Interreg Centre for Personalised Medicine
Unscheduled Care in Diabetes
Study 2: Inpatient Study

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TITLE
Interreg Centre for Personalised Medicine: Unscheduled Care in Diabetes
Study 2: Inpatient study

STUDY MANAGEMENT GROUP

Chief investigator:	Professor Sandra MacRury Professor of Clinical Diabetes School of Health University of the Highlands and Islands Inverness
Principle investigator:	Professor Vivien Coates Professor of Clinical Nursing Practice Research School of Nursing University of Ulster & Western Health and Social Care Trust Derry-London Derry
Co-investigator:	Ms Michelle Friel PhD Researcher University of Ulster Derry-Londonderry
Co-investigator:	Dr Neil Black Consultant Physician in Diabetes and Endocrinology Western Health and Social Care Trust Derry-Londonderry
Co-investigator:	Mr Kevin Blake Research Database Manager Letterkenny Institute of Technology Letterkenny
Co-investigator:	Dr Janet Heaton Research Fellow Rural Health and Wellbeing University of the Highlands and Islands Inverness
Co-investigator:	Dr Geraldine Horigan Freelance Clinical Research Consultant Clinical Translational Research and Innovation Centre University of Ulster Derry-Londonderry
Co-investigator:	Dr Brendan McCann Chief Scientific Officer Voscuris (previously Clinisent) Belfast
Co-investigator:	Dr Michael McCann Lecturer Letterkenny Institute of Technology Letterkenny

Co-investigator:	Dr Athinyaa Thiraviaraj Consultant Physician in Diabetes and Endocrinology Western Health and Social Care Trust Derry-Londonderry
Co-investigator:	Dr Hugo van Woerden Director of Public Health NHS Highland Inverness
Co-Investigator:	Charlotte Barr Lead Research Nurse NHS Highland Inverness

STUDY CENTRE
For general queries, supply of study documentation, and collection of data, please contact:

Professor Sandra MacRury
Rural Health and Wellbeing
University of the Highlands and Islands
The Centre for Health Science
Old Perth Road
Inverness, UK
IV2 3JH
Tel: +44 (0)1463 279583
Email: Sandra.macrury@uhi.ac.uk

SPONSOR

UHI	Professor Neil Simco Vice-Principal UHI Executive Office Ness Walk Inverness IV3 5SQ Email: neil.simco@uhi.ac.uk

CO SPONSOR

NHS Highland	Frances Hines NHS Highland R&D Manager Centre for Health Science Old Perth Road Inverness IV2 3JH Email: frances.hines@nhs.net

FUNDER Interreg, European Regional Development Fund

STUDY SYNOPSIS

Title	Interreg Diabetes Centre for Personalised Medicine - Unscheduled Care in Diabetes - Study 2: Inpatient Study
REC reference:	TBC
Design	Developmental study using mixed quantitative and qualitative research methods.
Primary objectives	To assess whether Flash Glucose Monitoring can be used in inpatient care for people with diabetes to improve clinical decision making and patient safety through more frequent glucose recording using a subcutaneous sensor.
Secondary objectives	To assess the potential for the use of Flash Glucose Monitoring in inpatient diabetes care to reduce average length of stay (LoS).
Participants: Inclusion criteria	**Phase 1: Retrospective data audit** – Adults (aged 18 years and older) – Diagnosed diabetes – Admitted to hospital in the previous year **Phase 2, Part A: Pilot study - Preliminary feasibility test** – Adults (aged 18 years and older) – Diagnosed with diabetes (patient participants only) – Admitted to hospital wards defined in phase 1 (patient participants only) – Employed on the hospital ward delivering diabetes care (HCP participants only) – Able to read and understand the participant information sheet (PIS) – Able to give written informed consent **Phase 2, Part B: Pilot study – Use of Flash Glucose Monitoring** – Adults (aged 18 years and older) – Diagnosed with diabetes – Admitted to hospital wards defined in phase 1 – Able to read and understand the participant information sheet (PIS) – Able to give written informed consent **Phase 2, Part C: Pilot study - Evaluation interviews** – Patients or HCPs that have participated in phase 2, part B. – Able to read and understand the participant information sheet (PIS) – Able to give written informed consent
Exclusion criteria	**Phase 1: Retrospective data audit** – Children or young people (aged younger than 18 years) – Not diagnosed with diabetes **Phase 2, Part A: Pilot study - Preliminary feasibility test** – Children or young people (aged less than 18 years). – Not diagnosed with diabetes (Patient participants only). – Admitted to hospital wards not defined in phase 1. – Pregnancy or gestational diabetes – Significant intercurrent illness and/or terminal diagnosis (Patient participants only).

Exclusion criteria (continued)	– Have a condition and/or treatment known to affect variability of blood glucose, such as on kidney dialysis. – Already using a Flash Glucose Monitoring or continuous glucose monitoring device. – Unable to read and understand the PIS. – Unable to give informed written/recorded consent. **Phase 2, Part B: Pilot study - Use of Flash Glucose Monitoring** – Children or young people (aged younger than 18 years). – Not diagnosed with diabetes. – Admitted to hospital wards not defined in phase 1 – Pregnancy or gestational diabetes – Significant intercurrent illness and/or terminal diagnosis. – Have a condition and/or treatment known to affect variability of blood glucose, such as on kidney dialysis. – Already using a Flash Glucose Monitoring or continuous monitoring device. – Unable to read and understand the participant information sheet (PIS). – Unable to give written informed consent. **Phase 2, Part C: Pilot study - Evaluation interviews** – Ongoing significant co-morbid illness – Unable to read and understand the participant information sheet.
Non-intervention group	**Phase 1: Retrospective data audit** N/A. **Phase 2, Part A: Pilot study - Preliminary feasibility test** N/A. **Phase 2, Part B: Pilot study – Use of Flash Glucose Monitoring** Usual point-of-care testing. **Phase 2, Part C: Pilot study - Evaluation interviews** N/A.
Sample size	**Phase 1: Retrospective data audit** N/A. **Phase 2, Part A: Pilot study - Preliminary feasibility test** A small sample of 4-8 participants (2-4 patients and 2-4 HCPs) per study site totalling 12-24 across the whole study. **Phase 2, Part B: Pilot study – Use of Flash Glucose Monitoring** A minimum of 60 participants is anticipated overall with a minimum of 20 participants per study site. **Phase 2, Part C: Pilot study - Evaluation interviews** A sample of 15-25 participants (approximately 10-15 patients and 5-10 HCPs) is anticipated per site.
Duration	The total duration of the study, including phases 1 and 2, is expected to be approximately 18 months. A staggered start will occur across the three sites.
Measurements	**Phase 1, Retrospective data audit** Blood glucose data from Freestyle Provision, POCcellarator and relevant databases. **Phase 2, Part A: Pilot study - Preliminary feasibility test** Feedback and EQ5D-5L questionnaires. **Phase 2, Part B: Pilot study – Use of Flash Glucose Monitoring**

