Study Protocol

Title:

AI-CARE: A Novel AI-Driven Mobile Insulin Calculator Integrating Image-Based Carbohydrate Estimation and CGM—A Feasibility Pilot Randomized Controlled Trial

1. Background

Diabetes mellitus (DM) is a chronic metabolic disorder affecting an estimated 537 million adults worldwide, with prevalence projected to increase to 643 million by 2030 (Magliano & Boyko, 2021). Poor glycaemic control is strongly associated with an increased risk of microvascular and macrovascular complications. Landmark trials, including the Diabetes Control and Complications Trial (DCCT, 1993) and the UK Prospective Diabetes Study (UKPDS, 1998), demonstrated that intensive glycaemic control achieved through multiple daily insulin injections (MDI) significantly reduces long-term complications. MDI typically consists of basal and bolus insulin therapy. Basal insulin is a long-acting insulin and is used to maintain background insulin levels and control glucose during fasting periods, including overnight and between meals. Bolus insulin, which is rapid-acting, is administered before meals to manage postprandial glucose excursions resulting from carbohydrate intake.

Clinical studies report that initiating MDI can reduce glycated haemoglobin (HbA1c) by approximately 1.5–2% within 3–4 months (Gibbons & Freeman, 2015; Rigalleau et al., 2022), with sustained reductions of up to 3–4% over 1 year (Shurter et al., 2013). Epidemiological data indicate that each 1% reduction in HbA1c is associated with a 37% decrease in microvascular complications (Stratton et al., 2001). Despite these benefits, a meta-analysis by Pitak et al. (2023) reported that only 23.75% of individuals with insulin-treated type 2 diabetes had HbA1c levels below 7%, while a cross-sectional study by Huo et al. (2020) found that only 20% of individuals with type 1 diabetes attained the same target. Achieving optimal glycaemic control in individuals treated with MDI requires accurate pre-meal glucose assessment, precise carbohydrate estimation, and appropriate bolus insulin dose calculation (Sussman et al., 2012). However, each of these components presents substantial real-world challenges.

Self-monitoring of blood glucose (SMBG) plays an important role in improving glycaemic control and empowering individuals with diabetes. It is particularly beneficial for those treated with insulin, as it helps determine bolus insulin dosing, facilitates insulin dose titration, and enables timely detection of hypoglycaemia. Despite strong recommendations for SMBG use among insulin-treated individuals (Karter, 2006; Muhali et al., 2024), its uptake remains suboptimal in many Asian countries (Bi et al., 2010; Mafauzy, 2006; Park et al., 2014). In many Asian settings, blood glucose monitors and test strips are paid out of pocket, creating substantial financial barriers to regular testing. Furthermore, finger-prick testing is often perceived as painful and inconvenient. Patients may avoid monitoring due to frustration with high glucose readings, embarrassment when testing in public, fear of needles, workplace constraints, or limited motivation and self-efficacy (Ong et al., 2014). Collectively, these

barriers result in inadequate pre-meal glucose monitoring, leading to inappropriate bolus dosing and suboptimal insulin titration, thereby contributing to poor glycaemic control despite insulin therapy.

Beyond glucose monitoring, carbohydrate counting—although a foundational component of MDI therapy—is cognitively demanding, time-consuming, and error-prone, particularly in multicultural dietary environments (Holt et al., 2021; Kawamura et al., 2015; Meade & Rushton, 2016). In Singapore and other Asian settings, meals are commonly consumed in hawker centres, food courts, and home-based contexts where dishes are mixed, visually complex, and rarely accompanied by standardized nutritional information. Staple foods such as rice, noodles, congee, roti prata, and mixed-economy rice involve variable portion sizes and composite ingredients, making accurate carbohydrate estimation particularly challenging (Chandran et al., 2024). Inaccurate estimation can lead to insulin underdosing or overdosing, resulting in postprandial hyperglycaemia or hypoglycaemia (Amorim et al., 2024). Notably, mean carbohydrate-counting accuracy among individuals using MDI has been reported to be only 59% (Meade & Rushton, 2016).

