Imperial College London

Type 2 Diabetes Exemplar (T2DEx): A remote care service for North West London

Study Management Group

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This protocol describes the *Type 2 Diabetes Exemplar (T2DEx): A remote care service for North West London* study and provides information about procedures for entering participants. Every care was taken in its drafting, but corrections or amendments may be necessary. These will be circulated to investigators in the study. Problems relating to this study should be referred, in the first instance, to the research team's project manager, Dr Jack Halligan.

Sponsor

Imperial College London is the main research Sponsor for this study. For further information regarding the sponsorship conditions, please contact the Head of Research Governance and Integrity.

Funder

Imperial College London (ICL) are funded through the Discover-NOW Health Data Research Hub, of which Imperial College Health Partners (ICHP) are lead partner and Imperial College London are an academic partner. Discover-NOW is funded by a grant from the UK Research and Innovation (UKRI) Industrial Strategy Challenge Fund (ISCF). Partial additional funding for the study (i.e., additional to the Hub grant funding) has been provided directly by ICHP.

The remote care service – 'Fresh Start' – being assessed by this research study has been designed and implemented as a collaboration between Discover-NOW partners, including ICL, ICHP, AstraZeneca, Huma and Collaboration Of North West London Clinical Commissioning Groups (NWL CCGs).

Extraction, cleaning and de-identification of the study dataset will be completed by ICHP and is funded by AstraZeneca. Integration of data from Huma into NWL's Whole of System Integrated Care (WSIC) database will be provided by InHealthcare as part of a pre-existing contract between the NWL CCGs Innovation Team and InHealthcare.

AstraZeneca have funded the pathway service design within their in-kind contributions to Discover-NOW. Huma are funding the remote monitoring platform (patient app and clinician dashboard) for 12 months, the associated deployments to sites, and individual licenses within their in-kind contribution to Discover-NOW. Discover-NOW are funding input from the NWL STP Diabetes Digital Transformation Lead (William Gilmour) and Clinical Director for Diabetes for NWL CCGs (Dr Tony Willis).

NHSX are funding the remote care innovation implementation that underpins the study and the procurement of devices and consumables from Huma. NHSX will also fund a clinical implementation support role to help new sites implement Fresh Start, including the provision of training for participating staff.

This study will adhere to the principles outlined in the UK Policy Framework for Health and Social Care Research It will be conducted in compliance with the protocol, Data Protection Act 2018 and General Data Protection Regulations (Europe) and other regulatory requirements as appropriate.

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1. Introduction

1.1 Background

Type 2 diabetes is a cardiometabolic disorder with associated vascular disease associated with half a decade of life years lost[1] or a decade and half among those with atherosclerotic cardiovascular disease (ASCVD).[2] Despite significant improvements in outcomes, mortality and morbidity remains higher among those with type 2 diabetes vs those without. A global approach starting with lifestyle and pharmacotherapy to address multiple risk factors is required to reduce the burden of disease. Observational data supports the notion that control of multiple risk factors attenuates the residual risk especially among younger subjects.[3] [4]

Broadly, complications of type 2 diabetes can be broken down into those that affect the macrovascular system (myocardial infarction, stroke, peripheral arterial disease) and those that effect the microvascular system (chronic kidney disease, retinopathy, neuropathy). The former requires control of multiple factors that affect cardiovascular disease such as lipid lowering, blood pressure control, and smoking cessation (among others). The latter is more closely related to long-term glycaemic control in particular, but potentially other factors such as BP control and use of specific therapies aimed at end organ preservation (e.g., RAS blockade, SGLT2 inhibitors).

Practice nurses (PNs) in primary care spend significant time in consultations with patients about managing their type 2 diabetes. Group consultations have been identified as an opportunity to improve outcomes and access, whilst engaging patients in a different way that offers the potential to provide a more social and less medical model of planned care.[5] Experience in other parts of England suggested that it could also improve staff experience by reducing repetition and creating more time to care and support patients.[5] Group consultations also have a strong evidence base of impact in type 2 diabetes, with seven randomised controlled trials showing improvements in HbA1c compared to one-to-one care.[6]

1.2 Study Rationale

As the prevalence of Type 2 Diabetes Mellitus (T2DM) grows the burden on healthcare is increasing in the form of additional consultations, hospital outpatient visits, death and disability. T2DM represents a large part of the disease and cost burden of healthcare in North West London (NWL) to the value of £600m annually. Patients with T2DM constitute over 40% of all NWL admissions, with complications of type 2 diabetes representing a significant factor in the morbidity and cost associated with this chronic disease. To this end, there is an urgent need for healthcare professionals to provide the same or better care without increasing healthcare expenditure. Digital interventions/ healthcare solutions may provide an opportunity to achieve these goals.

The Type 2 Diabetes Exemplar Programme has designed the Fresh Start service for use in primary care to demonstrate how real-world data and technology can improve health outcomes for T2DM patients. Fresh Start has been designed by the Discover-NOW Health Data Research Hub in a cross-industry collaboration between North West London CCGs, NHSX, AstraZeneca, Imperial College Health Partners and Huma. Fresh Start is offered to patients at high risk of developing complications from T2DM and combines video group consultations, a remote monitoring solution, and educational content.

Fresh Start seeks to support population stratification and strengthen population health management by providing better-tailored services and proactive interventions, particularly among population groups more at risk of the adverse impacts of COVID-19. Mortality risk from COVID-19 is approximately 25% higher in patients with T2DM and shielding has resulted in reduced primary care appointments for patients with T2DM. This has created an immediate need for primary care to adapt and provide remote care pathways to patients. Digital-first remote pathways could make care more accessible while finding time and cost efficiencies. By combining remote monitoring and video group consultations, we can inform the patient-clinician conversation making remote care in group settings safer, efficient and more personalised.

It is our opinion that generating credible evidence for digital health solutions remains an industry-wide challenge, hindering widespread adoption, and that traditional approaches present limitations for researchers to create evidence. Evaluation of digital health solutions has also been identified as requiring improvement and has been cited as a major obstacle for wider adoption.[7] [8] This study will use pragmatic methods to evaluate Fresh Start, with a view to support successful adoption of Fresh Start in primary care practices in the UK.