	Glucose data from Freestyle Libre Flash Glucose Monitoring devices, point of care (POC) blood glucose data, EQ5D-5L data, LoS data. **Phase 2, Part C: Pilot study - Evaluation interviews** Semi-structured interviews.
Study processes Study processes (continued)	**Phase 1, Retrospective data audit** Existing hospital staff members or members of the research team per study site will request access to the relevant databases to extract available data from capillary blood glucose monitoring on hospital wards. – The data will be extracted and collated from the relevant databases per study site. – The data will be analysed to determine incidence of hypoglycaemia and/or hyperglycaemia across the wards to identify which wards demonstrate the greatest variability. There will be no active participant involvement in this part of the study. **Phase 2, Part A: Pilot study - Preliminary feasibility test** – A test ward will be chosen from the ward(s) identified in Phase 1 to test the use of Flash Glucose Monitoring over the course of 2 weeks. – Ward staff will be approached by the study researcher and given an explanation of the study and a study pack outlining the purposes of the preliminary test and what will be involved. – A member of the clinical care team will make the first approach to patients, giving a brief explanation of the preliminary test and the role of the researcher, before asking if they are happy to be approached by the researcher. – Potential participants will be given a verbal explanation of the study and a study pack, which will include an invitation letter and PIS and be given the opportunity to discuss the study and ask any questions. – Written informed consent will be taken from willing participants to take part in the preliminary work. – Researchers and a research nurse on each site will be trained on the use of Flash Glucose Monitoring and application of the sensors. Whilst the risk of COVID-19 transmission is present, self-administration of the sensors will be recommended. There may be exceptional patients who are suitable for participation but physically are not able to apply the sensors. In this scenario the Inpatient DSNs will apply the sensor but will not be involved in any other aspects of the trial explanation or setting it up. Patients will be encouraged to swipe the sensor every two hours during waking hours alert ward staff of any values out with the acceptable range. For patients unable to carry this out, ward staff will be asked to swipe the sensor every two hours if possible and at the time of routine capillary glucose testing. Routine capillary testing will continue to be carried out as per hospital protocol at least four times daily. All measurements will be recorded on the bedside glucose monitoring chart along with a note of any action or intervention based on the glucose result. The full dataset of values will be downloaded by the researcher or research nurse daily to ' Libre view' software during the inpatient stay or at the end of the two week period if used following ward discharge. – Participants will wear the Flash Glucose Monitoring devices for 2 weeks or for the duration of their stay with a minimum of two days (if less than 2 weeks). Participants will be asked to complete EQ5D-5L questionnaire (appendix 21) at two timepoints – baseline and end of week two.

	– At the end of the 2 weeks the researcher will provide all patients and HCPs who have been involved with the study a questionnaire to gain their feedback on the use of Flash Glucose Monitoring and to tease out any problems with use of the devices and/or the study processes. – Patients who have consented will complete the demographic data questionnaire. **Phase 2, Part B: Pilot study – Use of Flash Glucose Monitoring** – A member of the clinical care team will make the first approach to patients, giving a brief explanation of the study and the role of the researcher, before asking if they are happy to be approached by the researcher. – Potential participants will then be approached by the researcher and given a verbal explanation of the study and a study pack, which will include an invitation letter and PIS, and be given the opportunity to discuss the study and ask any questions. – Written informed consent will be taken from willing participants to take part in the study and to be contacted following their discharge from hospital for the evaluation interviews (part C). – Participants will be randomised into either the active use of Flash Glucose Monitoring or non-intervention group using individual sequential randomisation. – The participants will ideally self-administer the glucose sensor for those randomised to use of Flash Glucose Monitoring. There may be exceptional patients who are suitable for participation but physically are not able to apply the sensors. In this scenario the Inpatient DSNs will apply the sensor but will not be involved in any other aspects of the trial explanation or setting it up. – Researchers and a research nurse on each site will be trained on the use of Flash Glucose Monitoring and application of the sensors. Patients will be encouraged to swipe the sensor every two hours during waking hours alert ward staff of any values out with the acceptable range. For patients unable to carry this out, ward staff will be asked to swipe the sensor every two hours if possible and at the time of routine capillary glucose testing. Routine capillary testing will continue to be carried out as per hospital protocol at least four times daily. All measurements will be recorded on the bedside glucose monitoring chart along with a note of any action or intervention based on the glucose result. The full dataset of values will be downloaded by the researcher or research nurse daily to 'Libre view' software during the inpatient stay or at the end of the two week period if used following ward discharge. – All participants in the active arm of the study will be given the choice to be sent home with a Flash Glucose Monitoring device to be used for up to 2 weeks in total following their discharge. – LoS will be recorded using site-specific databases and/or review of immediate discharge letters. LoS will be recorded in days and hours, including the time of day/night and the day of the week for both admission and discharge. – All participants will be asked to complete an EQ5D-5L questionnaire (appendix 25) at two timepoints including baseline and at three months. **Phase 2, Part C: Pilot study - Evaluation interviews** – Following their discharge from hospital, patient participants will be contacted to arrange a suitable date/time for the interview.

	– Following the completion of the study, HCP participants will be contacted to arrange a suitable date/time for the interviews. – Immediately prior to the interview, written/recorded informed consent will be obtained depending on whether the interviews are conducted face-to-face or via telephone. – Interviews will be audio-recorded, transcribed, anonymised and analysed to explore experiences of inpatient care and the use of Flash Glucose Monitoring both on the wards and at home following discharge.

