BLOOM Study

English translation of the original French document.

Research sponsor: Groupe Hospitalier de La Rochelle Ré Aunis

Coordinating investigator: Dr Didier GOUET

1. Administrative information

Title/Acronym (will be made public): Real-world data from people with diabetes using closed-loop insulin pump therapy (BLOOM)

Project team: Didier GOUET (hospital practitioner) / Caroline ALLIX-BEGUEC (PhD) / Harivola ANDRIANTAOLO (clinical research associate)

2. Objectives and purpose

a. Study background and objectives

In recent years, insulin pump systems coupled with continuous glucose sensors enabling semi-automated insulin delivery (closed-loop systems) have been developed.

Their use has been validated in clinical trials, but the international investigation centres participating in these trials are not always representative of French centres, and the patients they manage may also differ. Eligibility criteria in trials are stricter and more restrictive than those in routine practice in diabetology/endocrinology departments. Sociodemographic characteristics of trial participants - notably the male/female ratio, age, and ethnicity - do not necessarily reflect those observed in patients who actually use the device in real-world care.

Our objective is to evaluate, in real-world conditions, the impact of closed-loop systems on improving glycaemic control in people with diabetes managed in diabetology/endocrinology departments of general hospitals.

b. Ethical compliance

The purposes of data processing are defined, explicit and legitimate. An information letter is handed to patients in person or sent by post to their home. The data collected are adequate, relevant, and limited to what is necessary for the study.

c. Public interest justification

This study will measure the effectiveness and risks associated with the use of closed-loop insulin pumps in routine clinical practice.

d. Dissemination and publication

Peer-reviewed scientific article.

3. Methodology

a. Required data sources

☒Medical records
☐PMSI only
☐SNDS extraction
☐Registry
☐Survey / cohort
☒Other: diabetes platforms (CareLink / MyDiabby / YourLoops)

b. Study cohort description

Inclusion criteria:

- Age > 7 years
- Type 1 diabetes
- Equipped with a closed-loop insulin pump

Non-inclusion criteria:

- Presence of a legal protection measure limiting autonomous decision-making
- Patient or legal representative objecting to the use of data for research purposes

c. Methods, data processing and analysis

Data will be collected as follows:

i. At inclusion (baseline)

- Demographics: sex, age, weight, body mass index (automatically calculated).
- Medical history: retinopathy, nephropathy, coronary artery disease, stroke.
- Diabetes-related data: diabetes duration, HbA1c, year of insulin pump initiation, type of glucose monitoring (continuous glucose monitoring [CGM]; e.g., FreeStyle Libre or other - to be specified), year of CGM initiation.
- Data from the diabetes platform (CareLink) for the 3 months prior to closed-loop initiation and the last 14 days: time in range 70-180 mg/dL (TIR), time below range <70 mg/dL (TBR), time above range >180 mg/dL (TAR), mean glucose, coefficient of variation, mean number of capillary blood glucose tests per day, mean total daily insulin dose, basal/bolus ratio, grams of carbohydrates consumed per day.
- Number of severe hypoglycaemic events in the last 12 months.
- Ketosis or diabetic ketoacidosis in the last 12 months.
- Diabetes-related hospitalisations in the last 12 months.
- Device data: date of closed-loop initiation, closed-loop pump brand (MiniMed), configured glucose target, active insulin time in closed-loop mode.

ii. Follow-up at M3 (3 months after inclusion)

- Clinical characteristics: weight, BMI.
- Data from the diabetes platform for the last 14 days: HbA1c, time in SmartGuard, time in temporary basal, time in manual mode, TIR, TBR, TAR, configured glucose target, mean glucose, coefficient of variation,

mean number of capillary blood glucose tests per day, mean total daily insulin dose, basal/bolus ratio, grams of carbohydrates consumed per day.

- Device data: number of sensors used, number of sensor malfunctions; report transmitter and/or pump change if applicable (MiniMed, t:slim, DBLG1).
- Adverse events: number of severe hypoglycaemic events since the previous visit; number of episodes of ketosis or diabetic ketoacidosis since the previous visit; number of diabetes-related hospitalisations since the previous visit; other diabetes-related adverse events.

iii. Follow-up at M6 (6 months after inclusion)

- Clinical characteristics: weight, BMI.
- Data from the diabetes platform for the last 14 days: HbA1c, time in SmartGuard, time in temporary basal, time in manual mode, TIR, TBR, TAR, configured glucose target, mean glucose, coefficient of variation, mean number of capillary blood glucose tests per day, mean total daily insulin dose, basal/bolus ratio, grams of carbohydrates consumed per day.
- Device data: number of sensors used, number of sensor malfunctions; report transmitter and/or pump change if applicable (MiniMed, t:slim, DBLG1).
- Adverse events: number of severe hypoglycaemic events since the previous visit; number of episodes of ketosis or diabetic ketoacidosis since the previous visit; number of diabetes-related hospitalisations since the previous visit; other diabetes-related adverse events.

iv. Follow-up at M12

- Clinical characteristics: weight, BMI.
- Data from the diabetes platform for the last 14 days: HbA1c, time in SmartGuard, time in temporary basal, time in manual mode, TIR, TBR, TAR, configured glucose target, mean glucose, coefficient of variation, mean number of capillary blood glucose tests per day, mean total daily insulin dose, basal/bolus ratio, grams of carbohydrates consumed per day.
- Device data: number of sensors used, number of sensor malfunctions; report transmitter and/or pump change if applicable (MiniMed, t:slim, DBLG1).
- Adverse events: number of severe hypoglycaemic events since the previous visit; number of episodes of ketosis or diabetic ketoacidosis since the previous visit; number of diabetes-related hospitalisations since the previous visit; other diabetes-related adverse events.