2. Study aims and objectives

The aim of T2DEx is to assess the feasibility, usability, acceptability, cost-effectiveness and safety of a remote care service (“Fresh Start”) in primary care for people with ‘high risk’ or ‘very high risk’ Type 2 Diabetes in North West London.

The study will assess patient and clinician experience metrics, the feasibility of implementation including uptake and patient/physician acceptability for data collection procedures, and the resources needed to manage and implement Fresh Start . The study will also assess the impact of Fresh Start on clinical outcome measures (e.g., HbA1c, risk factor control, time at goal).

The results of this may support continuation of Fresh Start. A follow-up study with a larger number of participants and longer duration would be required to assess a statistically significant impact on secondary objectives.

Primary objectives:

1. To assess the **feasibility of uptake** amongst people with 'high risk' or 'very high risk' type 2 diabetes.
2. To assess the **usability** of Fresh Start amongst **people with 'high risk' or 'very high risk' type 2 diabetes**.
3. To assess the **usability** of Fresh Start amongst **HCPs**.
4. To assess the **acceptability** of Fresh Start amongst **people with 'high risk' or 'very high risk' type 2 diabetes**.
5. To assess the **acceptability** of Fresh Start amongst **HCPs**.
6. To assess the **cost-effectiveness** of delivering Fresh Start.

Secondary objectives (**EXPLORATORY** only and will not be demonstrated to a level of statistical significance):

1. To assess the **safety** of **Fresh Start**.
2. To assess the **impact of Fresh Start on clinical outcomes**.

3. Study design and methods

3.1 Design

An experimental feasibility study with a pre-test/post-test design using a matched control.

3.2 Study population

In response to the public health emergency posed by COVID-19, NHS England and NHS Improvement (London) are supporting clinicians to identify patients who are at the higher risk of adverse outcomes (based on available evidence) and prioritise the allocation of existing resources to these patients.

The study population therefore includes people with 'high risk' and 'very high risk' type 2 diabetes (see 'Inclusion criteria'), as defined by guidance for primary care from NHS England and NHS Improvement (London), entitled *Primary Care: Identification, risk stratification and interventions for patients at an increased risk*.

3.3 Sample size

The study will seek to collect and analyse data from a minimum of 300 participants to Fresh Start. With an estimated enrolment rate of 20%, 1,500 eligible patients will need to be identified and we will be able to estimate this rate within a 95% confidence interval of +/-3%, accounting for variance inflation due to clustering with the assumption of 10 GP practices and Intraclass Correlation Coefficient (ICC) of 0.05.

The study's secondary objectives are exploratory only and will not be demonstrated to a level of statistical significance in this study.

3.4 The Fresh Start service

This 12-week service has been designed to optimise patient care based on pro-active identification and prioritisation of clinical risk based on health, socioeconomic and demographic factors. `

Fresh Start seeks to assess whether alternative methods of healthcare delivery for people with high-risk or very high risk T2DM are safe, scalable, and cost-effective. Fresh Start has been co-designed with people with type 2 diabetes, healthcare professionals (GPs, specialists, nurses, podiatrists, dietitians) and commissioners from Collaboration Of North West London Clinical Commissioning Groups (NWL CCGs).

The North West London Diabetes Clinical Reference Group (CRG) reviewed and provided feedback on Fresh Start's design. The CRG comprised of three GPs, three endocrinologists, three vascular surgeons, two specialist podiatrists, two diabetes nurse specialists, one district nursing lead, one infection control lead, two commissioners/quality improvement leads and one psychiatrist.

Fresh Start will support delivery of the new Integrated Care System (ICS) and Primary Care Network (PCN) models currently being rolled-out across the NHS.
The Fresh Start service and SOPs have been specifically designed to enable a new model of care as part of the NHS Long Term Plan.

Individual primary care practices play a central role in service delivery. GPs, nursing staff and administrative staff from primary care practices have advised how best to adopt Fresh Start into the primary care clinical workflow and have helped to develop standard operating procedure (SOP) documentation to support participating practices.

The 12-week service comprises the following elements (overview provided at Appendix 1):

I. **Proactive risk stratification.** An electronic patient record (EPR) based risk stratification search is run at primary care practice level to identify T2DM patients at high risk of cardiovascular complications who may benefit from and be eligible for Fresh Start.

II. **Video Group Consultations (VGC)**. Each patient is invited to attend a total of three VGCs during the 12-weeks lasting approximately one hour and 15 minutes each. Each session is facilitated by a Practice Nurse (PN) and consists of 6-10 people with T2DM. The self-reported Huma app (see below) and patient EPR data are used to populate a "Discussion Dashboard" which is used in each VGC to facilitate discussion. During the first VGC session, patient goals are discussed and adjusted in a group setting with topics relevant to their condition covered by the PN. Between each VGC session, patients spend time working on their goals and continuing to enter self-reported metrics into the Huma app. During the second and third VGC sessions, each patient is discussed, along with their performance against agreed goals. The PN also uses pre-prepared content to discuss topics relevant to managing type 2 diabetes (e.g., staying motivated, low carb diets).

III. **Fresh Start educational email campaigns**. Each patient is signed up to a series of educational email campaigns to complement the VGC sessions and provide broader

education around type 2 diabetes management. Patients receive two emails per week during the 12-week service on a variety of topics.

IV. **Clinical protocols.** A series of best-practice CRG approved clinical protocols are in place to be triggered based on thresholds and values captured via the Huma app and as part of the VGC sessions. Protocol examples include medications review, foot care, renal, and mental health.

V. **Digital remote patient monitoring** using blood pressure and blood sugar devices in combination with a smartphone application ('the Huma app'). Participants are provided with home monitoring devices and download the Huma app. Participants are shown how to use the devices, how to input measurements into a smart phone and how to set personal goals. Data recorded via the Huma app is self-reported and includes activity data, diet information, blood glucose measurements, blood pressure measurements, weight, and the Diabetes Distress Scale (a self-reported questionnaire used to measure distress related to living with diabetes). A Health Care Assistant (HCA) observes these data via a Huma clinician dashboard that complements the Huma app. The HCA presents these data in combination with relevant EPR data to the PN for review ahead of each VGC appointment.