Even when glucose levels are measured and carbohydrate content estimated, bolus insulin calculation requires application of insulin-to-carbohydrate ratios (ICR), insulin sensitivity factors (ISF), and correction algorithms. This process demands numeracy and health literacy skills that are frequently limited among individuals with diabetes and are associated with poorer glycaemic outcomes (Marden et al., 2012). Difficulties in performing dose calculations may lead to reliance on fixed bolus doses, empirical estimation, incorrect administration, or omission of boluses (Gross et al., 2003; Sussman et al., 2012). Indeed, 64% of patients have been shown to inaccurately estimate their prandial insulin requirements (Ahola et al., 2010), and fixed-dose regimens have been associated with increased glycaemic variability and weight gain (Anyanwagu et al., 2017).

Collectively, these interrelated challenges—suboptimal glucose monitoring, inaccurate carbohydrate estimation, and numeracy burden in insulin dose calculation—contribute to postprandial glucose excursions and persistent hyperglycaemia despite insulin therapy. Addressing these barriers through integrated, automated clinical decision-support systems may therefore represent a promising strategy to enhance dosing accuracy, reduce cognitive burden, and improve overall glycaemic outcomes.

AI-CARE is an artificial intelligence–enabled clinical decision support mobile application designed to support prandial insulin dosing in individuals receiving MDI, incorporating a “human-in-the-loop” approach to ensure user verification of recommended doses. The application integrates AI-driven image-based carbohydrate estimation tailored to Asian dietary contexts, individualized patient-specific insulin parameters, and real-time CGM data to generate personalized insulin dose recommendations.

The system comprises several key components. First, the image-based carbohydrate estimation module enables users to capture meal images at standardized angles (45–55° and 90°), after which the AI engine automatically estimates carbohydrate content. User-in-the-loop features, including portion adjustment and manual editing, are incorporated to enhance accuracy and allow verification. Second, real-time CGM data are integrated into the system, allowing current glucose values to be incorporated into the insulin dose calculation algorithm. Third, the application calculates personalized insulin dose recommendations based on parameters such as the ICR, ISF, and target glucose level, with predefined maximum bolus limits to enhance safety.

To ensure safe use, the application incorporates multiple safety features and feedback mechanisms, including dose caps, prompts to review glucose levels prior to insulin administration, and reminders to confirm dosing decisions. Although AI-CARE provides insulin dose recommendations, the final decision remains patient-driven, and users retain full autonomy to accept, modify, or override the suggested dose.

2. Objectives

The primary objective of this study is to evaluate the feasibility, safety, and preliminary effectiveness of the AI-CARE mobile application among adults with diabetes receiving MDI. Feasibility will be assessed in terms of recruitment, retention, participant adherence, and application usability. Safety will be evaluated by monitoring the incidence of hypoglycaemia, hyperglycaemia, and other adverse events throughout the intervention period.

The study will also examine the preliminary effectiveness of AI-CARE on glycaemic and patient-reported outcomes compared with usual care. In addition, a qualitative process evaluation will be conducted to explore intervention participants' experiences and perceptions of using AI-CARE, including perceived ease of use, usefulness, acceptability, and barriers and facilitators to real-world implementation, and control participants' experiences of usual care and views on AI-assisted insulin dose recommendations. Findings from this phase will inform further refinement and optimization of the AI-CARE system and guide the design of a future large-scale randomized controlled trial.

3. Methodology

This study adopts a mixed-methods design, comprising a 12-week feasibility pilot randomized controlled trial (RCT) with an embedded qualitative process evaluation using focus group discussions.

3.1 Study Design and Setting

This study will be conducted as a single-centre, two-arm, stratified pilot randomized controlled trial with an embedded qualitative component at outpatient specialist diabetes clinics in Tan Tock Seng Hospital, Singapore.

