RESEARCH PROTOCOL

DiabetesMyWay: your home for online diabetes support

Contents

1) RESEARCH TEAM & KEY CONTACTS

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2) INTRODUCTION

Clinical problem: Type 2 diabetes (T2D) affects ~7% of the UK population. Suboptimal management of T2D leads to serious complications such as heart attacks, kidney failure and blindness. Poor patient knowledge about T2D contributes to sub-optimal levels of glucose and cardiovascular risk factors. There is major variation in the level of knowledge that patients have about diabetes; major variation in the quality of diabetes care across general practices in Greater Manchester (GM); practical and financial challenges for delivering behavioural interventions supporting healthier lifestyles; major blocks in clinical care because of diabetes-related psychological distress - all compounded by low attendance rates in clinics and structured education in some patient groups.[1-3] Effective diabetes management has been further negatively impacted my restrictions in access to traditional services due to the COVID-19 pandemic.

Aim: To assess whether digital interventions improve T2D self-management across GM during the COVID-19 pandemic.

Methods: From July 2019, digital interventions will be offered to patients with T2D across GM including access to educational resources, their medical records, personalised care planning, goal-setting tools, personalised care quality reporting against Care Standards and glucose monitoring displays through *MyDiabetesMyWay (DMW)*. Between July 2019 and 31 March 2021, sub-groups of patients will also have access to online behavioural interventions (*Oviva; Changing Health*), and a cognitive intervention (*MyCognition*). Clinicians will have access to patient data including information on the impact of intervention enabling personalised treatment plans.

Evaluation: The effectiveness of *DMW*, *Oviva* and *Changing Health, MyCognition* will be assessed by assessing changes in outcomes before vs. after intervention using a control group. The main focus will be on changes in glucose control and cardiovascular risk factors. There will be assessments of usability and other patient reported outcomes. Outcomes will be assessed across all patient groups and in ethnic minority and socially deprived subgroups.

Expected benefits: If the Intervention is found to support self-care and clinical care in T2D across GM then this evidence could justify rollout of these interventions across the NHS in England.

3) BACKGROUND

3.1. The clinical problem

Diabetes most commonly affects older people who are overweight (90% of diabetes is type 2 diabetes (T2D)). Diabetes currently affects more than 371 million people worldwide, and this number is expected to rise to 552 million by 2030. T2D affects more than 3.9 million people in the UK alone (to rise to 5 million people by 2025) [4] and in Greater Manchester there are more than 140,000 people with the condition. T2D is a serious long-term condition that can lead to premature death and morbidity due to diabetes-related complications including cardiovascular disease. Current approaches to managing diabetes are inadequate and there is an urgent need for novel interventions. Compelling practical, clinical and financial issues make *Digital Interventions* an attractive means of supporting effective self-management in people with T2D.

In the context of the COVID-19 pandemic, it is clear that digital interventions could be even more valuable to people with diabetes because access to face-to-face primary care interventions for people with type 2 diabetes have been extremely limited, and may remain so for many months. The digital interventions are designed to support self-management and could potentially reduce the need for direct contact with healthcare staff.

a) ***Patient knowledge about diabetes; level and variations in diabetes care quality across GM***: Clinical experience tells us that there is major variation in the level of knowledge that patients have about their diabetes. Data from Manchester Clinical Commissioning Groups indicates major variation in the quality of diabetes care across general practices in GM. For example, there is wide variation in the proportion of patients receiving the NICE-

recommended care processes such as having blood pressure checked; seven out of ten GM localities were rated 'requires improvement'; achievement of all treatment targets (e.g. good blood pressure control) ranged 38%-45%; GM's current self-management and learning offer is traditional group-based 'structured education' and uptake is poor.

b) ***Behaviour and weight change interventions***: There are major practical and financial challenges in delivering behavioural interventions supporting healthier lifestyles. For example, attendance at structured education was reported recently to range from 1%-4%. There are insufficient numbers of clinical staff to appropriately support and train 150K people with type 2 diabetes across GM.

c) ***Cognitive function, T2D self-management and diabetes distress***: The presence of type 2 diabetes has been linked to an increased risk of cognitive impairment and dementia.[5, 6] Cognitive impairment has been linked to reduced self-care in T2D.[7] Major blocks in clinical care occur because of diabetes-related psychological problems including depression, anxiety and diabetes-related distress.[8] There are major resource implications in relation to identifying and managing people with diabetes who have psychological issues that could impact on their diabetes management.

d) ***Poor clinic attendance***: In some patients, low rates of attendance at outpatient clinics and structured education sessions contribute to poor glucose control.[9]

3.2 Interventions and originality: The *DiabetesMyWay* project plans to implement multiple **digital interventions** to address the system-wide challenges and inequalities that limit patient learning, self-management and clinical care in T2D. Different people/communities live, work and operate in different ways, so our vision is a modern healthcare environment which embraces this and provides the tools and techniques to engage, educate and empower all people with T2D. This approach needs to be flexible; changing with peoples' needs and being accessible to people from different communities.

Between July 2019 and 31 March 2021 the interventions (DMW, Changing Health and Oviva, and MyCognition) will be offered to consenting patients.

Between 31 March 2021 and 30 April 2021 only the *DiabetesMyWay* intervention will be offered to consenting patients.

From 30 April 2021 onwards the *DiabetesMyWay* intervention will be part of routine clinical services offered by GP practices in GM. *DiabetesMyWay is not routinely available in other parts of the UK.*

Within our study we will uniquely assess the effectiveness of these interventions when used together. Study participants will all be offered access to DMW and selected participants will be invited to participate in **one other intervention** (a behavioural intervention (*Changing Health* or *Oviva*) or *My Cognition* (described below)). Other novel aspects of our study are that the Interventions will be delivered to large numbers of patients within the socially and ethnically diverse GM population. Each of these market-ready digital products has evidence supporting its use:

a) ***MyDiabetesMyW***ay ***https://www.mydiabetesmyway.scot.nhs.uk/:*** *My DiabetesMyWay* (DMW) is an award-winning interactive website for people with diabetes and their carers. It contains a variety of multimedia resources aimed at improving self-management, including: traditional information leaflets; interactive educational tools; and videos describing complications.[10] In addition to this general information and advice, DMW offers its users access to their clinical data via its novel electronic personal health record (ePHR). This service is currently available to all people with diabetes in Scotland; there are currently >30K users of the system.

This system in Scotland includes data from primary and secondary care, specialist screening systems (including retinopathy screening, podiatry) and laboratories. These data include diagnostic information, demographics, process outcomes, screening results, medication and clinical correspondence. The system provides a more complete overview of diabetes than would be available from any single data source, such as an isolated primary care or hospital clinic database. The DMW ePHR focuses on key diabetes indicators, such as HbA1c, blood pressure and body weight.

Alongside these data is descriptive text explaining each assessment, detailing why they are recorded and what normal range values are. Further educational materials are presented alongside clinical results and are tailored to those using the service. For example, foot care advice is based on the patient's recorded foot risk assessment category. History graphs and tables allow individuals to track changes over time for the full duration of their clinical record from multiple electronic data sources. DMW aims to provide highly tailored information and provides advice based on the Diabetes UK's "15 Healthcare Essentials" campaign. Patients can also manually enter home-recorded information (weight, blood pressure for example), or automatically upload blood glucose results. These features allow people to take control of their diabetes and become more empowered to enhance their self-management and care.

