ISRCTN16784568 https://doi.org/10.1186/ISRCTN16784568

Artificial intelligence (AI)-powered mealtime insulin dose-assisted decision-making system

Submission date	Recruitment status	[_] Prospectively registered
25/07/2023	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[X] Statistical analysis plan
09/08/2023	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
08/08/2023	Nutritional, Metabolic, Endocrine	[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Proper dosage titration is still the most effective way to mitigate intra- and inter-subject variations in insulin requirements and thus achieve euglycemic control in insulin therapy. Although the use of an artificial pancreas system for real-time basal rate adjustment has been extensively studied, the feasibility of automatic real-time meal bolus decisions with an intelligent closed-loop control algorithm is yet to be explored. We propose using an artificial-pancreas-like algorithm (AP-A) which could automatically determine the appropriate pre-prandial insulin dose based on intermittently scanned continuous glucose monitoring (isCGM) data trajectories in multiple-dose injection (MDI) therapy. The study aims to determine whether pre-prandial insulin dose adjustments guided by the AP-A under the supervision of physicians are as effective and safe as those guided by physicians alone.

Who can participate?
Type 2 diabetes patients aged over 18 years old

What does the study involve?
In this study, the participants wear an isCGM and insulin dosage is determined by either physician alone or AP-A recommendation before physician approvement.

What are the possible benefits and risks of participating?
Since the AP-A recommended dose will be reviewed and approved by physician, the benefits and risks are no more than standard care.

Where is the study run from?
Peking University People's Hospital (China)

When is the study starting and how long is it expected to run for?
December 2019 to July 2022

Who is funding the study?
Peking University People's Hospital Innovation Fund (China)

Who is the main contact?
Dr Wei Liu, liuwei03@bjmu.edu.cn

Contact information

Type(s)
Principal investigator

Contact name
Dr Wei Liu

ORCID ID
https://orcid.org/0000-0002-7613-3163

Contact details
Peking University People's Hospital
Xizhimennan Rd #11
Beijing
China
100044
+86-10-88324105
liuwei03@bjmu.edu.cn

Type(s)
Scientific

Contact name
Dr Wei Liu

Contact details
Xizhimennan Rd #11
Beijing
China
100044
+86-10-88324105
liuwei03@bjmu.edu.cn

Type(s)
Public

Contact name
Dr Wei Liu

Contact details
Xizhimennan Rd #11
Beijing
China
100044
+86-10-88324105
liuwei03@bjmu.edu.cn

Additional identifiers

Protocol serial number
Chictr.org number: ChiCTR2200055328

Study information

Scientific Title
Research on the adjustment scheme of insulin injection dose based on artificial intelligence

Study objectives
To verify the effectiveness and safety of an artificial intelligence algorithm that assists in guiding mealtime insulin doses.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 15/01/2021, Ethics Review Committee of Peking University People's Hospital (Xizhimennan Rd #11, Beijing, 100044, China; +86-10-88324516; rmyyllwyh@163.com), ref: 2020PHB338-01

Primary study design
Interventional

Study design
Single-blind parallel (two-arm) randomized controlled prospective non-inferiority trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Type 2 diabetes

Interventions
Meal insulin dose adjustment by AI-assisted
The study proposes an artificial pancreas-like algorithm (AP-A) that automatically determines the appropriate pre-prandial insulin dose based on intermittently scanned continuous glucose monitoring (isCGM) data trajectories in multiple-dose injection (MDI) therapy. The aim is to determine whether adjusting pre-prandial insulin doses guided by the AP-A under the supervision of physicians is as effective and safe as those guided by physicians alone. The study is taking place in a hospital setting, and participants are wearing isCGM (Freestyle Libre H, Abbott, US) devices after randomization to either the AP-A or physician arm. Randomization is stratified by age and glycated hemoglobin A1c (HbA1c) at screening using a computer-generated random sequence and random block size.

In the AP-A arm, isCGM data are being collected before meals and uploaded into the proposed closed-loop meal-bolus decision algorithm, which automatically outputs suggested insulin dosages. The physician reviews the suggested dosage and chooses whether to adopt it or override the recommended dosage. In the control arm, certified endocrinologists determine

insulin dosage adjustments based on current clinical strategies using isCGM readings. Meal-time insulin consists of insulin lispro (Humalog®, Lilly, USA.), while basal insulin is glargine U100 (Lantus®, Sanofi, US.).

Intervention Type
Other

Primary outcome(s)
Glucose in target range time measured using isCGM for glucose level during the insulin titration period (depending on how long the participants need multiple daily injections therapy)

Key secondary outcome(s)
1. Serum glycated albumin level measured using a standard laboratory test 14 days after enrollment, last visit
2. The proportion of glucose data <3.9mmol/L measured using isCGM during insulin titration
3. The proportion of glucose data <2.8mmol/L measured using isCGM during insulin titration
4. The proportion of glucose data >10.0mmol/L measured using isCGM during insulin titration
5. The proportion of glucose data >13.3mmol/L measured using isCGM during insulin titration
6. The area under the curve of glucose <10.0mmol/L in the AGP map measured using isCGM during insulin titration
7. The area under the curve of glucose <3.9mmol/L in the AGP map measured using isCGM during insulin titration
8. Average glucose data measured using isCGM during insulin titration
9. The standard deviation of glucose data measured using isCGM during insulin titration
10. The difference between the dose approved by the doctor and the dose recommended by the algorithm measured using the insulin dosage record during the titration period
11. The number of times that the doctor recommended the dose in the experimental group is different from that recommended by the algorithm measured using the insulin dosage record during the titration period
12. In the experimental group, the proportion of blood glucose in the range of 3.9mmol/L to 10.0 mmol/L within 4 hours after insulin injection when there was a difference between the doctor-approved dose and the algorithm-recommended dose measured using the insulin dosage record during the titration period

Completion date
30/07/2022

Eligibility

Key inclusion criteria
1. Type 2 diabetic subjects receiving intensive insulin therapy
2. Aged >= 18 years old
3. Poor blood sugar control, HbA1c>=8.0%

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Mixed

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. The subject is currently pregnant, intends to become pregnant, or is unwilling and unable to use contraception during the study (female only)
2. Abnormal mental state
3. Refuse to wear invasive examination equipment
4. There are clear reasons for not wearing dynamic glucose monitoring (severe allergies, skin diseases, etc.)
5. The subject has symptoms and signs such as skin lesions, scarring, redness, infection or edema at the sensor application site that will affect the sensor application or the accuracy of the interstitial fluid glucose measurement
6. Complicated serious diseases, including but not limited to heart disease, cerebrovascular disease, liver and kidney disease, severe diabetes-related complications
7. The subject has an appointment for X-ray, MRI or CT examination during the study period, and the appointment cannot be changed to before the start of the study or after the end of the study
8. Drugs that affect blood sugar such as glucocorticoids have been used within one month
9. Any other reasons judged by the investigator that would make the subject unsuitable to participate in the research

Date of first enrolment
01/11/2021

Date of final enrolment
20/07/2022

Locations

Countries of recruitment
China

Study participating centre
Peking University People's Hospital
Xizhimennan Rd #11
Beijing
China
100044

Sponsor information

Organisation
Peking University People's Hospital

ROR
https://ror.org/035adwg89

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Peking University People's Hospital Innovation Fund

Alternative Name(s)
, PKUPH

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
China

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from the corresponding author, Dr Wei Liu, liuwei03@bjmu.edu.cn. The type of data that will be shared is de-identified data. These data will be available after publication.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file		15/01/2021	04/08/2023	No	No
Statistical Analysis Plan	version 2.0	22/07/2022	04/08/2023	No	No