VI. **One-to-one routine patient review**. At the end of the 12-weeks participants are invited to a one-to-one review session with their primary care practice. The patient's progress over the 12-week service is reviewed and a decision is made whether to discharge patient, repeat them for another 12 weeks on Fresh Start, or escalate them to MDT.

3.5 Matched control group

A number of the study's objectives and associated outcome measures will require a control group for comparison. These objectives include:

- To assess the cost-effectiveness of delivering Fresh Start;
- To assess the safety of Fresh Start; and
- To assess the impact of Fresh Start on clinical outcomes.

This study will create a matched control group using propensity score matching (PSM),[9] a quasi-experimental method used to mimic the characteristics of a randomised control trial that has been shown to reduce biases.[10] PSM uses statistical techniques to construct an artificial control group by matching each study participant with a non-treated participant of similar characteristics. PSM computes the probability that a person would enrol in a program based on pre-defined characteristics, giving a 'propensity score'.

The propensity score for the study will be based on the following characteristics:

- Age
- Gender
- Risk category (see inclusion criteria)
- Geographical proximity
- Social deprivation index (by practice)

Each individual in the matched control group will be identified within one month of the index case.

The matched control group will be identified using NWL's Whole of Systems Integrated Care (WSIC) database. WSIC links provider data from four acute, two mental health and two community Trusts across eight CCGs, social care data from eight boroughs and 380 GP practices to generate an integrated care record.

3.6 Outcome measures

Primary objective	Outcome measure	Where is it recorded?	How often is it measured?	Compare with control?
To assess the **feasibility of uptake** amongst people with 'high risk' or 'very high risk' **type 2 diabetes**.	Patients offered Fresh Start vs. **enrolled**	EPR	Once	No
	Patients enrolled vs. **collecting** remote monitoring devices	EPR	Once	No
	Patients enrolled vs. downloading **Huma app**	Huma	Once	No
To assess the **usability** of Fresh Start amongst **people** with 'high risk' or 'very high risk' **type 2 diabetes**.	Number of **VGCs** attended	EPR	Every 4 weeks	No
	Number of **Fresh Start emails** opened	KD	Twice weekly	No
	Number of **blood glucose** measurements recorded	Huma	Daily	No
	Number of **blood pressure** measurements recorded	Huma	Daily	No
	Number of **weight** measurements recorded	Huma	Monthly	No
	Number of **Diabetes Distress Scale** measurements recorded	Huma	Monthly	No
To assess the **usability** of Fresh Start amongst **HCPs**.	System Usability Scale (**SUS**[11]) questionnaire	Online survey	Once (at 12 weeks)	No
To assess the **acceptability** of Fresh Start amongst **people** with 'high risk' or 'very high risk' **type 2 diabetes**.	**Interviews** with patients (x10)	Interview	At 12 weeks	No

To assess the **acceptability** of Fresh Start amongst **HCPs.**	**Interviews** with healthcare professionals (HCPs, x10)	Interview	After intervention period	No
To assess the **cost-effectiveness** of delivering Fresh Start.	**Number of primary care appointments** per patient	EPR	Data extracted from EPR	Yes
	Cost per appointment per patient	EPR	Data extracted from EPR	Yes
	Cost of **equipment** per patient	Huma	N/A	No
Secondary objective (Exploratory)*	**Outcome measure**			
To assess the **safety** of Fresh Start.	Number of **deaths**	EPR	Data extracted from EPR	Yes
	Number of **emergency department** admissions	WSIC	Data extracted from WSIC	Yes
	Number of **hospital** admissions	WSIC	Data extracted from WSIC	Yes
To assess the impact of Fresh Start on **clinical outcomes**.	**HbA1c**	EPR	Baseline, 12 weeks, 6 months	Yes
	Lipids, incl. LDL and non-HDL cholesterol	EPR	Baseline, 12 weeks, 6 months	Yes
	Weight	EPR	Baseline, 12 weeks, 6 months	Yes
	Diabetes Distress Scale score (**DDS**[12])	Huma	Monthly during service (and at 6 month follow-up appt.)	No
	Blood glucose time-in-range	Huma	Daily	Yes
	Systolic blood pressure (**SBP**)	Huma	Daily	Yes

**Note*: *Secondary objectives are exploratory only and will not be demonstrated to a level of statistical significance.*

3.7 Study procedures

This section provides detail on the procedures for delivering Fresh Start and data collection. Standard operating procedure (SOP) documents that go into greater detail have been developed for staff at primary care practices who will be delivering Fresh Start. These include SOPs for practice nurses (PNs), healthcare assistants (HCAs), and administrative staff. A training document has also been developed for participating primary care practices.

The below are the main steps involved to deliver Fresh Start. A high-level overview of study procedures is also provided at Appendix 2.

- Patient search
- Outreach, qualification and booking
- Onboarding
- Fresh Start educational emails
- Huma app, devices and clinician dashboard
- Video group consultations (VGCs)
- Discharge, repeat, or MDT escalation
- Interviews with patients and healthcare professionals
- Online System Usability Scale (SUS) survey

Patient search

EPR searches have been constructed based on the inclusion criteria for this study (see Section 4.3). This search will be run by administrative staff at participating primary care practices. Patients will then be invited to participate in the program.

Staff actions at primary care practice:

- Open practice management system and run report search
- Sense-check list of patients against risk stratification criteria
- Mark exported patients to receive outreach invitation to service

Outreach, qualification and booking

Outreach will involve a 10-minute initial conversation with patients identified in the search to speak to them about how Fresh Start may help them, find out if they are able to participate, and, if interested, book them onto the required appointments to start on Fresh Start. The participant must be able to download the Huma App to their smartphone or tablet.