A spinout company, MyWay Digital Health, created in Jan 2017, supplies DMW. The company received funding from NHS England's Small Business Research Initiative scheme, to demonstrate DMW's potential as a viable commercial product outside Scotland.

Benefits include substantial improvements in diabetes self-management along with population improvements in HbA1c, weight, lipids and blood pressure with anticipated long-term cardiovascular benefits. In a recently-reported survey of more than 1000 users of the service, the majority believed that online access to diabetes information had potential to improve their diabetes self-care.[11] The most valued features were personal clinical data associated visualisations.

In this study, DMW will be available to all participants and it will serve as gateway to the other interventions that will be offered to subgroups of the population. Our study will

enable the intervention to be evaluated in a large socially and ethnically diverse English population. Demonstration of effectiveness in this population will support efforts to make this available to all people with diabetes across the NHS in England.

b) ***Behavioural interventions***: ***Oviva*** ***https://oviva.com/uk/en/*** ***and Changing Health*** ***https://www.changinghealth.com/***: Lifestyle intervention, delivered through effective self-management, can improve glucose control and reduce cardiovascular risk factors. These benefits would be expected to reduce the long-term complications of diabetes, improve life expectancy and improve quality-of-life. Concerted efforts at lifestyle intervention supported by digital technologies (such as Oviva and Changing Health) can even induce remission of T2D. We plan to offer these behavioural interventions to subgroups of participants:

   i) ***Oviva*** offers 8-week personalised, frequent, one-to-one care from a diabetes specialist dietician using behaviour change techniques. An NHS-digital-approved mobile Oviva app is used to keep a food diary, track bodyweight, physical activity and progress towards personalised goals. The app or telephone is also used to keep in regular contact with the dietician. The intervention has been evaluated In 204 people with T2D recruited from practices in London.[12] Engagement with the *Oviva* intervention was associated with a 9 mmol/mol reduction in HbA1c, a 3kg reduction in body weight and a 9 mmHg fall in systolic blood pressure.[12] In our study we will build on this prior work by increasing participant numbers, recruiting from an ethnically and socially diverse population;

   ii) ***Changing Health*** offers a 12-week personalised programme consisting of an NHS-digital-approved and QISMET accredited app supported by a lifestyle coach trained in behaviour change techniques. The educational content on the app consists of short videos, articles and interactive activities on diet and exercise that participants can view at their convenience on their mobile phone or computer. Upon completion of the educational content, participants can book telephone appointments with their lifestyle coach at a time of their convenience. All participants will receive 100 minutes of coaching (1 x 20 minute introductory call, followed by 8 x 10 minute calls) across the 12 weeks. The intervention was evaluated in 41 people with T2D recruited from practices in London as above.[12] Engagement with the *Changing Health* intervention was associated with a 4 mmol/mol reduction in HbA1c, a 1.5kg reduction in body weight and a 1 mmHg fall in systolic blood pressure.[12] In our study we will build on this prior work by increasing participant numbers, recruiting from an ethnically and socially diverse population.

c) ***MyCognition*** ***https://mycognition.com/***: The intervention is designed to improve cognitive performance, enhance mental resilience and reduce the impact of stress through cognitive training exercises. The *MyCognition* intervention can be accessed via a mobile phone or computer. An online assessment tool (taking 15 mins to complete) provides a personal report on cognitive fitness. An online programme of personalised educational resources designed to increase cognitive performance follows on from this. MyCognition

also provides access to a personalised game-based training application that can be used 10-15 mins/day is also designed to increase cognitive performance. Healthy lifestyle choices are encouraged through the application. Several unpublished controlled studies have shown statistically significant improvements in cognitive performance through using the application. Other interventions designed to improve cognitive performance appear to improve T2D self-management in small studies.[13] In the study we plan to assess the impact of *MyCognition* on *diabetes related distress* in a large cohort of patients with T2D.

3.3 Research design addressing the research questions: Within the short time frame made available by the funders, a randomised control trial is not possible. Therefore the effectiveness of interventions will be assessed by a before and after comparison of those patients using the interventions with a control group of patient not using the intervention. The comparison will focus on risk factors such as glucose control as assessed by HbA1c levels.

The control group data will consist of a pseudonymised list of all patients within GM meeting the following criteria: a) age >18 years, b) type 2 diabetes, c) have not opted out of their data being used for research purposes, d) are not part of the cohort of patients taking part in the test bed project.

The information required from these patients will be limited to the following information held within the GP record: age, sex, ethnicity, GP postcode (to assess deprivation), diabetes type and duration, blood pressure, cholesterol, creatinine, eGFR, smoking and bodyweight/height/BMI, medication, diabetes clinic attendance in primary care, hospital visits including emergency visits.

The control data will be provided by Health Innovation Manchester and Graphnet via their Greater Manchester Care Record (GMCR).

3.4 Overview of evaluation*: DMW, Oviva, Changing Health* and *MyCognition* will be evaluated using quantitative and qualitative methods focusing on specific ethnic and socio-economic subgroups. For *DMW, Oviva and Changing Health*, changes in short-term metabolic risk factors such as HbA1c and body weight will be assessed. Cost-effectiveness will be assessed for *DMW, Oviva, Changing Health interventions*. For *MyCognition*, data on within-patient change in cognitive assessments delivered online will also inform the evaluation. For the DMW intervention, patient and clinical staff experience will be evaluated through focus groups and 1:1 interviews, details of which will be covered in a substantial amendment to the original ethics application.

3.5: Anticipated outcomes: If the Intervention is found to support self-care and clinical care in T2D across GM then this evidence could justify rollout of these interventions across the NHS in England.

4) STUDY AIMS and OBJECTIVES

4.1 Primary Aim:

To assess whether digital interventions improve T2D self-management across GM.

4.2 Objectives:

We will address specific research objectives in relation to individual interventions. Also see **Section 7** describing further detail of the outcome measures under these objectives:

a) DMW-related objectives

1. To assess changes in HbA1c, systolic blood pressure, cholesterol, smoking and bodyweight/BMI after controlling for risk factor changes in matched patients not using the intervention. Within person changes and risk factors will also be assessed in the intervention group;
2. To assess patient uptake (proportion offered intervention who take it up), engagement (time spent online and content viewed), user experience (usability, knowledge and ability to self manage), retention (proportion of people interacting with the intervention more than once), completion (proportion of people interacting with the intervention who use it within 2 months of the end date (31st June 2022) and healthcare utilisation (clinic and hospital attendance; medication use);
3. To assess how DMW is integrated into care pathways in primary care.

b) Behavioural interventions (Oviva and Changing Health)-related objectives

1. To assess changes in HbA1c, systolic blood pressure, cholesterol, smoking and bodyweight/BMI in participants using the intervention after controlling for risk factor changes in matched patients not using the intervention. Within person changes and risk factors will also be assessed in the intervention groups;
2. To assess patient uptake, engagement, user experience, retention, completion and healthcare utilisation (defined for DMW above (except for completion, which in the case of the behavioural interventions, will be completion of the course).

c) MyCognition-related objectives

1. To assess average within-person changes in *diabetes distress scores*;
2. To assess changes in cognition scores;
3. To assess within-person changes in referral rates for traditional psychological interventions.

d) Health economics objectives

1. To assess the net financial costs of the intervention for the health system;
2. To assess the costs to innovation partners of participating in the Test Beds programme;
3. To assess the net financial benefits of the intervention for the health system.

e) Process evaluation objectives

We will address the following objectives in a brief narrative report:

1. To describe the process through which the study was designed;
2. To explain if the interventions were delivered in line with original plans;
3. To explain if the governance arrangements for the intervention were effective and why;
4. To describe whether the partnership of NHS with innovator firms worked as intended and why;

5. To describe whether the innovator partnerships resulted in improved technology 'pull-through';
6. To describe whether the NHS has received better products or processes as a result of collaboration/testing/learning;
7. To describe the benefits to innovation partners of being part of the Test Bed programme;
8. To describe whether engagement by each party to the partnership been sufficient and why;
9. To describe whether changes were made during implementation to ensure effective delivery of the intervention, and why;
10. To describe whether there were barriers and facilitators to effective delivery (and uptake of technology/ services) and how were they overcome / ensured;
11. To describe any unintended consequences that needed to be managed and how was this done;
12. To describe to what extent is the intervention likely to be scalable and why.