APPENDICES

- Appendix 1 – Study 2, Phase 2, Part A: HCP Participant Invitation Letter
- Appendix 2 - Study 2, Phase 2, Part A: HCP Participant Information Sheet
- Appendix 3 - Study 2, Phase 2, Part A: HCP Participant Consent Form
- Appendix 4 - Study 2, Phase 2, Part A: Patient Participant Invitation Letter
- Appendix 5 - Study 2, Phase 2, Part A: Patient Participant Information Sheet
- Appendix 6 - Study 2, Phase 2, Part A: Patient Participant Consent Form
- Appendix 7 - Study 2, Phase 2, Part A: Feedback Questionnaire/Topic Guide
- Appendix 8 - Study 2, Phase 2, Part B: Patient Participant Invitation Letter
- Appendix 9- Study 2, Phase 2, Part B: Patient Participant Information Sheet
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- Appendix 11 - Study 2, Phase 2, Part B: Lifestyle/Demographic Questionnaire
- Appendix 12 - Study 2, Phase 2, Part C: Patient Participant Invitation Letter
- Appendix 13 - Study 2, Phase 2, Part C: Patient Participant Information Sheet
- Appendix 14 - Study 2, Phase 2, Part C: Patient Participant Consent Form
- Appendix 15 - Study 2, Phase 2, Part C: HCP Participant Invitation Letter
- Appendix 16 - Study 2, Phase 2, Part C: HCP Participant Information Sheet
- Appendix 17 - Study 2, Phase 2, Part C: HCP Participant Initial Expression of Interest Form
- Appendix 18 - Study 2, Phase 2, Part C: HCP Participant Consent Form
- Appendix 19 – Study 2, Phase 2, Part C: Patient Participant Topic Guide
- Appendix 20 – Study 2, Phase 2, Part C: HCP Participant Topic Guide
- Appendix 25 - Study 2, Phase 2, EQ5D-5L questionnaire
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KEY WORDS

Diabetes, unscheduled care, inpatient care, innovative technology

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1. INTRODUCTION

1.1 Background and rationale

Diabetes is a chronic and often debilitating condition that can involve a high degree of patient self-management and burden of self-care. The increasing prevalence of diabetes in the UK is a major cause for concern, with 3.7 million people diagnosed, but 4.6million estimated to actually live with the condition in the UK (1). The increased prevalence of diabetes has a reciprocal negative effect on costs for the National Health Service (NHS), with dramatic figures demonstrating that diabetes currently accounts for 10% of the entire health resource expenditure, with 80% of diabetes spending being used for potentially preventable complications (2).

Research has repeatedly demonstrated that people with diabetes are significantly more likely to be admitted to hospital than people without diabetes, with further excessive comparative length of stay (LoS) once admitted (3-10). In England, a comprehensive study demonstrated that diabetes had an independent effect on LoS, regardless of age, socio-economic status, type of admission or complexity of cases (10). The research concluded that people with diabetes stay in hospital on average twice as long, with 50% less chance to be treated as day cases, compared to those without diabetes.

Inpatient care has been long been identified as a priority in the government service frameworks for people with diabetes (11,12), yet the cost of diabetes inpatient care makes up 11% of the total NHS budget in England (7) and 12% in NHS Scotland (13). Despite such significant expenditure, care has been poor with avoidable complications seen due to medication errors, a lack of patient involvement or facilitation of self-management, and a lack of access to specialist diabetes teams (7, 14).

A prominent factor that can influence LoS in people with diabetes is appropriate management of extremes in blood glucose levels, with both hypoglycaemia (15,16) and hyperglycaemia (17,18) shown to significantly impact upon length of stay and mortality. Extremes in blood glucose can occur in hospital due to altered self-management patterns, nil-by-mouth requirements, delayed meal-times and inappropriate timing of medications (19). The quality of inpatient diabetes care has been comprehensively evaluated by in the National Diabetes Inpatient Audit (NaDIA) since 2010, which has long identified that hypoglycaemia is a significant concern. In their most recent report, they acknowledged that the incidence of hypoglycaemia has reduced from 26% in 2011 to 18% in 2017, although 31% of people still experienced medication errors, which can lead to iatrogenic hypoglycaemia (14).

A culture of clinical inertia has been identified in inpatient diabetes care, whereby ward staff demonstrate a reluctance to initiate or intensify treatment despite the identification and documentation of a necessity to act to rising or falling blood glucose levels (20-24). In a UK study exploring challenges faced by clinicians in providing adequate care for people admitted to hospital with diabetes, inertia resulting from a lack of confidence or adequate knowledge, as well as differences in approaches to care was identified (24). While a need for specialist support, in the form of inpatient diabetes specialist nurses, has been identified and recommended nationally (14), the study identified that ward staff can inadvertently become de-skilled as a result of relying on seeking specialist support. Ward staff followed routine

protocols with a lack of confidence in decision making, whereas specialists took a more holistic approach with higher-level decisions based on the complexity of each patient's presentation.

Although the NaDIA report (14) identified improvements since 2011, it highlighted a continued need for improvement, since both hypo- and hyperglycaemia are avoidable and preventable conditions. The report recommended innovative and improved systems for blood glucose monitoring in response to its findings. Similarly, in the study exploring complexity, resilience and quality in inpatient diabetes care, specialists identified a need for the development of decision support tools to bolster appropriate action in the response to blood glucose variability (24). An approach that holds the potential for such innovation is the use of Flash Glucose Monitoring which monitors glucose levels continually and provides additional data beyond a single reading including trends and trajectories over a 24 hour period of time for up to two weeks. The use of this innovative technology and its capability to provide additional data to routine ward point of care (POC) capillary testing and decision making between staff and patients could allow for faster recognition of changes in glucose levels and facilitate more timely responses in management of out of range levels.

2. AIMS

2.1 Aim

This study aims to explore the use of innovative technology for inpatient diabetes care to improve clinical decision making and patient safety through the potential stabilisation of glucose levels, and in time the reduction of LoS.

2.2 Primary objective

to assess whether Flash Glucose Monitoring can be used in inpatient care for people with diabetes to improve clinical decision making and patient safety through more frequent glucose recording using a subcutaneous sensor.

2.3 Secondary objectives

To assess the potential for Flash Glucose Monitoring in inpatient diabetes care can reduce average length of stay (LoS).

3. STUDY DESIGN

3.1 Methodology

This is a descriptive developmental mixed-methods study using both qualitative and quantitative approaches with two phases.

3.2 Sample size

Phase 1: Retrospective data audit

N/A

Phase 2, Part A: Pilot study - Preliminary feasibility test

An approximate sample of 2-4 patients and 2-4 HCPs is anticipated per study site.