The quantitative component will evaluate the feasibility, safety, usability, and preliminary effectiveness of the AI-CARE mobile application compared with usual care among adults with diabetes receiving MDI. Participants will be randomized in a 1:1 ratio to either the intervention or control group.

To complement the quantitative findings, a qualitative process evaluation will be conducted using a descriptive focus group design involving participants from both the intervention and control arms after completion of the 12-week study. Semi-structured focus group discussions, facilitated by a trained moderator, will be conducted separately for each arm with groups of approximately 4–5 participants. Intervention-arm discussions will explore their experiences and perceptions of AI-CARE, including usability, perceived usefulness, impact on self-management, and barriers and facilitators to implementation; control-arm discussions will explore their experiences of usual care and their views on AI-assisted insulin dose recommendations.

4. Study Participants

4.1 Sampling method

Participants for the randomized controlled trial (RCT) will be recruited using convenience sampling from outpatient diabetes clinics. Potentially eligible individuals will be identified by the clinical care team and screened against predefined inclusion and exclusion criteria. Eligible participants will include adults aged ≥21 years with type 1 or type 2 diabetes who are receiving MDI, have an HbA1c≥7%, are willing to wear a CGM sensor for 12 weeks, and are able to read and understand English. Individuals will be excluded if they are pregnant, have experienced severe hypoglycaemia or diabetic ketoacidosis within the preceding three months, have hypoglycaemia unawareness, insulin-to-carbohydrate ratio is below 8 or have significant cognitive impairment that may interfere with the use of the application. Eligibility will be confirmed through structured screening prior to enrolment.

For the qualitative process evaluation, participants will be recruited from those who have completed the intervention or control arm of the feasibility study. Recruitment will be conducted at the post-intervention visit, and participation will be voluntary, with written informed consent obtained prior to the focus group discussions. Each focus group will comprise approximately 4–5 participants from the same study arm, with additional groups

conducted as necessary to achieve data saturation. Purposive sampling will be used to ensure a diverse range of participant experiences within each study arm.

4.2 Sample size estimation

As this is a feasibility pilot trial, the study is not powered to detect statistically significant differences in effectiveness outcomes. Instead, the sample size is selected to estimate feasibility parameters (recruitment, retention, adherence), evaluate preliminary safety, and generate variance estimates for planning a future definitive RCT. A commonly recommended guideline for pilot trials is to recruit approximately 10–30% of the sample size required for a full-scale trial (Eldridge et al., 2010; Hertzog, 2008). Based on power calculations indicating that 64 participants per group (128 total) would be required in a full RCT to detect a medium effect size at $\alpha = 0.05$ with 80% power (Whitehead et al., 2016), a pilot sample of 40 participants (20 per arm) represents approximately one-third of the full trial size and is appropriate for feasibility objectives. Allowing for an anticipated attrition rate of 15%, a total of 48 participants (24 per arm) will be recruited to ensure that approximately 40 participants complete the 12-week follow-up.

4.3 Randomization

Participants will be randomized in a 1:1 ratio to either the intervention or control arm, with stratification by diabetes type (type 1 vs type 2) to ensure balanced representation across study groups. Block randomization with a fixed block size of four will be employed to maintain allocation balance throughout the recruitment period. The randomization sequence will be generated by an independent statistician using a computer-based random number generator. After enrolment, each participant will be assigned a unique study identification number, which will be entered into the randomization programme to determine group allocation.

4.4 Study Interventions

4.4.1 Intervention group

Participants randomized to the AI-CARE intervention arm will receive the intervention over a 12-week period, comprising five study contacts: a baseline visit (Visit 1), nurse-led telephone reviews at Week 1, 2 and 6, and a post-intervention visit (Visit 2) at Week 12. The intervention will be delivered through a hybrid model integrating an in-person onboarding session, application-based daily use, and early telemonitoring support.