5) STUDY DESIGN & PROTOCOL

5.1 Participants

a) **MyDiabetesMyWay** (DMW). Our aim is to offer DMW to all ~140K people with T2D in GM and a clinician-facing version will offered to all GM Primary Care staff. However, there may be limitations on numbers that can be offered depending for example on GP system vendor data integration issues. The aspiration is to make DMW available to all healthcare professionals in secondary and community care too, assuming we can easily define their patient population. We are planning a series of studies assessing the impact of DMW (see **section 9.1.1 for sample sizes**).

b) **Targeted digital interventions** (1-5 below). Selected study participants will be invited to participate in no more than **one other intervention.** These will be offered to DMW participants through the DMW interface as shown in **Figure 1** below. The *targeted digital*

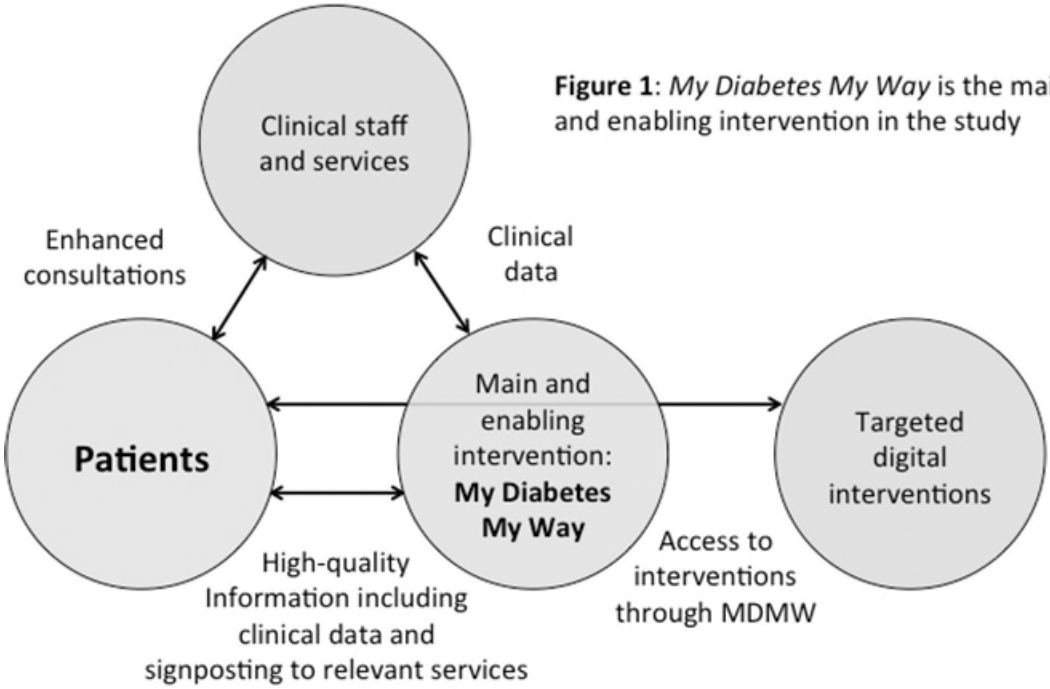


Figure 1: *My Diabetes My Way* is the main and enabling intervention in the study

interventions will be offered to a relatively small number of participants compared to those offered DMW.

1. **Behavioural interventions** (***Oviva*** **or** ***Changing Health***) will be offered and each provided to a total 600 attended patients (patients who take part in each intervention at least once). In subgroup analyses, we will assess the relationship of ethnicity and social deprivation with study outcomes;
2. ***MyCognition*****:** cognitive assessment will be offered to all DMW participants and the intervention on cognitive function will be offered and provided to the first 1000 participants. In subgroup analyses, we will assess the relationships of ethnicity and social deprivation with outcomes;

5.2 Study Intervention and/or Procedures

5.2.1: Identification of participants July 2019 to 30 April 2021 (DMW); July 2019 to 31 March 2021 (Oviva, Changing Health and MyCognition)

In this study, the digital interventions will be offered as an adjunct to current diabetes care to all people with a diagnosis of T2D within GM (~140K patients across 10 CCGs and 450+ Practices). Enrolment to the study will be entirely voluntary.

Based on current DMW usage (10% of the Scottish diabetes population), we anticipate that there will be ~7000-14,000 active users at the end of the intervention period. It is anticipated that the service will go live during July 2019.

Once live, DMW and the targeted digital interventions will be promoted locally via primary and secondary care health care professionals and by the GM Diabetes Clinical Research Network team.

The research team based at the Strategic Clinical Network has well-established lines of communication with 10 CCGs and >450 primary care sites that will be involved in this research.

Identification of potential participants will take place primarily through searches of primary care practice databases to identify patients with T2D. Practice searches will be facilitated by GCP-trained staff of the NIHR Clinical Research Network Greater Manchester (CRN) whenever possible. Additionally, the 'Research for the Future' team in the CRN will invite type 2 diabetes patients who have already registered their interest in taking part in research studies on a volunteer database organised by the CRN '*Help BEAT Diabetes*' campaign and provided their consent to be contacted. People who are registered on the *Help BEAT Diabetes* database who meet the inclusion criteria and who live in Greater Manchester will be invited by email or post (see ***RfF DMW Patient Invite***) by the CRN Research for the Future Team to register via the Diabetes My Way website; they will also be provided with the patient information sheet (see ***Participant Information for the DiabetesMyWay Study***) at this point.

We anticipate that letters from the practice will, in most cases, make initial contact with potential study participants (see ***Participant Information for the DiabetesMyWay Study***). In some cases a text message (see ***Text for the DiabetesMyWay Study***) from the practice to the patient or an email message (see ***email for the DiabetesMyWay Study***) sent from the practice to the patient will be used.

We are also planning to publicise the study through local diabetes networks, pharmacies, opticians, external media and through 3rd party organisations including Diabetes UK.

The GM Strategic Clinical Network has a Communications & Recruitment policy in place for the roll out at the programme, which will include promoting the study through community groups. For example, North Manchester has excellent links with their community groups and Bolton have the very successful *Community Champions Scheme* which could attract participation from ethnic and more socially deprived cohorts.

We expect that a small number of patients with T2D will be identified through their clinical teams based in hospital clinics (the majority of people with T2D are managed in primary care) and those attending Allied Health clinics (e.g. eye screening, podiatry etc.), BUZZ (https://buzzmanchester.co.uk/: health and well-being services) and community groups.