Staff actions at primary care practice:

- Phone patients on the outreach list
- Qualify if patients are eligible for service
- Organise device collection from the practice
- Book patient onto onboarding appointment
- Keep track of the uptake of Fresh Start
- Book patient for **baseline measurements**, which will include:
    - HbA1c
    - Lipid panel
    - Weight

Onboarding

A 30-45 minute onboarding appointment will be completed by a practice nurse (PN), healthcare assistant (HCA) or a member of the administrative staff from the participant's primary care practice (at the discretion of the participating practice). The onboarding appointment can be completed via Microsoft Teams or face-to-face (at the discretion of the participant/primary care practice). The onboarding appointment will be used to explain the Huma app, video group consultations (VGCs), and the educational emails from Fresh Start. An onboarding guide and associated script has been developed to support the onboarding process.

Staff actions at primary care practice:

- Run one-to-one appointment via Microsoft Teams or a phone call
- Explain how to download and use Huma app & devices
- Book onto VGCs (x3)
- Sign up for Fresh Start emails

Fresh Start educational emails
Patients will be instructed to sign up for Fresh Start educational emails during the onboarding appointment. These emails will be twice-weekly and will ensure patients get supportive information and education on how to improve their type 2 diabetes.

Staff actions at primary care practice:

- Sign patients up to first two Fresh Start emails in onboarding call
- Sign patients up to full Fresh Start campaign in first VGC

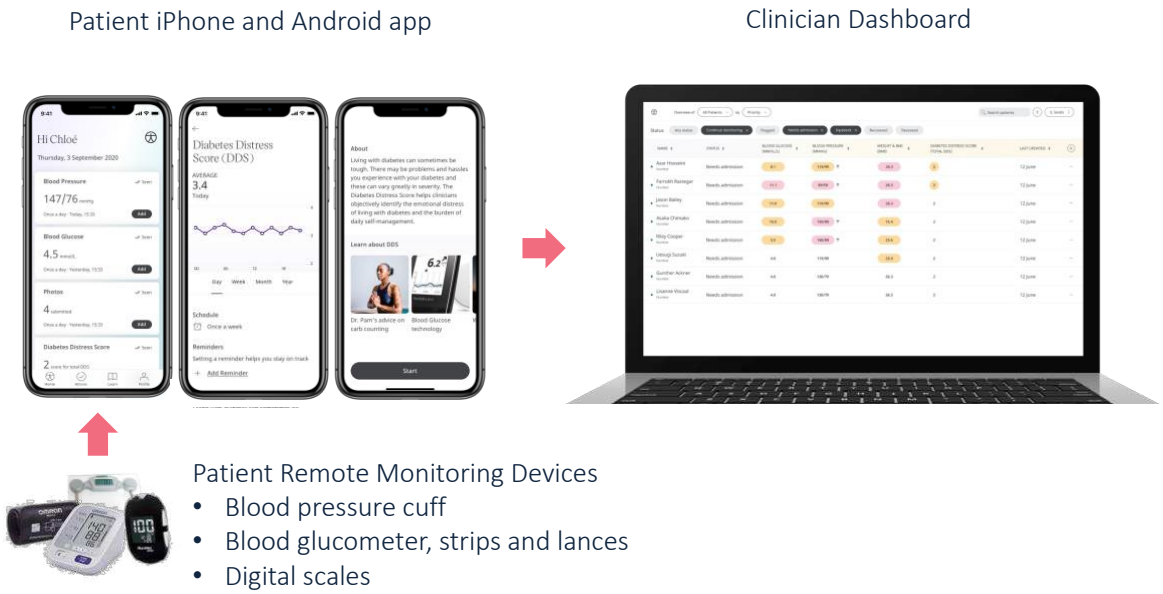
Huma app, devices and Clinician Dashboard
The Huma app will enable particiapnts to report their own clinical metrics, feelings, goals and behaviour activities (e.g. photos of food). At the onboarding appointment, participants will be instructed how to download the Huma app from the App Store (for iPhone users) or from the Google Play Store (for all other smartphones). Participants will also be shown how to use their blood pressure cuff and glucometer device, walked through the Diabetes Distress Scale questionnaire, and shown how to set goals and actions in the Huma app.

Participants will be asked to enter results from their first measurements into the Huma app. The HCP who is running the onboarding appointment will check whether results have appeared on the Huma clinician dashboard. If data has not appeared HCPs are advised to contact Huma at support@huma.com.

Huma will also provide a "Clinician Dashboard" to review patient reported data to inform care decisions. The Huma Clinician Dashboard will be used to monitor the blood pressure and blood glucose measurements of participants as they are entered into the Huma app. A HCA at each practice will review the Huma clinician dashboard and escalate any urgent readings to the GP. Data from the dashboard will be provided to PNs in advance of VGCs and will be used to trigger non-urgent care protocols before and after VGC sessions.

Staff actions at primary care practice:

- Review Huma Clinician Dashboard daily
- Escalate to GPs when there has been an urgent reading



Video group consultations (VGCs)

VGCs will be booked and the process for VGCs explained during onboarding. Participants will be booked onto their first VGC approximately one week from the date of the onboarding session, with the second and third booked at four week intervals. Reminder emails containing the Microsoft Teams link to join the session will also be set up during this session. Each VGC will last for 1 hour and 15 minutes in total.