Phase 2, Part B: Pilot study – Use of Flash Glucose Monitoring

The final sample size will be dependent on the number of eligible participants willing to participate but we envisage a minimum of 20 participants per study site.

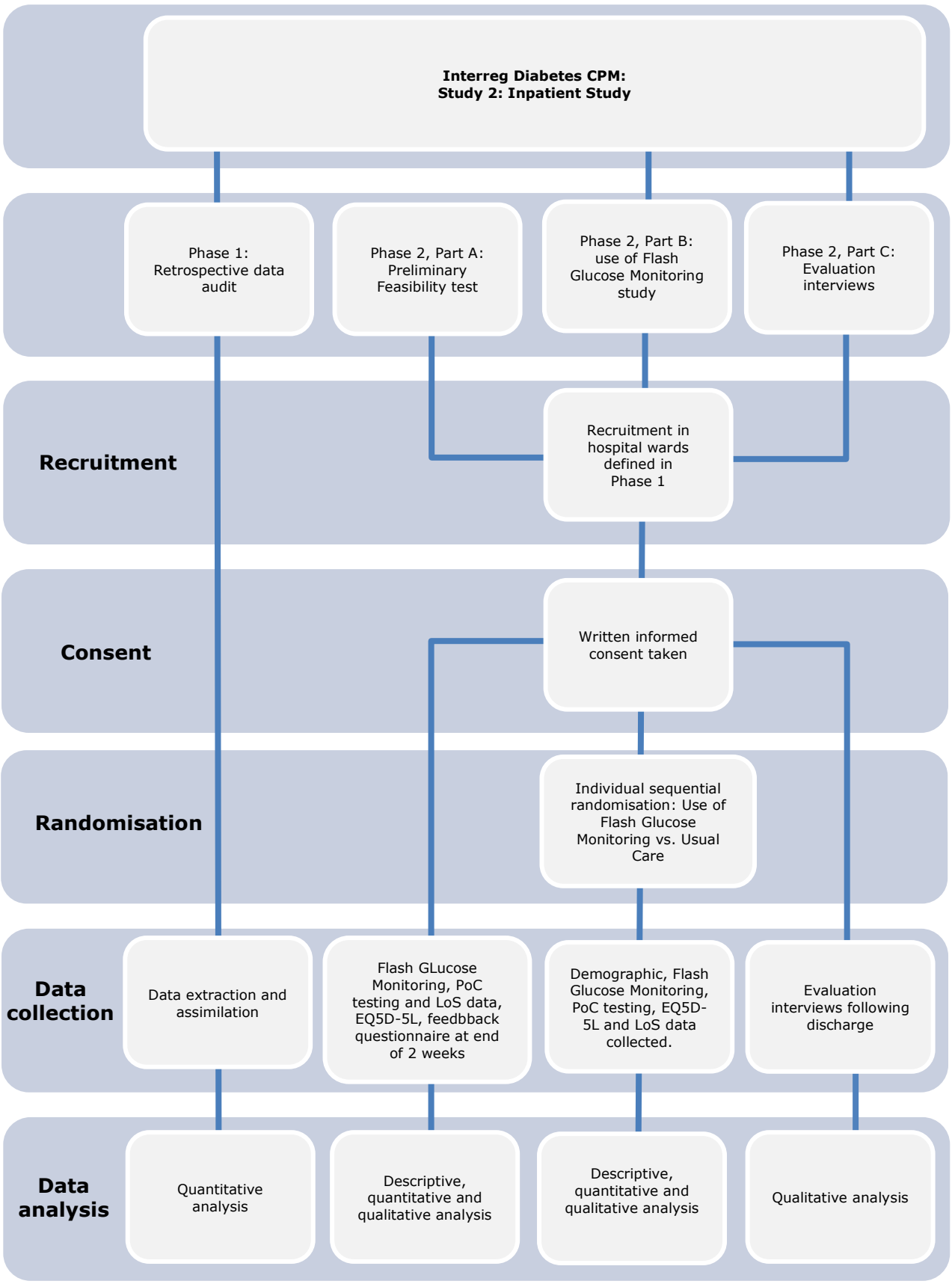
Phase 2, Part C: Pilot study - Evaluation interviews

As with Part B, the final sample size will be dependent on the number of eligible participants that are willing to participate, but we anticipate 15-25 participants per study site, consisting of both patients who were enrolled into, and HCPs who were involved in the delivery of, the pilot study Part B (approximately 10-15 patients and 5-10 HCPs per study site).

3.3 Study overview

Please see Figure 1 (overleaf) for an outline of the steps in this study.

Figure 1: Overview of study processes for Interreg Centre for Personalised Medicine: Unscheduled Care in Diabetes, Inpatient Intervention Study



4. PARTICIPANT ENTRY

4.1 Population

The overall target population for this study will be individuals who have been admitted to hospital as an inpatient in Raigmore Hospital, Inverness, Altnagelvin Hospital, Derry-Londonderry, or Letterkenny University Hospital, Co Donegal. The specific inclusion and exclusion criteria for each phase and part of this study differ slightly please see section 4.2 and 4.3.

4.2 Inclusion Criteria

Phase 1: Retrospective data audit

There will be no active participation in this phase of the study, however the data collected will relate to individuals with the following criteria:

- Adults (aged 18 years or over).
- Diagnosed with diabetes.
- Admitted to hospital as an inpatient in the previous year.

Phase 2, Part A: Pilot study - Preliminary Feasibility Test

- Adults (aged 18 years or over).
- Diagnosed with diabetes. (Patient participants only)
- Admitted to hospital ward defined in Phase 1. (Patient participants only)
- Employed on the hospital ward delivering diabetes care (HCP participants only)
- Able to read and understand the participant information sheet (PIS).
- Able to give informed written/recorded consent to participate.

Phase 2, Part B: Pilot study – Use of Flash Glucose Monitoring

- Adults (aged 18 years or over).
- Diagnosed with diabetes.
- Admitted to hospital ward defined in Phase 1 as an inpatient.
- Able to read and understand the PIS.
- Able to give informed written/recorded consent to participate.

Phase 2, Part C: Pilot study - Evaluation interviews

- Participation in Phase 2, Part B.
- Adults (aged 18 years or over).
- Diagnosed with diabetes. (Patient participants only)
- Admitted to hospital as an inpatient. (Patient participants only)
- Employed on the hospital ward delivering diabetes care for Phase 2, Part B (HCP participants only)

- Able to read and understand the PIS.
- Able to give informed written/recorded consent to participate.