In summary, copies of the following documents are provided in this ethics application:

1) Communication with patients
   a) Introductory letter DMW 22March19
   b) Introductory text DMW 22March19
   c) Introductory email DMW 22March19
   d) Patient information Sheet DMW 22March19 (provided by email)
   e) Patient information Sheet Oviva 22March19 (provided by email)
   f) Patient information Sheet Changing health 22March19 (provided by email)
   g) Patient information Sheet MyCognition 22March19 (provided by email)

2) Communication clinical staff
   a) GP information letter DMW via email 22March19
   b) GP information letter Oviva via email 22March19
   c) GP information letter Changing Health via email 22March19
   d) GP information letter MyCognition via email 22March19

5.2.2: Identification of participants for Diabetes My Way, 30 April 2021 onwards:

From 30 April 2021 the Diabetes My Way intervention will be offered to patients as part of their routine diabetes care. Patients will not be asked to consent to participate in a research study. Instead, users register for Diabetes My Way and authenticate their identity via the NHS Login process. The Diabetes My Way terms and conditions, which participants consent to, include sharing data for research purposes. The NHS Login service has its own Ts&Cs at https://access.login.nhs.uk/terms-and-conditions. For the screens seen by patients please see ***Diabetes My Way on boarding process v1***

The decision to make Diabetes My Way part of routine diabetes care in Greater Manchester was taken by the Greater Manchester Strategic Clinical Network as part of their initiatives to improve the care of those with diabetes. Implementing the intervention into routine care required the on boarding process to be simplified to facilitate the regional roll out. .

6) STUDY PARTICIPANTS

The study is designed to be as inclusive as possible so that the results are generalisable. Therefore there are very few/exclusion criteria involving the DMW intervention:

6.1 Inclusion Criteria for the main intervention (DMW), July 2019 to 30 April 2021:

- Age ≥18 years
- T2D (as determined by primary or secondary care records)
- Registered with GP in GM
- GP or other diabetes care provider is linked to DMW
- Self-certified understanding of spoken and written English or available support from family or friends
- Able to access a digital device including having a mobile phone and an email address

6.2 Exclusion Criteria for the main intervention (DMW) July 2019 to 30 April 2021:

- Age <18 years
- No T2D (as determined by primary or secondary care records)
- Not registered with GP in GM
- GP or other diabetes care provider e.g. hospital is not linked to DMW
- Unable to access a digital device

6.3 Additional selection criteria for participants/practices offered other digital interventions July 2019 to 31 March 2021:

DMW will apply *additional* selection criteria (described under *a-d* below) prior to patients being offered access to *targeted digital interventions*. Once offered, participants will be encouraged to discuss the option of their participation with these *targeted digital interventions* with their regular clinical team members responsible for their diabetes care. The final decision to participate in these *targeted digital interventions* will rest with patient.

- **a) *Behavioural interventions*** (***Oviva*** or ***Changing Health***) will be offered and each provided to 600 participants**.** We will exclude people self-reporting *current pregnancy,* those treated with insulin (*Changing Health* only), those with no contraindication for weight loss or physical activity (*Changing Health* only) and those receiving diabetes care at a location other than their GP surgery.
- b) ***MyCognition*** assessment will be offered to all DMW participants and the ***MyCognition*** intervention will be offered and provided to the first 1000 participants who complete the assessment (as explained above). There will be no additional selection criteria.

6.4 Recruitment:

Recruitment will require a 2-stage registration process:

a. ***Registration with online Patient Services:*** If participants are interested to take part after reading the introductory letter, email, text and patient information sheet (see submitted documents), then they will be invited to register for online *Patient Services* with their GP practice staff. Patients will probably be invited to fill in a paper form in order to do this (will depend on the system in place at each practice). Patient registers their basic information with *Patient Services* and unique codes provided by *Patient Services* enable signup to the system (https://www.patient-services.co.uk/login) and on-going communications with their primary care provider.

b. ***Registration with DiabetesMyWay:*** When participants are accepted for online Patient Services they will be able to register online with *DiabetesMyWay* (patients are provided web address via the patient information sheet), which will give participants access to the system. Patients will be given access to terms and conditions and privacy notices. Patients will be invited to confirm that they have T2D and are 18 years of age or older. Potential participants will have as much time as they need to decide to take part. Informed consent will be provided through reading the patient information sheet, conditions and notices and will be captured on first system access.

Enrolment to the other targeted digital interventions, July 2019 to 31 March 2021, will be via the DMW website: Study participants enrolled and using the DMW intervention will be invited to take part in additional sub-studies involving *targeted digital interventions* from the list below and as also described in **section 6.3** above:

- ***Behavioural interventions*** (***Oviva*** or ***Changing Health***); allocated to alternate eligible participants to achieve similar recruitment numbers for each intervention
- ***MyCognition***

Selection criteria for studies involving targeted digital interventions: Offers to participate in studies of targeted digital interventions will be based on selection criteria described in **Section 6.3** above.

Participation Information and consent: Selected participants will be invited to read the intervention-specific **Participant Information Sheets** (**see section 5.2.1**). The final decision to participate will rest with patient. There will be no obligation to take part and their decision to take part will not influence their involvement in the DMW intervention or their usual clinical care. Informed consent will be provided through reading the patient information sheet, conditions and notices and will be captured on first system access to these targeted interventions. Consent will be assumed by acceptance and use of the apps and by completion of the questionnaires.

6.5: Interventions

a) DiabetesMyWay July 2019 to 31 March 2022: The DiabetesMyWay interactive website and mobile app will provide participants with high-quality information about diabetes including access to the information in their medical records. Information is presented in the form of videos, interactive content and carefully worded and easily understood text. Participants will be provided with the ability to plan their care, set goals and look at their sugar and other results in a way that is

easy to understand. These tools are expected to greatly support people in managing your diabetes.

b) Enrolment to the behavioural intervention, Oviva, July 2019 to 31 March 2021: The Oviva programme provides 8 weeks of one-to-one support from a diabetes specialist dietitian, along with providing high-quality information about healthy lifestyles.

Participants can either use their online resources and app or choose to keep in contact with the team through phone calls, printed materials and DVD content sent to their home. The online programme can be accessed anytime and anywhere via phone or computer including dietitian coaching at a convenient time.

The research will monitor changes in sugar levels (HbA1c), weight, blood pressure and cholesterol.

At the end of the programme participants will be invited to complete an online questionnaire to assess the usability of the programme (see usability questionnaire Oviva 22March19). Usability questionnaires have been developed with the individual intervention providers in line with the requirements the funder.

c) Enrolment to the behavioural intervention, Changing Health, July 2019 to 31 March 2021: Changing Health provides a 12-week programme starting with short videos and articles about type 2 diabetes, diet, exercise and goal setting via the app. Then, via phone, participants will meet a personal lifestyle coach who will support lifestyle changes. The Changing Health app allows participants to monitor meals, weight loss and track goals.

The research will monitor changes in sugar levels (HbA1c), weight, blood pressure and cholesterol monitored from GP records.

At the end of the programme participants will be invited to complete an online questionnaire to assess the usability of the programme (see usability questionnaire Changing Health 22March19).

d) Enrolment to MyCognition intervention July 2019 to 31 March 2021: The MyCognition app involves playing a fun video game over 12 weeks. Before starting, participants will be invited to perform 5 short questionnaires to assess which of their brain functions can be improved (these questionnaires are part of the app; please see https://mycognition.com/). Participants will be invited to complete an online questionnaire assessing their current ability to cope with living with diabetes (please see diabetes distress score questionnaire), and in particular their level of distress linked to the condition.