Staff actions at primary care practice **before each VGC**:

- Open Huma Clinician Dashboard patient template side-by-side and manually port patient-reported data from the Huma app into the EPR as follows for patients due to attend VGC session
    - 1 x latest blood pressure reading
    - 1 x latest blood glucose

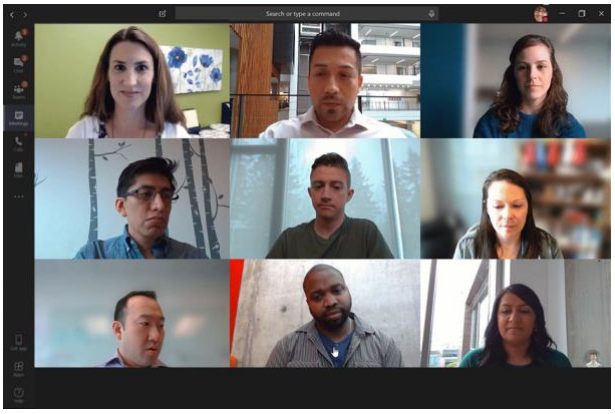
    - 1 x latest Diabetes Distress Score
    - 1 x latest weight (BMI automatically calculated)
    - Average daily step count for the last week (total for the week / 7)
- Open VGC Discussion Board slide and populate using EPR data
    - Blood pressure – latest reading
    - Blood glucose – latest reading
    - DDS – latest reading
    - BMI – latest reading
    - Average daily step count for the last week (total for the week / 7)
- Review food pictures in Huma dashboard
    - Decide whether to discuss food pictures for that patient on VGC session

Staff actions at primary care practice **during each VGC**:

- Set-up Teams meeting and troubleshoot potential problems with participants (15mins before session start time)
- Take consent
- Share link for Fresh Start emails
- Introductions and theme (video played – 10/15 slides talked to)
- Answer questions in the chat
- Review VGC Discussion Board (see Appendix 3 for example)
    - Speak with each patient one-by-one
    - Set actions for each person

Staff actions at primary care practice **after each VGC**:

- Review VGC Discussion Board and notes from VGC session
- Discuss each patient and possible clinical protocols to apply (e.g. medication, footcare, mental health, renal etc.)
- Make changes to care plan in practice management system
- Refer or book one-to-one appointments with patients (as required)



Microsoft Teams

3 x 1h15m sessions

Huma app data is used to inform and structure conversations with patients

- 6-10 patients
- 1 facilitator
- 1 clinician

Discharge, Repeat or MDT Escalation

At 12 weeks each participant will be formally reviewed and decisions can be made for their future care-plan.

Staff actions at primary care practice:

- Review patient's progress
- Decide whether to discharge patient, repeat them for another 12 weeks on Fresh Start, or escalate them to MDT
- Complete **12-week measurements**, including:
  - HbA1c
  - Lipid panel
  - Weight

Interviews with patients and HCPs.
After the intervention period, interviews will be conducted with 10 people with type 2 diabetes who have participated in Fresh Start and with 10 healthcare professionals from participating primary care practices who have delivered Fresh Start.

Online System Usability Scale (SUS) survey
After the intervention period, the SUS will be distributed via email to all healthcare professionals at participating primary care practices. The SUS is a reliable tool for measuring the usability of a system or service. It consists of a 10-item questionnaire with five response options via a Likert scale, ranging from 'Strongly agree' to 'Strongly disagree'.

3.8 Training

The aim of the T2DEx training is to equip clinicians and practice staff with sufficient understanding of Fresh Start's objectives and operations to deliver it autonomously at their respective sites. The training will be divided **into three sessions lasting approximately 1.5 hours each**. These sessions will be led by a member of the ICHP team or a clinical implementation role funded through NHSX.

Training sessions will be run via Microsoft Teams using training slide decks that has been created by ICHP. The slide decks form part of the virtual resource pack hosted in Teams, which includes all materials required for Fresh Start delivery. The trainer will walk the attendees through the slide deck, allowing time for questions during the session and at the end. Attendees will receive a feedback form at the end of each session to record their feedback on the training. After each session the trainer will share a copy of the deck with all attendees and invite the attendees to send any questions.

- **The first session** will provide an introduction to the Fresh Start objectives and an overview of all the Fresh Start components. Staff tasked with delivering Fresh Start should attend the full session. This will likely include PNs (practice nurses), healthcare assistants (HCAs), and administrative staff. General practitioners (GPs) or advanced nurse practitioners (ANPs) involved with running the VGCs should also attend the full session. It is recommended that other staff attend the first 15 minutes of this session if they will assume responsibility for any Fresh Start components when their colleagues are absent or on annual leave. At the end of the first session, attendees will be shown the virtual resource pack in Teams. The aim is to show the attendees a summary of the resource pack materials and the location of the materials they will require for their role in Fresh Start. All attendees should be given access to

the resource pack to review and the opportunity to contact the training team with questions.

- **The second session** will cover the search, outreach, qualification and booking, onboarding and Huma Clinician Dashboard monitoring components of Fresh Start . Staff responsible for these components should attend the full session. This will likely include HCAs and administrative staff. A representative from the Huma Customer Success team will join the session to demonstrate the Huma sign-up process and answer questions on the application and dashboard functionality. At the end of the second session attendees will be shown the resource pack folders relevant to the Fresh Start components covered in the session. All attendees should be given access to the demo versions of the Huma App and the Huma Clinician Dashboard to test in their own time. Attendees may have questions about the app and dashboard, which might require an additional session with Huma. It is recommended that short role-play sessions on onboarding and Clinician Dashboard monitoring are held before Fresh Start is formally launched.

- **The third session** will cover the VGC elements of Fresh Start; before, during and after. Staff responsible for these components should attend the full session. This will likely include HCAs, administrative staff, PNs, GPs or ANPs. A clinician familiar with the VGC content can join the session to deliver the 'during' section. At the end of the second session attendees will be shown the resource pack folders relevant to the Fresh Start components covered in the session. It is recommended that staff involved with delivering VGC session run a practice session to test Microsoft Teams and the content and structure of the session.

3.9 Follow-up

Patient's will be assessed at follow-up appointment with their primary care practice at month 6 (i.e., 3 months after completing the programme). Outcome measures recorded at this appointment will include:

- HbA1c
- Blood pressure
- Blood glucose
- Lipids
- Diabetes Distress Scale (DDS)

3.10 Study timeline

The below table gives a high-level overview of the study timeline.

Month	1	2	3	4	5	6	7	8	9
Recruit GP practices and train clinicians									
Recruit participants									
Deliver the intervention									

Follow-up period									
Interviews with patients and HCPs									
Analysis and write-up									

3.11 Data analysis

The research team will not have access to any personal or identifiable patient data as part of the project. Data will be de-identified before being transferred to WSIC's de-identified data (DID) environment and made available to approved researchers. Any data extracted from the secure environment after analysis by the research team will be at an aggregate level only.