At the baseline visit, participants will attend a structured training session in which they will be introduced to the AI-CARE mobile application and trained in standardized procedures for capturing meal images. Following onboarding, participants will use the application

independently in their daily routines to support prandial insulin dosing decisions. Physician oversight will be maintained throughout the study for the setting and adjustment of individualized insulin parameters, including total daily dose (TDD), ICR, ISF, target glucose level, and maximum bolus dose, based on the participant's clinical profile and hypoglycaemia risk.

Structured nurse-led telephone reviews at Week 1, 2 and 6 will be conducted to support early adoption, monitor safety, and address usability concerns. During these sessions, a trained study nurse will review CGM data with participants, with particular attention to time below range, hypoglycaemia risk, glycaemic variability, and insulin dosing patterns to ensure early safety monitoring. Subsequent insulin adjustments, if clinically indicated, will be performed in accordance with standard outpatient care practices under physician supervision.

Participants will be instructed to use the AI-CARE application prior to each main meal (typically two to three times daily) throughout the intervention period. Application usage data, including the frequency of meal image capture and acceptance of insulin dose recommendations, will be automatically recorded to assess intervention adherence and user engagement. A structured support infrastructure will be provided, including access to a study contact line during office hours and a predefined escalation pathway for urgent clinical concerns.

Following completion of the study, participants who provide consent will be invited to participate in semi-structured focus group discussions. Each focus group will explore user experiences, perceived usefulness, ease of use, impact on self-management, and barriers and facilitators to implementation. All discussions will be audio-recorded.

4.4.2 Control group

Participants randomized to the usual care arm will continue to receive standard diabetes self-management practices without access to the AI-CARE application. Usual care includes manual carbohydrate counting using conventional methods, such as estimating carbohydrate content based on food labels, dietary guides, or prior diabetes education. Prandial insulin dosing will be calculated manually by participants using their individualized ICR and ISF, or according to instructions provided by their treating physician. All participants in this arm will wear a CGM sensor for study measurement purposes throughout the study period. Routine diabetes management and follow-up will continue in accordance with standard outpatient care practices. The study visit schedule for the usual care group includes two in-person visits: Visit 1 at baseline for enrolment, baseline assessments, and CGM sensor application, structured nurse-led telephone reviews at Week 1, 2 and 6, and Visit 2 at Week 12 for post-intervention outcome assessment. Following completion of the study, participants who provided consent will be invited to participate in semi-structured focus group discussions.

4.5 Data Collection Procedure

Data will be collected at three key time points: baseline (Week 0), early follow-up telephone reviews (Week 1, 2 and 6), and post-intervention assessment (Week 12).

At baseline, demographic and clinical characteristics will be recorded, including age, sex, type and duration of diabetes, and current treatment regimen. Clinical and biochemical measurements will include HbA1c, low-density lipoprotein (LDL) cholesterol, and anthropometric parameters such as body weight, body mass index (BMI), and blood pressure. A CGM sensor will be applied to all participants to monitor glycaemia throughout the study period. Participants will also complete patient-reported outcome measures, including the Diabetes Treatment Satisfaction Questionnaire (DTSQ) (Bradley & Gamsu, 1994), the Audit of Diabetes Dependent Quality of Life (ADDQOL) questionnaire (Bradley et al., 1999), and Diabetes Distress Scale (DDS17). In addition, individualized insulin therapy parameters, including ICR, ISF, target glucose level, and TDD, will be documented.

Structured telephone reviews will be conducted at Week 1, 2 and 6, to support early safety monitoring and adherence. These reviews will include assessment of CGM data, identification of hypoglycaemia and other adverse events, and evaluation of participant adherence and usability of the intervention application.

At Week 12 (post-intervention visit), clinical and biochemical measurements will be repeated, including HbA1c and LDL cholesterol, as well as anthropometric parameters such as body weight, BMI, and blood pressure. CGM data will be downloaded to derive glycaemic metrics, including time in range (TIR), time above range (TAR), time below range (TBR), and glycaemic variability (GV). Participants will again complete the DTSQ, DTSQc (Bradley, 1999), DDS17 and ADDQOL questionnaires, and those in the intervention arm will additionally complete the mHealth App Usability Questionnaire (MAUQ) (Zhou et al., 2019) to evaluate application usability. A final adverse event review will also be conducted to document any safety concerns occurring during the study period. A summary of the data collection procedures will be presented in Annex 1.