4.3 Exclusion Criteria

Phase 1: Retrospective data audit

- Children or adolescents (aged less than 18 years).
- Not diagnosed with diabetes.

Phase 2, Part A: Pilot study

- Children or adolescents (aged less than 18 years).
- Not diagnosed with diabetes (Patient participants only).
- Admitted to hospital wards not defined in phase 1
- Pregnancy or gestational diabetes
- Significant intercurrent illness and/or terminal diagnosis (Patient participants only).
- Have a condition and/or treatment known to affect variability of blood glucose, such as on kidney dialysis (Patient participants only).
- Already using a Flash Glucose Monitoring
- Unable to read and understand the PIS.
- Unable to give informed written/recorded consent.

Phase 2, Part B: Pilot study – Use of Flash Glucose Monitoring

- Children or adolescents (aged less than 18 years).
- Not diagnosed with diabetes.
- Pregnancy or gestational diabetes
- Significant intercurrent illness and/or terminal diagnosis.
- Have a condition and/or treatment known to affect variability of blood glucose, such as on kidney dialysis.
- Already using Flash Glucose Monitoring or continuous glucose monitoring device.
- Unable to read and understand the PIS.
- Unable to give informed written/recorded consent.

Phase 2, Part C: Pilot study - Evaluation interviews

- Significant intercurrent illness (Patient participants only).
- Unable to read and understand the PIS.
- Unable to give informed written/recorded consent.

4.4 Withdrawal Criteria

Phase 1: Retrospective data audit

N/A

Phase 2: Pilot study

All participants recruited in Phase 2, parts A, B and/or C, will be informed of their right to withdraw at any point within the study, without needing to provide a reason, and any participants expressing a wish to do so will be withdrawn immediately. Should participants choose to withdraw from participation, they will be asked if they are happy for any existing data to remain in the study. Should participants wish to have any existing data removed from the study they will be free to do so and data will be removed immediately and destroyed by the relevant IT departments across the study sites. Interview data was analysed will not be retrievable.

5. STUDY PROCEDURES

5.1 Phase 1: Retrospective data audit

Existing NHS staff members of the study team will access blood glucose data from the Freestyle Precision database in NHS Highland, and the POCcellarator database in Altnagelvin Hospital and Letterkenny University Hospital, Co Donegal to identify the incidence of hypoglycaemia (<4mmol/L) and hyperglycaemia (>12mmol/L) combined with demographic and LoS data across hospital wards.

The data will be extracted, collated and anonymised by existing NHS staff before being securely transferred to the study researcher. The study researcher will analyse the data set to identify wards (excluding intensive care or high dependency units) that have the greatest incidence of extremes in blood glucose. Anonymised data will be stored on a password-protected database to which only the main investigators and designated researchers will have access.

5.2 Phase 2 Part A: Pilot study - Preliminary feasibility test

A test ward will be chosen from the ward(s) identified in Phase 1 to test the use of Flash Glucose Monitoring over the course of 2 weeks, the maximum lifetime of a single Flash Glucose Monitoring sensor. Ward staff will be approached via email by the study researcher and provided an explanation of the study and a study pack outlining the purpose of the preliminary work and what will be involved. The study pack will include an invitation letter (appendix 1), PIS (appendix 2) and a consent form to be printed and completed by HCPs who are interested in taking part (appendix 3). The researcher will be available by phone for any questions they may have.

A member of the clinical care team will identify potential patient-participants and will make the first approach to confirm that patients are happy to be approached by the researcher. Willing participants will be approached by the researcher or research nurse and given a verbal explanation of the study and a study pack, which will include an invitation

letter (appendix 4), a PIS (appendix 5), and be given the opportunity to discuss the study and ask any questions. Written informed consent (appendix 6) will be taken from willing participants to take part in the preliminary work.

Researchers will hold a research passport and an honorary NHS contract and along with a research nurse will receive structured training in the use and application of the Flash Glucose Monitoring system through attendance at an area training session. Participants will ideally be provided guidance to self-administer the Freestyle Libre Flash Glucose Monitoring sensor for those randomised to the intervention group. Whilst the risk of COVID-19 transmission is present, self-administration of the sensors will be recommended. There may be exceptional patients who are suitable for participation but physically are not able to apply the sensors. In this scenario the Inpatient DSNs will apply the sensor but will not be involved in any other aspects of the trial explanation or setting it up. Patients and staff will be advised of the need for the sensor to be in place for 1-2 hours before recording will commence and also of the anticipated time delay between simultaneous sensor and blood glucose readings. Patients will be advised to scan the sensors every two hours during waking hours with at least one scan between 10pm and midnight and 6-8am. For patients unable to carry this out, ward staff will be asked to swipe the sensor every two hours if possible and at the time of routine capillary glucose testing. Routine capillary testing will continue to be carried out as per hospital protocol at least four times daily. All measurements will be recorded on the bedside glucose monitoring chart along with a note of any action or intervention based on the glucose result. During the inpatient stay for patients and ward staff to enhance decision making the full dataset of values will be downloaded by the researcher or research nurse daily from the monitor to 'Libre view' software and printed out in the ward for patients and staff to view. Scanners will be placed on a table and wiped down with disinfectant and gloves before and after data is downloaded. If the patient prefers they may use the Libre phone app linked to 'Libre view' software. The researcher will download the full data set at the end of the two week period and note any changes the patient has made to therapy if the sensor is used following discharge from the ward.

Participants will wear the Flash Glucose Monitoring devices for 2 weeks or for the duration of their stay with a minimum of two days (if less than 2 weeks). At the end of the duration the researcher will provide all patients and HCPs involved in the testing with a questionnaire sent via email (appendix 7) to gain their feedback on the use of Flash Glucose Monitoring, tease out any problems with use and identify the best ways to facilitate the study processes.

Participant duration will start at the point of consent being taken, and will end at the point of their feedback data being collected. Participation is anticipated to be no longer than 2 weeks depending on patient LoS.

Linked anonymised information will be held in locked filing cabinets in locked rooms and/or on a password-protected database to which only the main investigators and delegated researcher will have access. All paperwork will be handled with gloves and placed into storage immediately after being passed back to the researcher.