All outcomes will be reported using descriptive statistics with tables and graphical presentations of findings. Continuous variables will be presented as means and standard deviations if normally distributed, and as medians and inter-quartile ranges for skewed data, whilst categorical variables will be presented as frequencies and percentages.

To assess the pre-test/post-test change on clinical outcomes the appropriate generalized mixed model approach will be used to account for repeated measurements and clustering of GP practices and including important covariates in the model.

To create a matched control group from NWL's WSIC database, a 1:1 propensity score matching (PSM) analysis will be performed using age, gender, risk category, geographical proximity and social deprivation index as matching variables. R statistical software will be used for estimating PS by logistic regression and for balance and sensitivity checks.

Comparisons with the control group for clinical outcomes will be exploratory and differences with 95% CI will be reported using the appropriate generalized mixed model.

Interviews conducted with participants and healthcare professionals will be analysed using NVivo, where responses will undergo thematic analysis using an inductive approach to derive key themes.

3.12 Data privacy and security

The research team will not have access to any personal or identifiable patient data as part of the project. Data will be de-identified before being transferred to WSIC's de-identified data (DID) environment and made available to approved researchers. Any data extracted from the secure environment after analysis by the research team will be at an aggregate level only.

A single WSIC analyst who is responsible for flagging patients in the matched control group will have access to the personal identifiable data (PID) environment. This WSIC analyst has

a substantive contract with the data controller and is authorised to execute the flagging in the PID.

The WSIC dataset is a PID hosted by UKCloud in a secure cloud-based environment, which is ISO27017 certified. This is an Identifiable data set which supports clinicians and health care professionals to provide joined-up care, decision-support and workflow automation. This information feeds into a wide range of bespoke assets for example clinical facing WSIC dashboards and the Health Information Exchange (HIE) for use by clinicians, and the Care Information Exchange (CIE) and coordinate my care for use by citizens.

Discover Dataset is de-identified dataset hosted in a secure Azure environment and to be hosted by IBM in a new Trusted Research Environment (TRE). This depersonalised data set is for quality improvement planning and research, it is controlled by NWL data controllers, and access to it is mediated by the NWL Data Access Committee. It is accessible via Discover-NOW Health Data Research Hub for Real World Evidence through their data scientists specialists hosted by Imperial College Health Partners (ICHP) and IG committee-approved analysts to conduct research within the safe environment.

Data collected on the Huma platform is hosted in the UK by Google Cloud Platform (GCP) who manage all physical servers, resources and networking hardware to enable all business logic and higher-level services. All communications are secured by TLS. Huma follows NIST approved encryption techniques for encrypting data-at-rest. Huma's cloud provider provides Key Management Services (KMS) for data storage services using an encryption key. Key rotation is performed. Huma practises the concept of least-privileged permissions for services. Huma also conforms to the following accreditations and standards:

- NHS Data Security and Protection Toolkit certification (organisational code: YGMA8)
- ISO13485 Certified Quality Management System with robust Risk Management Plan that includes Data Security & Protection, Business Continuity, Disaster Recovery, & implementation of Corrective & Preventive Actions

4. Recruitment

4.1 Recruitment to Fresh Start

Participants will include patients from participating primary care practices in NWL with ‘high risk’ and ‘very high risk’ of developing complications from T2DM. Risk stratification has been defined by guidance for primary care from NHS England and NHS Improvement (London) entitled *Primary Care: Identification, risk stratification and interventions for patients at an increased risk*. EPR searches have been constructed based on this risk stratification. Selected patients will then be invited to participate in the program, with those who accept being onboarded (see Section 3.7 for more detail).

4.2 Recruitment for interviews – people with type 2 diabetes (x10) and HCPs (x10)

A total of 10 people with type 2 diabetes and 10 HCPs will be recruited to participate in interviews to assess the acceptability of Fresh Start to HCPs. Potential interviewees will be sent an email invitation to take. Those that express an interest in taking part will be emailed a participant information sheet and consent form by a member of the research team. Interviews will be carried out via Microsoft Teams and the duration of each interview will be approximately 45 minutes.

Participants will have a choice on the consent form to allow the researchers to audio-record the interview for the sole purpose of analysing the transcript in NVivo. All recordings will be deleted once transcription has been completed using a service such as PageSix. Alternatively, participants who do not wish to be audio recorded can still take part, the researcher will be responsible for capturing written notes during the session.

Participants in the interviews to assess Fresh Start's acceptability will be remunerated. Public participants (i.e., people with type 2 diabetes) will be paid £30 per hour for this online engagement (£25 per hour for their involvement plus an additional £5 to cover for WiFi/electricity). This is as per latest INVOLVE guidelines on patient and public involvement in research activity. All clinicians will be paid £100 per hour for their involvement.

4.3 Inclusion criteria

- Patients over the age of 18 with the capacity to give consent
- Patients with 'high risk' OR 'very high risk' T2DM as defined by:
- **Very high risk** - **T2DM with existing ASCVD** OR T2DM without ASCVD but with any **3 of the following**:
    - HbA1c >58 mmol/mol
    - SBP >140 mm Hg
    - Non-HDL >3.35 mmol/L or LDL-C >2.5 mmol/L
    - Nephropathy (eGFR <45 ml/min, or Urine ACR >3 mg/mol)
    - Retinopathy
    - Neuropathy (including moderate/high risk feet, previous foot ulceration and erectile dysfunction)
    - Currently smoking
- **High risk** - T2DM without ASCVD but with any **2 of the following**:
    - HbA1c > 58 mmol/mol
    - SBP >140 mm Hg
    - Non-HDL >3.35 mmol/L or LDL-C >2.5 mmol/L
    - Nephropathy: eGFR <45 ml/min or Urine ACR >3 mg/mol
    - Retinopathy

- Neuropathy (including moderate/high risk feet, previous foot ulceration and erectile dysfunction)
- Currently smoking
- Black, Asian and minority ethic (BAME) status

4.4 Exclusion criteria

- Participants too ill to participate in the study (i.e., presence of a life-threatening condition, expected survival less than 3 months, clinically unstable)
- Participants who have previously participated in efforts that have informed the design of this research.
- Participant without access to a smartphone.
- Non-English language (the remote monitoring technology currently does not support additional languages).
- Visual disability (the remote monitoring technology currently does not natively support visual assistance).
- Active severe mental illness (SMI).
- Alcohol / drug abuse.
- Severe frailty (identified via the Electronic Frailty Index – eFI).
- Housebound / living in nursing home.
- Currently on the REWIND Programme (a NWL total diet replacement programme for patients with type 2 diabetes).