These brief questionnaires are followed by playing a fun video game, which is personalised to participants' test results, for 15 minutes a day with increasing challenges designed to improve memory, learning skills and concentration and decision-making skills. The app also provides tips and guidance on everything from diet to exercise and practical guidance on sleep and work habits.

At the end to the programme participants will be invited to complete the brief questionnaires again looking for improvements in cognitive function and level of diabetes distress.

At the end of the programme participants will be invited to complete an online questionnaire to assess the usability of the programme (see usability questionnaire MyCognition 22March19).

e) Enrolment to 1:1 Interviews and focus groups: We will be inviting a small number of Will be inviting a small number of participants (<40) to take part in *1:1 Interviews and focus groups* with a research psychologist. ***Details will be provided in a substantial amendment to this ethics application.*** In short, we will focus recruitment primarily, but not exclusively, on research-active practices currently supported by the Diabetes Clinical Research Network. Initial contact will be made with participants through clinical contact, posters describing the study in GP surgery waiting rooms, patient support groups and DMW newsletters.

6.6 Participants who withdraw consent or lose capacity to take part:

Right to withdraw consent: Participants can withdraw from the study entirely, or any targeted intervention that forms part of it, at any time without giving any reason, as participation in the research is voluntary, without their care or legal rights being affected. Patients can leave the study at any time by either choosing not to engage with the service or by contacting the system administrators at DMW or the targeted intervention and asking that their account is closed.

Outcome of data in participants who withdraw consent: For patients who withdraw their consent to participate, it will not be possible to remove their data from the project once it has been pseudonymised and forms part of the aggregated dataset. Patients are advised of this fact at the time of enrolment and are asked whether they agree to take part on this basis. The wording of the patient information sheet reads as follows, ”I understand that it will not be possible to withdraw my health records from the project once my personal information has been removed and the information has been sent to the University.”

Capacity: We do not plan to monitor capacity for two reasons: First, patients will remain under the care of their regular clinical teams; the interventions provided are designed to improve and not to replace usual care. Second, should the patient lose capacity then they are very unlikely to be harmed by any of the interventions used in this research.

7) OUTCOME MEASURES

7.1: Primary, secondary and tertiary endpoints

a) ***DMW*, *Oviva* and *Changing Health* behavioural interventions**
Primary endpoint: Change in HbA1c: a) relative to controls not using the intervention and b) within-person change
Secondary endpoints

i) Changes in bodyweight/BMI, blood pressure, cholesterol and smoking;

ii) Uptake, engagement, user experience, retention, completion and healthcare utilisation;
iii) Modifying effect of cognitive function and digital uptake on primary and secondary outcomes;
iv) Economic impacts (see below);
v) Impact in primary care staff on care processes (will be assessed using a questionnaire described in a subsequent substantial amendment).

b) ***MyCognition***
Primary endpoint: Within-group change in *diabetes distress score* (see *diabetes distress score* questionnaire).
Secondary endpoints

i) Within-group change in cognition scores;
ii) Referral rates for traditional psychological interventions compared to age-sex-ethnicity-deprivation-matched individuals.

7.2: Outcomes involved in the *process evaluation*
Through dialogue with the digital intervention teams, the evaluation team will provide a brief narrative report on processes leading to the programme design, whether partnerships and interventions were delivered as planned and the effectiveness of governance arrangements.

The team will assess technology 'pull-through' and whether the Test Bed and NHS benefitted from better products as result. The adequacy of the contribution of individual partners will be assessed and how barriers, facilitators and unintended consequences of the implementation plan were handled. Assessment of the benefits to individual partners and whether the intervention is scalable will be reported.

7.3: Outcomes involved in the economic evaluation: The economic evaluation will focus on cost effectiveness. The main outcomes that we expect to change will vary across the digital interventions evaluated in the programme.

The main analysis will focus on obtaining reliable estimates of how intervention affects key risk factors such as HbA1c and costs across population groups. Costs will be direct NHS costs assessed from intervention-related costs and changes in routine healthcare utilisation as assessed from rates of primary care consultations and hospital attendances during the observation period.

The data required for the economic evaluation will include: within-group changes in bodyweight/BMI, blood pressure, cholesterol, smoking, medication and healthcare utilisation.

In exploratory analyses, expected reductions in rates of cardiovascular events, and other adverse patient outcome, through modifying cardiovascular risk factor levels will be modelled using data from relevant meta-analyses and the UKPDS Outcomes Model. Net financial costs to the NHS per patient will be assessed from each partner in the Test Bed.

7.4: Outcomes involved in assessing *user experience* focussing on *usability*: We will assess these patient reported outcomes for each digital intervention using the same brief standard questionnaires delivered through the DMW platform after 3 months of using each intervention.

a) Usability will be assessed using questionnaires developed in collaboration with the digital intervention partners. Participants will be invited to complete these questionnaires towards the end of the intervention period. Copies of these following questionnaires are provided for review:

a) Usability questionnaire DMW 22March19 (provided by email)
b) Usability questionnaire Oviva 22March19 (provided by email)
c) Usability questionnaire Changing Health 22March19 (provided by email)
d) Usability questionnaire MyCognition 22March19 (provided by email)

***b) Knowledge and ability to self-management T2D*:** this will be assessed from the DMW usability questionnaire (Usability questionnaire DMW 22March19) presented in this ethics application. We will also assess *Knowledge and ability to self-management T2D* through *Focus groups* and *1:1 qualitative interviews* performed by the study psychologist; further details of which will be provided in a substantial amendment to this ethics application.

7.5: Outcomes involved in assessing *impact of DMW on primary care pathways*: These outcomes will be assessed from *Focus groups* and *1:1 qualitative interviews* performed by our study psychologist. Further details of these assessments will be provided in a substantial amendment to this ethics application.

7.6: Outcomes involved in assessing user engagement with digital intervention: A range of metrics will be used with no additional burden to participants. Measures will include:

- Number of users offered the intervention
- Number of users registering for the intervention
- Number of Inactive users (registered but not logged onto the intervention)
- Number and % of users who have viewed all learning content
- Number and % of users who have booked a coaching session (for behavioural interventions)
- Number and % of users who attended a coaching or dietician session (when appropriate)
- Number and % completing Digital Structured Education (for behavioural interventions)

7.7: Extrapolating intervention costs and comparisons with other services: The cost of the DMW intervention in all patients with T2DM across GM has been captured in the original grant application (including costs borne by the innovators). The costs delivering the other digital interventions to all people with T2D across Greater Manchester will be calculated through scaling the numbers assessed in this study.

Unit costs of delivering traditional face-to-face behaviour change intervention; psychological intervention and costs of clinic non-attendance locally are available in GM enabling meaningful cost comparisons.

