# MobilE artificaL Intelligence Solution for DiabeteS Adapted care (MELISSA) – The Randomized Controlled Multicentre Trial Protocol

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## Rationale

Approximately **200 million people with diabetes** worldwide require intensive insulin therapy, most using **multiple daily injections** (MDI) (1). MDI remains the **standard treatment**, as (hybrid) closed-loop systems are not universally accessible or desired (2).

MDI consists of:

- **Basal insulin** for continuous insulin needs in the fasted state
- **Bolus insulin** for meals and hyperglycaemia correction

Achieving glycaemic control requires **frequent insulin dose adjustments** based on dynamic factors, including glucose levels, physical activity, and carbohydrate intake etc. Insulin adjustment is a **time-consuming, complex, and error-prone process** (3,4), leaving many not reaching glycaemic targets and at **increased risk of diabetes complications** (5,6).

**Innovative digital tools** have emerged to support self-management. However, **clinical effectiveness remains modest** (7), as many rely on i) accurate user input and ii) static decision algorithms. Therefore, we developed the MELISSA app, which provides **personalised insulin dose recommendations** based on two Artificial Intelligence-driven features **(Adaptive Basal-Bolus Advisor and goFOOD™)**.

## Objectives

1) ***To clinically validate and demonstrate glycaemic superiority of the MELISSA app as compared to standard care in people with type 1 diabetes on MDI, reflected by time-in-range***

2) To assess the impact of the MELISSA app on additional glycaemic outcomes, insulin usage, and patient-reported-outcomes

3) To evaluate the feasibility and acceptability of the MELISSA app in type 2 diabetes

## Methods

**Study design:** a 22-week multi-centre prospective randomised open-label blinded endpoint trial (Fig. 1)

**People with type 1 (n=402) and type 2 diabetes (n=90) on MDI**

**Denmark (n=120), Germany (n=90), Greece (n=112), Netherlands (n=120)**

The **MELISSA app** consists of two AI-features:

- **Adaptive Basal-Bolus Advisor (ABBA):** provides basal and bolus insulin advice by using an actor–critic reinforcement-learning method. The actor selects actions based on predefined rules, while the critic evaluates and adjusts them. The model is trained on individual glucose and insulin data from weeks 4–6. Prior and current glucose levels, insulin-on-board, and estimated carbohydrate intake (from goFOOD™ or manual entry, supported by national food databases) are incorporated in the algorithm. Likewise, a correction bolus when glucose is >10 mmol/L and a correction snack when glucose is <3.9 mmol/L are suggested.
- **goFOOD™ :** automatically estimates carbohydrates content by processing meal images utilising machine-learning based segmentation and food recognition. A geometric method generates a depth map from two images to build a 3D model of each item to estimate volume. Estimated volume and food category are then matched to national food databases to provide the carbohydrate estimation. Users can accept or adjust each step.

**Primary outcome:** time-in-range measured by continuous glucose monitoring (CGM)

**Secondary outcomes:** other CGM metrics, insuline usage and patient-reported-outcomes (e.g., quality-of-life, diabetes distress, and hypoglycaemic awareness)

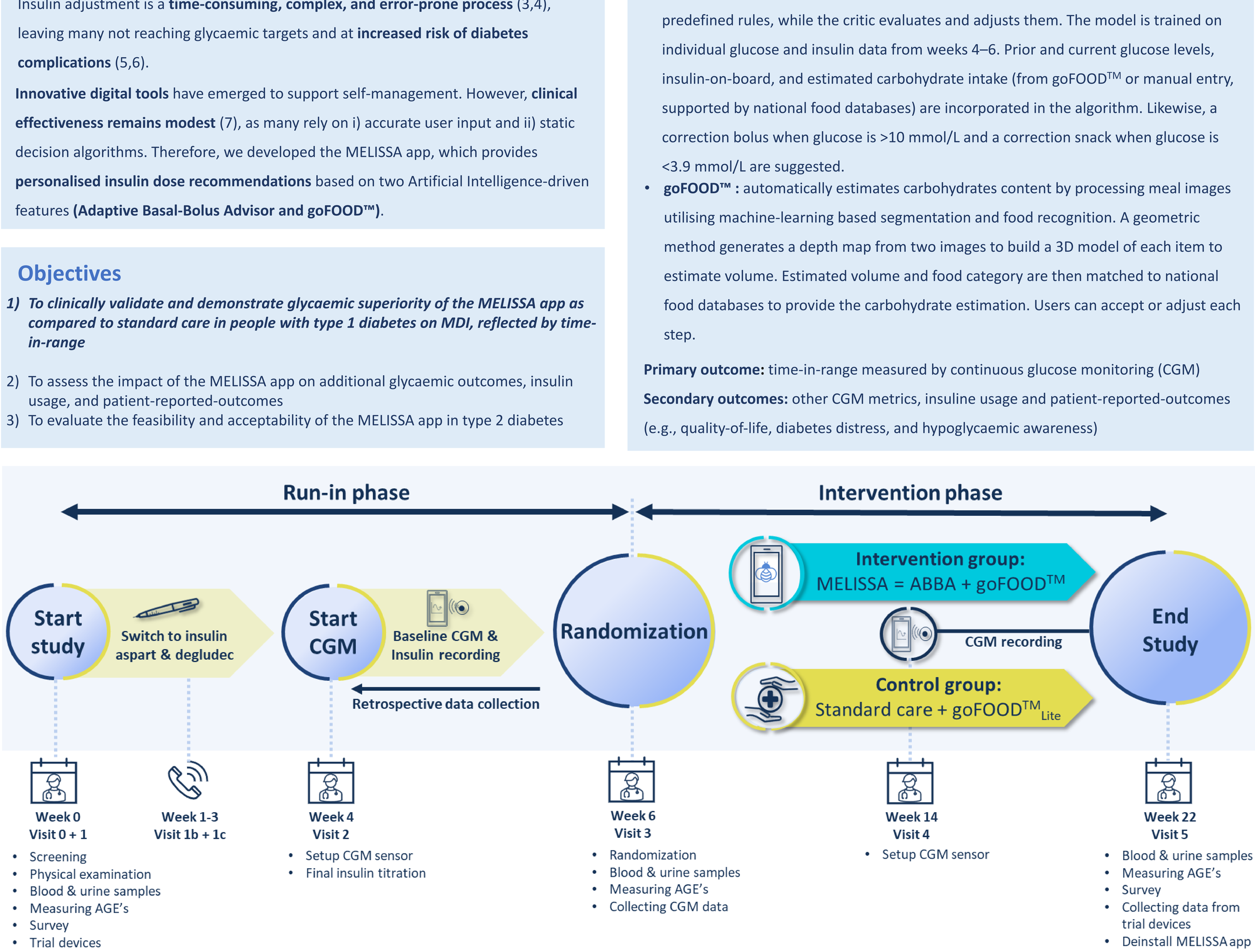


**Figure 1:** Overview of study timeline and study procedures. AGEs = Advanced Glycated End-products, CGM = Continuous Glucose Monitoring, ABBA = Adaptive Basal-Bolus Advisor

## Conclusions

This trial aims to address the current gaps by **validating a device-independent, adaptive solution that learns from individual data, and supporting personalized insulin optimization in diverse real-word settings**. The MELISSA app has the potential to **improve quality of life** and to **reduce diabetes related complications**. The trial outcomes will generate necessary evidence for **obtaining Conformité Européenne certification** (class IIb), paving the way for broader clinical adoption.

## Participants needed

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## recruitment is ongoing

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## References

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