5.3 Phase 2, Part B: Pilot study – Use of Flash Glucose Monitoring

The researcher will approach the ward staff and provide a detailed overview of the study and training on the use of Flash Glucose Monitoring for the pilot study Part B (developed in part A).

Potential participants will be approached by a member of the clinical care team in the first instance and given a brief explanation of the study and will be asked if they are happy to be approached by the researcher. If patients provide verbal consent to this, a member of the research team will then approach the patients and provide them with a more detailed verbal explanation of the study and a study pack, including an invitation letter (appendix 8) and a PIS (appendix 9). Patients will be free to choose whether they wish to participate there and then, and if willing, they will be consented into the study using a written informed consent procedure (appendix 10). Patients that would like more time to consider the information and/or speak to their family/friends or care team will be given 2-4 hours to do so. Due to the time-sensitive nature of the intervention and the potential loss of critical clinical data, further time will not always be possible as this could impact the viability of the study. In some exceptional circumstances up to 24 hours may be given to patients to process the information. Any patients that are undecided after this period will not be included. Potential participants will be informed of the randomisation procedure and that they may be placed into the intervention or non-intervention arm prior to consent being taken.

The consent form will include their agreement to be randomised into either the intervention or non-intervention group, to wear a Flash Glucose Monitoring device for the duration of their admission (if randomised into the intervention group), to have their case notes reviewed by the study researcher to extract relevant data for the study, to compete a demographic and lifestyle questionnaire, and to have their contact details stored for the study researcher to contact them following their discharge from hospital to arrange the evaluation interview.

Participants who consent will be sequentially randomised into either the use of Flash Glucose Monitoring arm or the usual care arm and data will be collected for the duration of their stay. All participants will be asked to complete an EQ5D-5L questionnaire at two timepoints including baseline and at three months, or the researcher will complete it with them, to collect socioeconomic and health status data (appendix 21). This data will contribute to the wider demographic CPM study data base held in University of Ulster. It includes questions which may identify mood disorder or depression and while the University of Ulster CPM data team will carry out formal analysis the researcher will highlight to the ward clinical team any participant whose scores suggest the possibility of a depressive illness.

Participants in the intervention group will be provided with a Freestyle Libre Flash Glucose Monitoring sensor and asked to self-apply the sensor with guidance from the research nurse. There may be exceptional patients who are suitable for participation but physically are not able to apply the sensors. In this scenario the Inpatient DSNs will apply the sensor but will not be involved in any other aspects of the trial explanation or setting it up. Patients and staff will be advised of the need for the sensor to be in place for 1-2 hours before recording will commence and also of the anticipated time delay between simultaneous sensor and blood glucose readings. Patients will be advised to scan the sensors every two hours during waking hours with at least one scan between 10pm and midnight and 6-8am. For patients unable to carry this out, ward staff will be asked to swipe the sensor every two hours if possible and at the time of routine capillary glucose testing. Routine capillary testing will continue to be

carried out as per hospital protocol at least four times daily. All measurements will be recorded on the bedside glucose monitoring chart along with a note of any action or intervention based on the glucose result. During the inpatient stay for patients and ward staff to enhance decision making the full dataset of values will be downloaded by the researcher or research nurse daily from the monitor to 'Libre view' software and printed out in the ward for patients and staff to view. If the patient prefers they may use the Libre phone app linked to 'Libre view' software. The researcher will download the full data set at the end of the two week period and note any changes the patient has made to therapy if the sensor is used following discharge from the ward.

Participants in the usual care group will receive standard POC capillary blood glucose testing according to hospital protocols. All participants' case notes will be reviewed to collect the frequency of tests, the blood glucose readings and whether any intervention was needed. All participants in the intervention group will be given the option to take the Flash Glucose Monitoring device to use at home for up to 2 weeks, if less than 2 weeks use as an inpatient, following their discharge from hospital.

Participant duration will vary depending on the group into which patients are randomised and individual LoS. All participation will start at the point of consent. For patients randomised into the usual care group or the intervention group who do not choose to take the Flash Glucose Monitoring device home, participation will end at the point of discharge from the hospital. For patients randomised into the intervention group who choose to take home the Flash Glucose Monitoring device, participation will end up to 2 weeks following discharge depending on how long they have already worn the sensor. Due to the multiple variables involved in the study, participation is anticipated to be on average between 1 to 6 weeks.

Linked anonymised information will be held in locked filing cabinets in locked rooms and/or on a password-protected database to which only the main investigators and delegated researcher will have access.

5.4 Phase 2, Part C: Pilot study – Evaluation interviews

Patients that participated in Phase 2, Part B and gave prior consent to being contacted at the end of their participation will be sent a study pack following their discharge from hospital consisting of an invitation letter (appendix 12) and PIS (appendix 13).

The study researcher will allow time for the pack to arrive and follow-up with a telephone call to answer any questions and confirm continued willingness to participate in the interview. If the participant demonstrates continued interest in participating, the researcher will arrange a suitable date and time for a phone or online video interview. On the date of the interview, the researcher will ensure understanding and willingness before taking written informed consent (appendix 14) immediately prior to the commencement of the interview. If patients have family members or carers present who would like to include their experiences and opinions of the intervention these will also be explored, with separate consent being taken for these individuals (appendix 15).

To recruit HCPs involved in the pilot study, the researcher will provide ward managers with study packs to distribute to relevant HCPs. The study pack will include an invitation letter (appendix 16), PIS (appendix 17) and an initial expression of interest form (appendix 18). HCPs will be asked to complete the form and return it to a designated secure drop box in the ward that the researcher will collect. The researcher will contact all HCPs demonstrating an

interest in participating through the means of communication they have provided to arrange a suitable date and time for the interview. Written informed consent (appendix 19) will be taken online immediately prior to the commencement of the interview.

Participation in the evaluation interviews will start at the point of consent and end at the end of the interviews. Interviews will be semi-structured and facilitated by a separate topic guide for patients (appendix 20) and HCPs (appendix 21). Duration is expected to last between 20 and 40 minutes. Linked anonymised information will be held in locked filing cabinets in locked rooms and/or on a password-protected database to which only the main investigators and delegated researcher will have access.

6. STATISTICAL PLAN

6.1 Phase 1: Data audit

Once all available data are extracted and collated, primary cumulative frequency analyses of the data pool will be performed to determine the wards (excluding intensive care or high dependency units) with the highest incidence of hypoglycaemia and hyperglycemia. Hypoglycaemia will be defined as a blood glucose reading below 4 mmol/L(72mg/dL) and hyperglycaemia will be defined as a blood glucose reading over 12 mmol/L(216mg/dL) in accordance with hospital guidelines on the acceptable range for blood glucose levels.