v. Follow-up at M18 (end of study)

- Clinical characteristics: weight, BMI.
- Data from the diabetes platform for the last 14 days: HbA1c, time in SmartGuard, time in temporary basal, time in manual mode, TIR, TBR, TAR, configured glucose target, mean glucose, coefficient of variation, mean number of capillary blood glucose tests per day, mean total daily insulin dose, basal/bolus ratio, grams of carbohydrates consumed per day.
- Device data: number of sensors used, number of sensor malfunctions; report transmitter and/or pump change if applicable (MiniMed, t:slim, DBLG1).
- Adverse events: number of severe hypoglycaemic events since the previous visit; number of episodes of ketosis or diabetic ketoacidosis since the previous visit; number of diabetes-related hospitalisations since the previous visit; other diabetes-related adverse events.

vi. Analyses

- Describe demographic and clinical characteristics of the type 1 diabetes population initiated on closed-loop therapy (M0).
- Assess changes in glycaemic control at M3, M6, M12 and M18 versus M0 (TIR, TBR, TAR, HbA1c, mean glucose and glucose coefficient of variation).
- Assess adherence to closed-loop use at M3, M6, M12 and M18 (percentage of time in SmartGuard, manual mode, on closed-loop pump, and reasons for discontinuation).
- Assess changes in insulin requirements at M3, M6, M12 and M18 versus M0 (mean total daily insulin dose, basal/bolus ratio, carbohydrate intake).
- Assess safety (number of diabetes-related hospitalisations, diabetic ketoacidosis, severe hypoglycaemia) and device vigilance (pump/transmitter changes, number of sensors used, defective sensors) at M3, M6, M12 and M18.
- Assess self-monitoring practices at M3, M6, M12 and M18 (mean number of capillary blood glucose tests).

d. Data flow and record linkage

Data will be extracted from the electronic medical record and the closed-loop device software (CareLink, MyDiabby, YourLoops) and entered into an eCRF.

Data in the eCRF will be pseudonymised. The paper correspondence table (re-identification key) will be kept at the investigator site and destroyed after acceptance of the publication.

The database will be transferred to the statistician for analysis via a secure channel. It will then be stored and archived on the clinical research department server.

Only aggregated data will be presented in the study report and scientific publications.

e. Planned timeline and feasibility

- May-August 2022: preparation of study documents, selection of participating centres, and design of the eCRF.
- September 2022: study initiation.
- September 2022-August 2023: retrospective data collection for patients already using closed-loop pumps, and prospective inclusion of patients newly initiated on closed-loop therapy.
- A one-month delay between sending information letters and starting data collection will be respected.
- September 2023-January 2025: follow-up of prospectively included patients.
- February-March 2025: data analysis.
- April-May 2025: manuscript drafting.
- Mid-2025: submission.

4. Privacy, security and confidentiality of data

a. Patient information and protection of rights

☒Individual information of patients/service users, etc.
☐Collective information
☒Data media and security

☐Request for exemption from individual information (to be justified):

5. References

[1] Pleus S, Baumstark A, Jendrike N, Mende J, Link M, Zschornack E, et al. System accuracy evaluation of 18 CE-marked current-generation blood glucose monitoring systems based on EN ISO 15197:2015. BMJ Open Diabetes Res Care 2020;8. https://doi.org/10.1136/bmjdrc-2019-001067.

[2] The Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group. Continuous Glucose Monitoring and Intensive Treatment of Type 1 Diabetes. New England Journal of Medicine 2008;359:1464–76. https://doi.org/10.1056/NEJMoa0805017.

[3] Knox ECL, Quirk H, Glazebrook C, Randell T, Blake H. Impact of technology-based interventions for children and young people with type 1 diabetes on key diabetes self-management behaviours and prerequisites: a systematic review. BMC Endocr Disord 2019;19:7. https://doi.org/10.1186/s12902-018-0331-6.

[4] Pease A, Lo C, Earnest A, Kiriakova V, Liew D, Zoungas S. The Efficacy of Technology in Type 1 Diabetes: A Systematic Review, Network Meta-analysis, and Narrative Synthesis. Diabetes Technol Ther 2020;22:411–21. https://doi.org/10.1089/dia.2019.0417.

[5] Di Molfetta S, Di Gioia L, Caruso I, Cignarelli A, Green SC, Natale P, et al. Efficacy and Safety of Different Hybrid Closed Loop Systems for Automated Insulin Delivery in People With Type 1 Diabetes: A Systematic Review and Network Meta-Analysis. Diabetes/Metabolism Research and Reviews 2024;40:e3842. https://doi.org/10.1002/dmrr.3842.

[6] Peacock S, Frizelle I, Hussain S. A Systematic Review of Commercial Hybrid Closed-Loop Automated Insulin Delivery Systems. Diabetes Therapy 2023;14:839–55. https://doi.org/10.1007/s13300-023-01394-5.

[7] Rothwell PM. External validity of randomised controlled trials: "To whom do the results of this trial apply?" The Lancet 2005;365:82–93. https://doi.org/10.1016/S0140-6736(04)17670-8.

[8] Leelarathna L, Choudhary P, Wilmot EG, Lumb A, Street T, Kar P, et al. Hybrid closed-loop therapy: Where are we in 2021? Diabetes, Obesity and Metabolism 2021;23:655–60. https://doi.org/10.1111/dom.14273.