Following completion of the intervention phase, participants in both the intervention and control arms will be invited to participate in a semi-structured focus group discussion. The purpose, procedures, and voluntary nature of participation, including audio recording, are described in the study informed consent form; written informed consent will be obtained at enrolment and re-confirmed verbally prior to the discussion. The focus group discussion will be facilitated by the researcher using arm-specific semi-structured topic guides. The intervention-arm guide will explore usability, user experience, perceived benefits and

challenges, trust in AI-generated insulin dose recommendations, and suggestions for improvement. The control-arm guide will explore experiences of usual care, views on and trust in AI-assisted insulin dose recommendations, and perceived barriers and facilitators to using such tools. Both guides share a set of common questions (e.g., impact on self-management, intention to use, barriers and facilitators) to allow comparison across arms. Sessions will be conducted either in person or virtually (e.g., via Zoom or Microsoft Teams), depending on participant availability, and will last approximately 60 to 90 minutes.

All discussions will be audio-recorded and supplemented with field notes taken by a co-facilitator. Recordings will be transcribed verbatim and anonymized prior to analysis. Data will be analysed thematically using Braun and Clarke's framework, employing both inductive and deductive coding to identify key themes that will inform refinement and future implementation of the AI-CARE application.

5. Outcome Measures

5.1 Feasibility outcome

Feasibility outcomes will be assessed to determine the practicality and methodological readiness to conduct a future full-scale randomized controlled trial with a similar study design. Recruitment feasibility will be evaluated by measuring the time required to achieve the target sample size, the eligibility rate (the proportion of eligible participants among those screened), and the recruitment rate (the proportion of enrolled participants among those eligible). Retention and attrition rates will also be calculated, with attrition defined as the proportion of participants who withdraw or are lost to follow-up during the 12-week intervention period. Intervention engagement will be assessed through application usage metrics, including the frequency of daily insulin calculator activation and the proportion of meals supported by AI-CARE. Usability will be evaluated using the validated MAUQ (Zhou et al., 2019), which will be administered at Week 12. Acceptability will be further inferred from usage patterns and participant feedback. Safety will be monitored throughout the study, with adverse events including severe hypoglycaemia (requiring third-party assistance), diabetic ketoacidosis, and clinically significant hypoglycaemia identified through CGM data review. Any serious or potentially intervention-related adverse event will prompt immediate clinical review and, if necessary, consideration of protocol modification.

5.2 Preliminary effectiveness outcomes

Preliminary effectiveness outcomes will be explored to provide early signals of potential clinical benefit and to inform outcome selection and sample size estimation for a future definitive trial.

- **Clinical outcomes.** Changes in glycaemic control will be assessed using HbA1c measured at baseline and Week 12, along with continuous glucose monitoring–derived

metrics, including TIR, TAR, TBR, and glycaemic variability. Cardiometabolic and anthropometric parameters, including body weight, BMI, blood pressure, and LDL cholesterol, will also be evaluated to explore broader metabolic effects of the intervention.

- **Self-reported outcomes.** Patient-reported outcomes will assess changes in diabetes treatment satisfaction and quality of life using validated questionnaires, including DTSQ, DTSQc, ADDQoL, DDS17 and MAUQ. These measures will provide insight into whether the AI-CARE intervention influences perceived treatment burden, confidence in insulin dose calculation, and overall satisfaction with diabetes self-management.

6. Data Analysis

All quantitative statistical analyses will be performed using R (version 4.5.1), with statistical significance defined as a two-sided p-value < 0.05. Descriptive statistics will be used to summarize baseline participant characteristics and feasibility outcomes, including recruitment, retention, attrition rates, and application usage metrics. Continuous variables will be presented as means and standard deviations or medians and interquartile ranges, depending on data distribution.