6.2 Phase 2, Part A: Pilot study - Preliminary work

The qualitative feedback data collected from the preliminary work will be analysed using thematic analysis method to identify themes within the data in the context of Flash Glucose Monitoring use in an inpatient setting. Thematic analysis (25) was developed to facilitate applied policy research. This approach shares many elements of other qualitative analyses, consisting of five key stages: i) familiarisation, ii) identifying a thematic framework; iii) indexing; iv) charting and; v) mapping and interpretation. Index-weighting profiles will be used in the analysis of the EQ5D-5L data.

6.3 Phase 2, Part B: Pilot study – Use of Flash Glucose Monitoring

Descriptive statistical analyses will be used to summarise and interpret the data including mean, median, range, and standard deviation to understand and explore the sample characteristics, glucose ranges and interventions during inpatient stay and (if applicable) following discharge, average LoS. Index-weighting profiles will be used in the analysis of the EQ5D-5L data.

6.4 Phase 2, Part C: Pilot study - Evaluation interviews

As with Phase 2, Part A, the qualitative data collected in the evaluation interviews will be analysed using thematic analysis and use a framework charting approach to aid exploration and interpretation of the themes identified in relation to inpatient diabetes care and Flash Glucose Monitoring use. While no a priori thematic concepts will be held, the process of

analysis will be facilitated by considering how any themes that are identified might be applied to potential care policy design.

7. MONITORING

7.1 Risk assessment

This study is considered to be low risk as the use of interventions requires only subcutaneous application of a glucose sensor device, carrying minimal health risks, the devices are safe and easy for patients to self administer. Low-risk to patients will be further ensured through confidential and anonymous storing of their data, and giving participants the opportunity to express their thoughts and opinions about the service they received without judgment or influence.

Due to the risk of COVID-19 transmission Facemasks will be worn at all times as well as other appropriate PPE. Hand sanitising/washing on entry and exit from Hospital and individual wards will also be undertaken. Researchers will refrain from touching face or other surfaces during and after entry and clothes will be changed and washed on returning home.

Consent forms will be done online for staff and physical copies will be printed straight before entry, handled only with gloves, and filed immediately after consent taken.

All patient researcher contact will be avoided and physical distancing observed. No COVID-positive patients will be recruited. During the need for any dialogue with participants who are inpatients appropriate PPE will be employed.

In accordance with the amended study protocol patients must self-administer the glucose sensor under supervision from the researcher and interviews will be conducted using online video software or by telephone.

7.2 Monitoring at study centre

All consent forms and study documentation will be checked by the designated researchers.

8. REGULATORY ISSUES

8.1 Clinical Trials Registration

N/A

8.2 Ethics Approval

NHS ethical approval will be sought from a NHS research ethics committee (REC) with NHS Highland as the lead NHS site and site specific approval requested for Altnagelvin Hospital, Derry-Londonderry using the Integrated Research Application System (IRAS). A separate equivalent application will be made in parallel to the ethics committee for Letterkenny University Hospital, Letterkenny, Co Donegal to approve the research in this site.

8.3 Consent

8.3.1 Phase 1: Retrospective data audit

No patient consent will be sought for the retrospective anonymised data audit as this will not involve active participation; however organisational consent has already been given per study site.

8.3.2 Phase 2, Part A: Pilot study - Preliminary work

Consent to enter the intervention study preliminary work will be sought from each participant at the time of recruitment, only after a full explanation has been given, PIS offered and time allowed for consideration. Participants will be given the opportunity to ask any questions regarding the study (appendices 3 and 6).

8.3.3 Phase 2, Part B: Pilot study – Use of Flash Glucose Monitoring

Consent to enter this part of the pilot study will be sought from each participant only after a full explanation has been given, PIS offered and time allowed for consideration. Participants will be given the opportunity to ask any questions regarding the study. Signed participant consent will be obtained immediately before entering the intervention study (appendix 10). Consent will include an optional point to have contact details stored for the purpose of contacting them following their discharge from hospital to participate in the evaluation interview study (Part C).

8.3.4 Phase 2, Part C: Pilot study - Evaluation interviews

For patient participants who have agreed to being contacted following their involvement in Part B, a separate written informed consent procedure will be conducted immediately before commencing the evaluation interviews (appendix 14). For healthcare professionals involved in the study who have provided an initial expression of interest to participate in the interviews, a consent procedure will be conducted immediately prior to the interviews commencing (appendix 19).

The right of the participant to refuse to participate without giving reasons will be respected. All participants are free to withdraw at any time from the study without giving reasons and without prejudicing further treatment.

8.4 Confidentiality

No patient identifiable data will be recorded for the retrospective data audit (phase 1) since the cumulative frequencies of hypoglycaemia and hyperglycaemia are all that will be required for the analyses.

Participant identifiable data will be required for the registration process for the intervention preliminary work, pilot study and the evaluation interviews (phase 2). Once enrolled in the study, the delegated researcher will preserve the confidentiality of participants taking part by application of individual study code numbers for use throughout the study.

8.5 Sponsor

The University of the Highlands and Islands will act as sponsor for the study. Details can be found on page 2 of this protocol. NHS Highland will co-sponsor the study.

8.6 Funding

This project, as part of the wider project entitled Centre for Personalised Medicine: Clinical Decision Making and Patient Safety (CPM), is funded by the Interreg European Regional Development Fund and Special EU Programmes Body.

8.7 Audits and Inspections

The study may be subject to inspection and audit by Ulster University/University of the Highlands and Islands, and by Altnagelvin Hospital or NHS Highland under their remit as co-sponsor, and other regulatory bodies to ensure adherence to Good Clinical Practice (GCP).

9. STUDY MANAGEMENT

A study management group (SMG) consisting of the principle investigators and all co-investigators will be appointed and will be responsible for reviewing and appraising the progress of the study overall. Professor Vivien Coates has overall responsibility of the wider study, whilst the day to day management of the study will be coordinated by a researcher in NHS Highland and a PhD student and research nurse at Altnagelvin Hospital and Letterkenny University Hospital, Co Donegal respectively. All data from the study will be stored securely and only accessed and analysed by the research team. The data will be stored for the duration of the wider study and destroyed after 10 years from the end of funding. Data will be destroyed through the IT services per study site to ensure that the files are appropriately and safely disposed of.