7.8: Potential clinical benefits of positive results across the NHS and wider

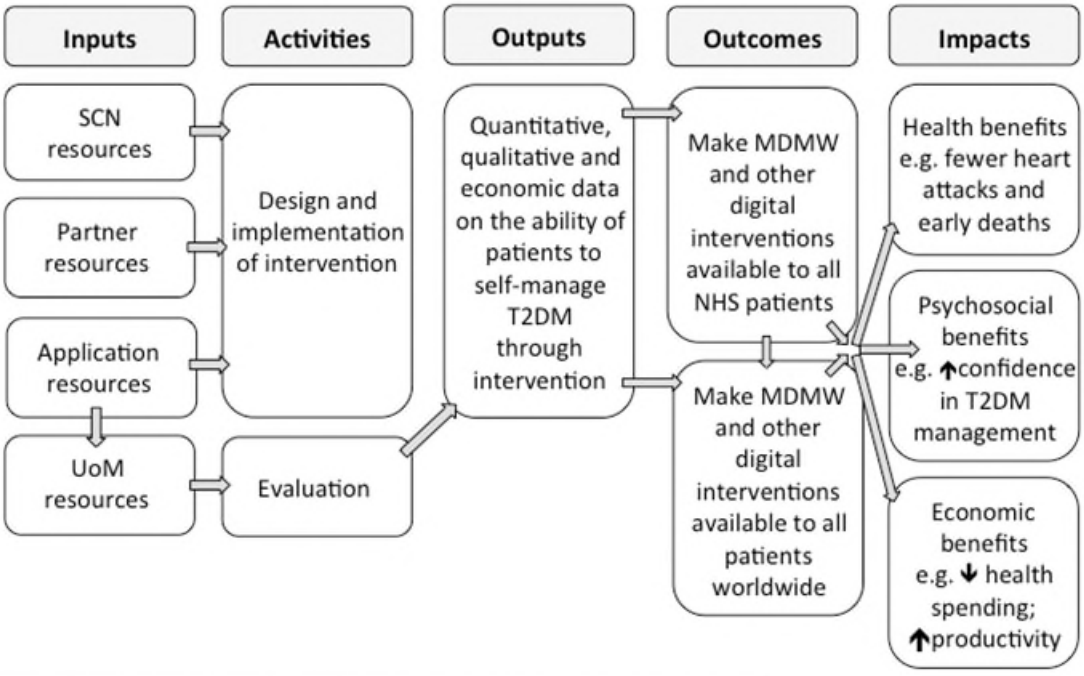
a) **Demonstration of improved T2D self-management and risk factor levels**: If the evaluation shows that My DiabetesMyWay (DMW) and the linked digital behavioural interventions (Oviva and Changing Health) can improve self-management and risk factor levels in people with T2DM then this could lead to a step-change in diabetes management across the NHS and wider. If the economic analysis shows cost savings compared to traditional care then this would lead to global changes in healthcare delivery. Therefore the clinical, psychological, social, economic and healthcare resource benefits observed through this application could have global reach.
b) **Demonstration of improved diabetes distress scores through MyCognition**: If MyCognition can improve psychological health in people with T2D then these data could be used to promote this approach being rolled out across the NHS, which could reduce the huge public health burden of psychological illness associated with T2D.

7.9: Potential research, economic and policy implications of positive results

The broad implications of this study are summarised in the high-level logic model shown in **Figure 2** (below) and include research, economic and health policy impacts:

a) **Research implications:** There is a major global epidemic of T2D that is being followed by a wave of cardiovascular disease and premature mortality. If we are able to show that digital interventions in patients with diabetes can have major clinical, societal and economic benefits then this will be a massive global stimulus to research in this area. Researchers and healthcare managers will be interested in the context in which the interventions were delivered (patients and healthcare system) and the methods of implementation adopted in the Test Bed. The research will have implications for pharmaceutical companies and other companies involved in producing treatments, interventions and digital interventions in diabetes care.

Figure 2: High-level logic model defining inputs and expected outputs



MDMW, My Diabetes My Way, SCN, Strategic Clinical Network; T2DM, type 2 diabetes; UoM, University of Manchester

b) **Economic implications**: In 2011, diabetes consumed 10% (£10 billion) of the NHS budget and when indirect costs were included (mortality data, sickness data, loss of productivity and informal care) the cost was estimated at £23 billion. If digital interventions have only a small impact on the self-management of T2D and its complications, then the absolute economic benefits may still be large. The largest cost of managing diabetes comes from the cost of managing its complications. If interventions targeting the management of cardiovascular risk (DMW and behavioural interventions primarily) are successful then this could have major financial benefits in the UK and globally.

c) **Policy implications:** The treatment of T2D is central to the Government's 2011 National Service Framework (NSF) for diabetes. Our research addresses key NSF standards. NSF standard 4 states that, "All adults with diabetes will receive high-quality care…to optimise the control of their blood glucose, blood pressure and other risk factors for developing the complications of diabetes." If our research shows the expected outcomes then we will work with leading figures in the Department of Health, Public Health England, NHS England and NICE to ensure that future policies and guidance include appropriate reference to our work. This project also maps to the aims of: i) **The NHS 10-year Plan (2019)**; ii) **The NHS England Digital Health Strategy**; iii) the **National Information Board Personalised Health and Care 2020 plan** and iv) The **'State of the Nation'** report (2016) produced by Diabetes UK.

8) DATA COLLECTION, SOURCE DATA AND CONFIDENTIALITY

8.1. Data collection & management

8.1.1: Overview of data items and source of data by intervention

a) DMW

- **Participant data from GP records via DMW and Greater Manchester Care Record 1st April 2016-31st March 2022:** Age, Sex, Ethnicity, GP postcode (to assess deprivation), diabetes type and duration, blood pressure, HbA1c, cholesterol, creatinine, eGFR, urinary albumin creatinine ratio, smoking and bodyweight/height/BMI, medication, diabetes clinic attendance in primary care, hospital visits including emergency visits.
- **Participant data from DMW :** ethnicity (self provided (unreliable from primary care due to missing data), user experience, service use and website activity. These data will be provided for all DMW users enrolled from July 2019 onwards
- **Control data from Greater Manchester Care Record on people not using DMW, 1st April 2016-31st March 2022:** Age, Sex, Ethnicity, GP postcode (to assess deprivation), diabetes type and duration, blood pressure, HbA1c, cholesterol, creatinine, eGFR, urinary albumin creatinine ratio, smoking and bodyweight/height/BMI, medication, diabetes clinic attendance in primary care, hospital visits including emergency visits.
- **Participant data from focus groups and 1:1 interviews conducted by the research study psychologist with consent:** user experience, knowledge and ability to self manage.
- **Primary care staff data from focus groups and 1:1 interviews conducted by the research study psychologist with consent:** user experience and impact on care pathways.

b) Behavioural interventions: Oviva and Changing Health

- **Participant data from GP records via DMW and Greater Manchester Care Record 1st April 2016-31st March 2022:** as DMW (above)
- **Control data from Greater Manchester Care Record on people not using Oviva and Changing Health, 1st April 2016-30th June 2022:** as DMW (above)
- **Participant data from Oviva and Changing Health via DMW:** as DMW (above)
- **Participant data from Oviva and Changing Health:** usability data.

c) MyCognition

- **Participant data from GP records via DMW and Greater Manchester Care Record 1st April 2016-31st March 2022**: as DMW (above)
- **Control data from Greater Manchester Care Record on people not using MyCognition, 1st April 2016-31st March 2022:** as DMW (above)
- **Participant data from DMW**: as DMW (above) plus cognition scores, diabetes distress scores (see online diabetes distress score questionnaire 22March19) and usability data.