4.5 Withdrawal criteria

Subjects may be withdrawn from the study at the discretion of the investigator team due to a safety concern or if judged non-compliant with trial procedures. Reasons for withdrawals and discontinuation of any subject from the protocol will be recorded by the investigator team.

A subject must be withdrawn from treatment if one of the following applies:

- Subject chooses to withdraw from the study (at any time)
- Major violation of the study protocol
- Other circumstances that would endanger the health of the subject if he/she were to continue his/her participation in the trial

5. Adverse events

5.1 Definitions

Adverse Event (AE): any untoward medical occurrence in a patient or clinical study subject.

Serious Adverse Event (SAE): any untoward and unexpected medical occurrence or effect that:

- **Results in death**

- **Is life-threatening** – *refers to an event in which the subject was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe*

- **Requires hospitalisation, or prolongation of existing inpatients' hospitalisation**
- **Results in persistent or significant disability or incapacity**
- **Is a congenital anomaly or birth defect**

Medical judgement should be exercised in deciding whether an AE is serious in other situations. Important AEs that are not immediately life-threatening or do not result in death or hospitalisation but may jeopardise the subject or may require intervention to prevent one of the other outcomes listed in the definition above, should also be considered serious.

5.2 Reporting procedures

All adverse events should be reported. Depending on the nature of the event the reporting procedures below should be followed. Any questions concerning adverse event reporting should be directed to the Chief Investigator in the first instance.

5.2.1 Non serious AEs

All such events, whether expected or not, should be recorded- it should be specified if only some non-serious AEs will be recorded, any reporting should be consistent with the purpose of trial end points.

5.2.2 Serious AEs

An SAE form should be completed and emailed to the Chief Investigator within 24 hours. However, hospitalisations for elective treatment of a pre-existing condition do not need reporting as SAEs.

All SAEs should be reported to the Bromley Research Ethics Committee (bromley.rec@hra.nhs.uk) where in the opinion of the Chief Investigator, the event was:

- 'related', ie resulted from the administration of any of the research procedures; and
- 'unexpected', i.e., an event that is not listed in the protocol as an expected occurrence

Reports of related and unexpected SAEs should be submitted within 15 days of the Chief Investigator becoming aware of the event, using the NRES SAE form for non-IMP studies. The Chief Investigator must also notify the Sponsor of all SAEs.

Local investigators should report any SAEs as required by their Local Research Ethics Committee, Sponsor and/or Research & Development Office.

Contact details for reporting SAEs
RGIT@imperial.ac.uk
CI email (and contact details below)
Please send SAE forms to: k.ray@imperial.ac.uk and Cc j.halligan@imperial.ac.uk
Tel: +447742161980 (Mon to Fri 09.00 – 17.00)

6. Regulatory issues

6.1 Ethics approval

The Principal Investigator has obtained approval from the Health Research Authority via the Bromley Research Ethics Committee. The study will be conducted in accordance with the recommendations for physicians involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions.

6.2 Consent

Consent to enter the study will be sought from each participant only after a full explanation has been given, a patient information sheet offered, and time allowed for consideration. Signed participant consent will be obtained. The right of the participant to refuse to participate without giving reasons will be respected. All participants are free to withdraw at any time.

6.3 Confidentiality

The Principal Investigator will preserve the confidentiality of participants taking part in the study and fulfil transparency requirements under the General Data Protection Regulation for health and care research. Data and all appropriate documentation will be stored for a minimum of 10 years after the completion of the study, including the follow-up period.

6.4 Indemnity

Imperial College London holds negligent harm insurance policies which apply to this study.

6.5 Sponsor

Imperial College London will act as the main sponsor for this study.

6.6 Funding

Imperial College London (ICL) are funded through the Discover-NOW Health Data Research Hub, of which Imperial College Health Partners (ICHP) are lead partner and Imperial College London are an academic partner. Discover-NOW is funded by a grant from the UK Research and Innovation (UKRI) Industrial Strategy Challenge Fund (ISCF). Partial additional funding for the study (i.e., additional to the Hub grant funding) has been provided directly by ICHP.

We expect Imperial College London's research study budget to be 135,000 GBP based on the activities and approach outlined above. The study's funding is covered under the term's of the Consortium Agreement relating the Discover-NOW Digital Innovation Hub entered into between Imperial Collee of Science, Technology and Medicine and ICHP effective 20 November 2019.

This consortium was formed in connection with the Parties' successful application in response to the Digital Innovation Hub Prospectus issued by the Medical Research Council (MRC) on behalf of UK Research and Innovation (UKRI), working together with Health Data Research UK Limited (HDRUK), for funding through the Industrial Strategy Challenge Fund (ISCF).

6.7 Audits

The study may be subject to inspection and audit by Imperial College London under their remit as sponsor.

7. Publication policy

The Investigators and representatives of the collaborating organisations will be involved in reviewing drafts of the manuscripts, abstracts, press releases and any other publications arising from the study. Authors will acknowledge that the study funding as detailed in Section 6.6 above. Authorship will be determined in accordance with the ICMJE guidelines and other contributors will be acknowledged.

