; serving on advisory boards for Medtronic and Ypsomed; and facilitating workshops for the Australian Diabetes Society. All other authors declare no competing interests.

**Data sharing**

De-identified individual data for low-glucose alert settings are available in the appendix (p 2). Additional de-identified data relating to this manuscript will be made available for research purposes for up to 12 months after publication on reasonable request by email to the corresponding author.

**Acknowledgments**

This work was funded by JDRF (3-SRA-2018-667-M-R), the Diabetes Australia Research Program, and St Vincent’s Hospital (Melbourne) Research Endowment Fund. Medtronic supplied discounted insulin pumps and glucose monitoring devices for the study. SAM is supported by a JDRF Research Award. We are grateful to the study volunteers for their participation. We acknowledge support by the research nurses, diabetes educators, and dietitians at St Vincent’s Hospital Melbourne and the Royal Melbourne Hospital. Parts of these findings were presented at the 14th International Conference on Advanced Technologies & Treatments for Diabetes, virtual meeting, June 2–5, 2021.

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