8.1.2: Clinical and biochemical data *in study participants*

Clinical data collected by health care professionals during routine clinical care will entered onto the appropriate clinical management system (e.g. General practitioners using the EMIS health primary care electronic health record). Pseudonymisation is a technique that replaces or removes all information that could be used to identify an individual. The process involves replacing names or other identifiers that are easily attributed to individuals with a **study reference number**. DMW will provide pseudonymised data on study participants and controls to the University of Manchester (see data flow map in **figure 3)**.

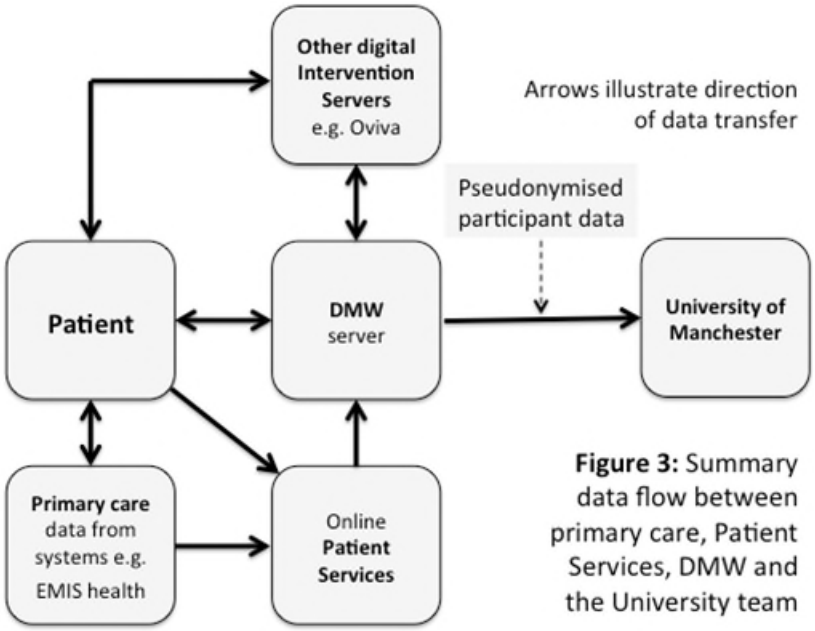


Figure 3: Summary data flow between primary care, Patient Services, DMW and the University team

Clinical data: The clinical data of interest includes: age, sex, ethnicity, deprivation, diabetes type, weight, height, BMI, HbA1c, blood pressure level, diabetes medication, blood pressure medication, lipid lowering therapy and service usage data (attendance and non-attendance at diabetes clinics; emergency hospital visits) will be taken from Primary Care records. Ethnicity will be taken from in self-reported data provided at enrolment with DMW (White/South Asian/Black/Mixed/other (if 'other' participants will be invited to specify using text). Deprivation will be assessed from the GP postcode to reduce the likelihood of participants being identified.

Biochemical data: All blood sampling (e.g. HbA1c and serum lipids) will be conducted via routine clinical care. Participants who have not had a blood sample taken within the preceding 3-6 months will be advised through a message on the DMW website to arrange a diabetes review (weight, blood pressure, smoking status, medication review, HbA1c and lipids) with their practice team at the time of enrolment ***in line with standard clinical care according to NICE guidance 28***.[14] Participants will be advised to have repeat weight, blood pressure, medication review and blood tests every 3-6 months in line with standard clinical care according to NICE guidance 28.[14] Study participants will not be subject to any investigations outside of their routine care unless clinically indicated. Blood tests results will be transferred to DMW from the primary care record.

Duration of data access: Through DMW, the University of Manchester will request primary care data on study participants for the period: **1st April 2016-31st March 2022**. This will enable a 3-year assessment of "baseline" levels of risk factors such as HbA1c and blood pressure prior to study commencement (July 2019), and up to the end of the intervention (31st March 2022).

8.1.3: Clinical and biochemical data from Greater Manchester Care Record *in participants and in controls not providing consent:*

Our study involves comparing intervention-related changes in risk factors, such as is HbA1c, in study participants with the changes occurring in a control patient cohort not receiving the intervention.

Greater Manchester Care Record will provide GP data on all patients with Type 2 Diabetes across Greater Manchester (approximately 160K people) between: 1st April 2016-31st March 2022. The core data items will include: Age, Sex, Ethnicity, GP postcode (to assess deprivation), diabetes type and duration, HbA1c, blood pressure, cholesterol, creatinine, eGFR, urinary albumin creatinine ratio, smoking and bodyweight/height/BMI, medication, diabetes clinic attendance in primary care, hospital visits including emergency visits.

In order to distinguish between DMW participants and non-participants in Greater Manchester Care Record data the following steps will be taken:

1. DMW will supply Graphnet with details of DMW participants including:
    a. NHS numbers
    b. GP practice with which the participant is registered
    c. DMW generated study ID
    d. Whether the participant is using Oviva, Changing Health or MyCognition
2. Graphnet will use NHS numbers of participants to create a 'DMW participant flag' within the Greater Manchester Care Record. NHS Numbers will then be removed
3. Graphnet will supply the University of Manchester with Greater Manchester Care Record data for patients from Greater Manchester with Type 2 diabetes
4. University of Manchester will store and analyse these data in accordance with the Greater Manchester Care Record requirements and Data Sharing Agreement

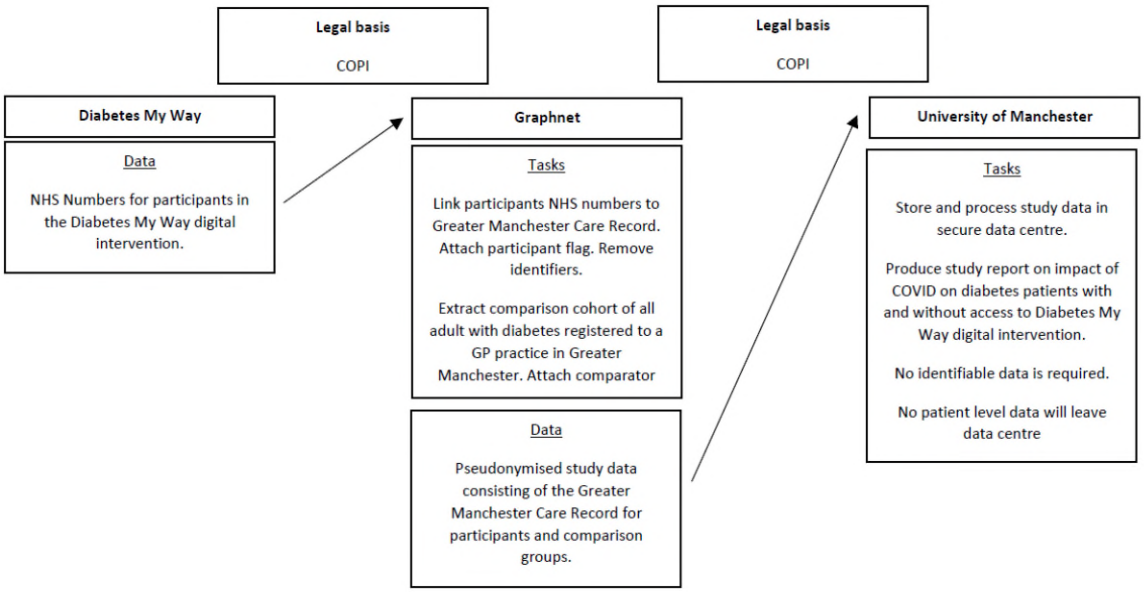
Our study design requires that control participants are matched to participants receiving the intervention on age, sex, ethnicity, deprivation (defined by GP postcode). We therefore require information on these 4 characteristics in addition to the clinical and biochemical data. Deprivation level will be assessed from the GP postcode to minimise the risk of patients being identified. The University of Manchester will not receive any information that will enable DMW participants or control participants to be identified.