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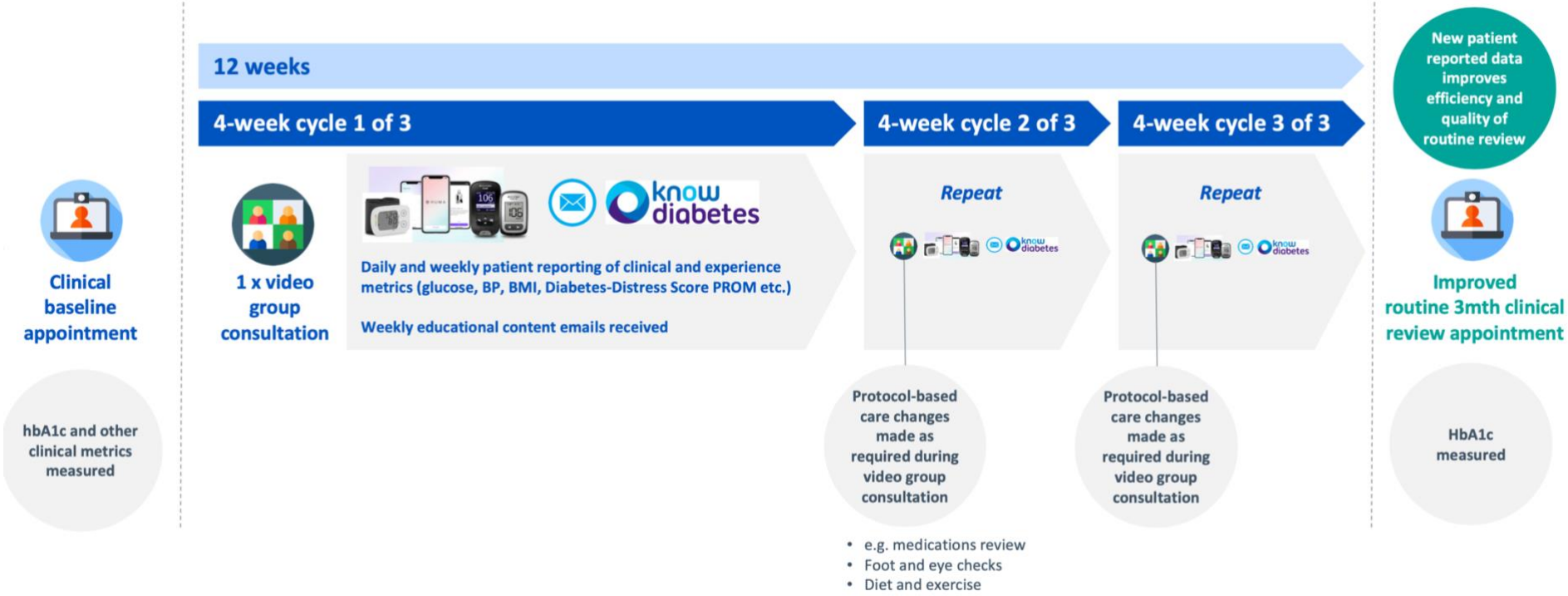
Appendix 1: Fresh Start overview



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Appendix 2: Overview of study procedures

Step	Patient search	Outreach, Qualification & Booking	Onboard	Know Diabetes Emails	Huma App and Devices	Virtual Group Consultations (VGC)			12wk Review Discharge, Repeat or MDT
						Before	During	After	
Staff actions at primary care practice	Run EPR search report to find list of patients.	Contact patients by phone, invite them to the service and ensure they can participate. Book them onto a formal onboarding appointment and book bloods if missing. Book to collect devices.	Run virtual appointment or phone call to onboard patient onto the service. Provide Huma app, book 3 x VGC sessions, sign up for Know Diabetes emails, answer questions Patient collects devices from practice.	Sign the patient up by email and make sure they are receiving emails OK.	Check Huma clinician dashboard daily for safety (red flags) and to see whether patients are using app. Escalate care if red flag spotted. Patients set their own goals.	Look at Huma dashboard, move some key data into EPR. Fill out VGC "discussion board" slide and agree talking points for VGC session. Discuss possible clinical and care plan decisions.	Run VGC session with 6-10 patients. Review and discuss patient goals and clinical metrics. Identify and note clinical treatment or care plan changes and referrals required.	Internally discuss notes and actions from VGC after session. Refer to clinical protocols; agree and action any required care plan and treatment changes or referrals.	Decide whether to discharge patient, repeat service for 12-weeks or escalate them to an MDT for further support.
How long it should take?	5m total	10m per patient	30m-45m per patient	1m per patient	1-2m per patient	1hr total	1hr15m total	1hr total	1hr total
How often it should be done?	Once, at beginning of 12 weeks	Once, at beginning of 12 weeks	Once, at beginning of 12 weeks	Twice, at beginning and at first VGC session	Daily	Before each VGC	During each VGC	After each VGC	Once, at end of 12 weeks

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Appendix 3: Example VGC discussion board

Name	HbA1c	Blood Pressure	Non-HDL cholesterol	Body Mass Index (BMI)	Diabetes Wellbeing	Goal	Actions
	Your average blood sugar over 3 months, the higher the result, the higher the sugar. **Ideally below 53 normally**	Good blood pressure reduces risk of strokes and heart attacks. **Ideally less than 130/80**	Cholesterol is essential for life and can be good (HDL) and bad (non-HDL). Bad cholesterol increases your risk of heart disease. **Ideally below 3.35**	Your weight against your height. You have a 90% chance of achieving remission if you manage to lose 15kg or more. **Ideally 20-25 (18-23 if South Asian)**	Living with diabetes can be really challenging. The Diabetes Distress Scale is a questionnaire we use to measure this. **Ideally below 2**	Being clear about what you want to see happen will help you achieve it!	91% of people who write down their action plan will stick to it.
John	67	156/98	3.7	34.8	3	Lose 5kg weight over next 3 months to improve quality of life	Reduce carb intake, walk 5000 steps per day
Manoj	109	145/67	3.2	29.0	2	Feel more energy, reduce my HbA1c to reduce complications	Cut back on fruit juice and fizzy drinks
Alex	56	132/77	3.0	33.7	1	Lose 10kg weight and get into remission within 6 months	Join REWIND and go on low calorie soups and shakes

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