10. PUBLICATION POLICY

All publications and presentations relating to the study will be reviewed and authorised by the SMG. Members of the SMG, where appropriate, will be listed as authors/contributors and will be cited by name.

11. REFERENCES

(1) Diabetes UK. Diabetes Prevalence 2017 (November 2017). 2017; Available at: https://www.diabetes.org.uk/professionals/position-statements-reports/statistics/diabetes-prevalence-2017. Accessed 28 Feb, 2018.
(2) Hex N, Bartlett C, Wright D, Taylor M, Varley D. Estimating the current and future costs of Type 1 and Type 2 diabetes in the UK, including direct health costs and indirect societal and productivity costs. Diabetic Med 2012;29(7):855-862.
(3) Aro S, Kangas T, Reunanen A, Salinto M, Koivisto V. Hospital use among diabetic patients and the general population. Diabetes Care 1994 Nov;17(11):1320-1329.

(4) Bo S, Ciccone G, Grassi G, Gancia R, Rosato R, Merletti F, et al. Patients with type 2 diabetes had higher rates of hospitalization than the general population. J Clin Epidemiol 2004 Nov;57(11):1196-1201.
(5) Comino EJ, Harris MF, Islam MF, Tran DT, Jalaludin B, Jorm L, et al. Impact of diabetes on hospital admission and length of stay among a general population aged 45 year or more: a record linkage study. BMC health services research 2015;15(1):12.
(6) Donnan PT, Leese GP, Morris AD, Diabetes Audit and Research in Tayside, Scotland/Medicine Monitoring Unit Collaboration. Hospitalizations for people with type 1 and type 2 diabetes compared with the nondiabetic population of Tayside, Scotland: a retrospective cohort study of resource use. Diabetes Care 2000 Dec;23(12):1774-1779
(7) Kerr M. Inpatient Care for People with Diabetes: The Economic Case for Change. 2011; Available at: https://www.diabetes.org.uk/resources-s3/2017-10/Inpatient%20Care%20for%20People%20with%20Diabetes%20%20The%20Economic%20Nov%202011_1.pdf?_ga=2.229416030.313368823.1508765802-1498355072.1474465387. Accessed 04/02, 2018.
(8) Khalid J, Raluy- Callado M, Curtis B, Boye K, Maguire A, Reaney M. Rates and risk of hospitalisation among patients with type 2 diabetes: retrospective cohort study using the UK General Practice Research Database linked to English Hospital Episode Statistics. Int J Clin Pract 2014;68(1):40-48.
(9) Rosenthal MJ, Fajardo M, Gilmore S, Morley JE, Naliboff BD. Hospitalization and mortality of diabetes in older adults. A 3-year prospective study. Diabetes Care 1998 Feb;21(2):231-235.
(10) Whitston M, Chung S, Henderson J, Young B. What can be learned about the impact of diabetes on hospital admissions from routinely recorded data? Diabetic Med 2012;29(9):1199-1205.
(11) Department of Health. National Service Framework for Diabetes. 2001.
(12) The Scottish Government. Diabetes Improvment Plan. 2014.
(13) Govan L, Wu O, Briggs A, Colhoun H, McKnight J, Morris A, et al. Inpatient costs for people with type 1 and type 2 diabetes in Scotland: a study from the Scottish Diabetes Research Network Epidemiology Group. Diabetologia 2011;54(8):2000-2008.
(14) NHS. The National Diabetes Inpatient Audit (NaDIA) - 2016 - Full Report. 2017; Available at: file:///C:/Users/EO02NP/Downloads/nati-diab-inp-audi-16-rep%20(2).pdf;. Accessed March 23.
(15) Turchin A, Matheny ME, Shubina M, Scanlon JV, Greenwood B, Pendergrass ML. Hypoglycemia and clinical outcomes in patients with diabetes hospitalized in the general ward. Diabetes Care 2009 Jul;32(7):1153-1157.
(16) McEwan P, Thorsted BL, Wolden M, Jacobsen J, Evans M. Healthcare resource implications of hypoglycemia-related hospital admissions and inpatient hypoglycemia: retrospective record-linked cohort studies in England. BMJ Open Diabetes Research and Care 2015;3(1):e000057.
(17) Umpierrez GE, Isaacs SD, Bazargan N, You X, Thaler LM, Kitabchi AE. Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. The Journal of Clinical Endocrinology & Metabolism 2002;87(3):978-982.
(18) Gofir A, Mulyono B, Sutarni S. Hyperglycemia as a prognosis predictor of length of stay and functional outcomes in patients with acute ischemic stroke. Int J Neurosci 2017;127(10):923-929.

(19) Baker H, Stephenson S, Sumner J, Hammersley M. Managing hypoglycaemia in hospital. Journal of Diabetes Nursing 2007;11(3):108.
(20) Clement S, Braithwaite SS, Magee MF, Ahmann A, Smith EP, Schafer RG, Hirsch IB (2004) Management of diabetes and hyperglycemia in hospitals. Diabetes Care 27:553–591
(21) Giangola J, Olohan K, Longo J, Goldstein JM, Gross PA (2008) Barriers to hyperglycaemic control in hospitalised patients: a descriptive epidemiologic study. Endocr Pract 14(7):813–819
(22) Cook CB, McNaughton DA, Braddy CM, Jameson KA, Roust LR, Smith SA, Roberts DL, Thomas SL, Hull BP (2007) Management of inpatient hyperglycemia: assessing perceptions and barriers to care among resident physicians. Endocr Pract 13(2): 117–124
(23) Cook CB, Jameson KA, Hartsell ZC, Boyle ME, Leonhardi BJ, Farquhar-Snow M, Beer KA (2008) Beliefs about hospital diabetes and perceived barriers to glucose management among inpatient midlevel practitioners. Diabetes Educator 34(1):75–83
(24) Ross, A. J., Anderson, J. E., Kodate, N., Thompson, K., Cox, A., & Malik, R. (2014). Inpatient diabetes care: complexity, resilience and quality of care. Cognition, technology & work, 16(1), 91-102.
(25) Ritchie, J. & Spencer, L. Qualitative data analysis for applied policy research. Analysing Qualitative Data London: Routledge; 1994. p. 173-194.