For exploratory effectiveness analyses, between-group differences will be assessed using independent samples t-tests for normally distributed data or Mann–Whitney U tests for non-normally distributed data. Within-group changes from baseline to post-intervention will be evaluated using paired t-tests or Wilcoxon signed-rank tests, as appropriate. All analyses will follow the intention-to-treat principle. Missing data will be handled using single imputation (mean or median, depending on the data distribution) to preserve sample size for exploratory analyses. Given the pilot nature of the study and the relatively small sample size, findings from hypothesis testing will be interpreted with caution and considered exploratory.

Qualitative data from the focus group discussions will be analysed using thematic analysis following the framework described by Braun and Clarke (2006). Audio-recorded discussions will be transcribed verbatim and analysed using both inductive and deductive coding approaches to capture emergent themes as well as those informed by the study objectives and relevant theoretical frameworks. NVivo software will be used to facilitate data management, coding, and organization. The analysis will generate key themes to inform further refinement and future implementation of the AI-CARE application. To ensure rigor and trustworthiness of the qualitative findings, several strategies will be employed. Credibility will be enhanced through accurate transcription and independent coding by members of the research team. Dependability and confirmability will be supported by maintaining an audit trail and conducting peer debriefings throughout the analytic process. Transferability will be

strengthened by providing detailed descriptions of the study context and participant characteristics.

Integration of quantitative and qualitative findings will be undertaken during the interpretation phase to provide a comprehensive understanding of the feasibility, usability, and real-world applicability of AI-CARE, and to inform the design of a future large-scale randomized controlled trial.

7. Significance of the Study

This feasibility pilot RCT will provide critical preliminary evidence on the safety, acceptability, and practical implementation of the AI-CARE mobile insulin decision-support system in adults with diabetes receiving MDI. The findings will determine whether progression to a full-scale definitive RCT is warranted. Evaluation of usability and acceptability will inform iterative refinements to both the AI-CARE application and user training procedures, with the aim of enhancing user engagement, adherence, and overall intervention effectiveness. Continuous safety monitoring will further ensure that the intervention does not introduce unintended clinical risks.

In addition, a qualitative process evaluation will be conducted to gain in-depth insights into participants' experiences, perceived usefulness, and the barriers and facilitators influencing the use of AI-CARE in routine diabetes self-management. Data from focus group discussions will elucidate how the intervention is implemented in real-world settings and identify key factors that affect user engagement and sustainability. These insights will provide essential contextual understanding to support intervention optimisation and guide future implementation strategies.

Furthermore, this study will generate preliminary estimates of outcome variability and responsiveness, which are essential for refining outcome measures and informing sample size calculations for a future definitive trial. Collectively, these findings will enhance trial readiness, reduce methodological uncertainty, and support the safe and effective translation of AI-enabled insulin decision support systems into clinical practice and diabetes self-management.

References

Bradley C. Diabetes Treatment Satisfaction Questionnaire: Change version for use alongside status version provides appropriate solution where ceiling effects occur. Diabetes Care. 1999; 22:530–532. doi: 10.2337/diacare.22.3.530.

Annex 1: Schedule of study visits

	Visit 1: Baseline	**Phone Call (1,2 and 3)**	**Visit 2: Completion**
	Day 0	Phone call 1: 1 week from visit 1 (+/- 3 days) Phone call 2: 2 weeks from visit 1 (+/- 3 days) Phone call 3: 6 weeks from visit 1 (+/- 3 days)	12 weeks from visit 1 (+/- 7 days)
Informed Consent	X		
Randomization	X		
Demographic	X		
Clinical Characteristics	X		
Clinical Measurements	X		X
CGM Wearable	X		
Training for CGM and app (for intervention group)	X		
Questionnaires: PROMS	X		X
CGM Monitoring		X	X
Adverse Event Monitoring		X	X
Focus Group Discussion (optional; both groups; after Visit 2)			X