The legal basis under which the University of Manchester is accessing these data is the Health Service Control of Patient Information (COPI) Regulations 2002 and Article 6 (1)(E) [Public Task] and Article 9 (2)(j) (Research) of the General Data Protection Regulation. The COPI notice means we are accessing this data to learn more about Covid-19, specifically how people with diabetes have managed their care during the pandemic.

Through the COPI mechanism, the University of Manchester will be provided with data on participants and controls. **No data will be provided by the University of Manchester to the Commercial partners.**

Processing of Greater Manchester Care Record data

- DiabetesMyWay will provide Graphnet with the NHS numbers of those individuals who are participating in the interventions along with GP practice, the DMW generated study ID and whether the participant is also using Oviva, Changing Health or MyCognition. These data represent the only flow of data into Graphnet. This will be patient level data.
- Pseudonymised Greater Manchester Care Record data will flow out of Graphnet. This will be patient level data.
- There are no subsequent flows of data
- Greater Manchester Care Record data will be processed to determine whether the DiabetesMyWay app provides effective self-management support for people with type 2 diabetes across Greater Manchester during the Covid-19 pandemic. The data will be analysed using the statistical packages Stata and R. Statistical regression methods will be used which will output regression results tables. No record level data will be produced as an output at any stage, only aggregated date (with small numbers suppressed in line with the Greater Manchester Care Record guidance). Descriptive statistics tables of the data will be produced which will aggregate the data by year/month. Graphs will be produced to describe the data and these graphs will also aggregate the data by year. The outputs produced cannot be used to identify patients or sensitive information.
- There are no data linkages.
- There will be no requirement/attempt to re-identify individuals.
- Data processing will only be carried out by substantive employees of the University of Manchester who have been appropriately trained in data protection and confidentiality.
- The data will be stored within an access restricted data share on the University's network storage infrastructure, which is the recommended location for storing sensitive or critical University data. The storage infrastructure is hosted across two data centres for resilience and disaster recovery purposes.
- Physical access to the data centres is strictly limited to data centre staff and a limited number of authorised IT Services staff. The data centres are protected by physical and electronic access security systems, swipe card access in and out of the data centres and CCTV coverage.
- Processing of the data will take place on the iCSF infrastructure of the University of Manchester.



8.1.4: Secure data extraction and transfer

The DMW service relies on the availability of near-real time clinical data – see data flow map in **figure 3**. These data will be extracted from ***Patient Services*** via an automated nightly secure file transfer. All primary care practices linked to Patient Services within GM are eligible to participate. ***Patient Services*** will be invited to sign up to an Information Sharing Agreement (ISA) with DMW. No data will be transferred from primary care practices that have not linked to ***Patient Services***. DMW will store clinical data including contact details for 5 years on an encrypted database within a secure server that complies with GDPR. MDWM data is hosted with BrightSolid: Approved NHS Scotland Managed Hosting Partner – www.brightsolid.com. BrightSolid hold ISO Accreditation, including IS027001 and ISO22301.

Data from the other digital interventions in the project e.g. Oviva data will be transferred to the DMW database on a daily basis. The DMW cipher will be used to re-identify the patient to allow storage of patient data from other digital intervention databases within the DMW patient record.

8.1.5: Transfer of pseudonymised data to the University of Manchester

The DMW chief technical officer will extract study data from the DMW database. Data will be pseudonymised and transferred via a secure file transfer system. The data controller for identifiable clinical data is DMW and will maintain control over the pseudonymisation cipher.

8.1.6: Data management system within the University of Manchester

Following transfer to the University of Manchester (UoM) research team, the pseudonymised data extract will be held for 5 years after the end of the study (31st March) within a password controlled, encrypted UoM computer. Data will be backed up within the university server.

The data analysis will follow the study protocol and the individual requirements of the investigators. The study database will be compliant with University of Manchester standard operating procedures including the Data Management Policy for Clinical Research and others listed below:

a) The University of Manchester Research Data Management Policy
http://documents.manchester.ac.uk/DocuInfo.aspx?DocID=33802%20
b) The University of Manchester Records Management Policy
http://documents.manchester.ac.uk/display.aspx?DocID=14916
c) The University of Manchester Data Protection Policy
http://documents.manchester.ac.uk/display.aspx?DocID=14914
d) The University of Manchester Publications Policy
http://documents.manchester.ac.uk/display.aspx?DocID=28526
e) The University of Manchester Intellectual Property Policy
http://documents.manchester.ac.uk/display.aspx?DocID=24420
f) The University of Manchester IT policies and guidelines
http://www.itservices.manchester.ac.uk/aboutus/policy/

The database will be managed in line with all applicable principles of medical confidentiality and UK law on data protection, namely, the Data Protection Act 2018, which brought UK law into line with the EU Data Protection Directive, the General Data Protection Regulation (GDPR) and Common Law Duty of Confidentiality.

9. STATISTICAL CONSIDERATIONS

9.1 Statistical Analysis

9.1.1: Anticipated cohort sizes for the main study and sub-studies:

a) ***DMW*** (n=7,000-14,000; with smaller subgroups also involved in sub-studies)

We anticipate that 7,000-14,000 participants will be enrolled between from the date of REC/HRA approval 2019 and 31st March 2022;

b) ***Behavioural interventions: Oviva*** (n=600) and ***Changing Health*** (n=600)

We will invite up to participants to enrol with either *Oviva* or *Changing Health* behavioural interventions until 600 have attended with each intervention. These interventions will be offered to alternate participants ensuring that numbers receiving each intervention remain similar.

c) ***MyCognition*** (n=1000)

All DMW participants will be provided with the option of completing the *MyCognition* online cognitive assessment and will be offered the *MyCognition* intervention until 1000 have completed the intervention. When 1000 people have completed intervention, DMW participants will continue to be offered the option of completing the *MyCognition* online cognitive assessment but will not be offered the *MyCognition* intervention. Participants will be invited to complete the *MyCognition* online cognitive assessment every 3 months during the study (maximum 3 times). Those completing these assessments, but without receiving the intervention, will act as a control group.

9.1.2: Design

DMW, the **behavioural interventions**: (***Oviva*** and ***Changing Health***), ***MyCognition*** will be controlled before-after studies. Intervention-related changes in endpoints such as glucose level will be assessed from changes in HbA1c and other endpoints (see **section 7.1**)

9.1.3: Sub-groups: we will assess outcomes in South Asians, Blacks, and Whites and in those in the least and most deprived quintiles.

9.1.4: Modifying factors: we will consider the influence of age, sex, ethnicity, deprivation, cognitive function (assessed by *MyCognition*), and level of engagement with digital interventions on outcomes using stratification and interaction effects as appropriate.

9.1.6: Modelling

In addition to analyses comparing outcomes within groups, statistical modelling will be performed to assess the impact of interventions (***DMW***, the **behavioural interventions**: (***Oviva*** and ***Changing Health***), ***MyCognition interventions***) after controlling for clinical covariates***:*** For example linear or logistic regression models will assess changes in outcomes after adjusting for baseline: age, sex, ethnicity and deprivation, smoking status, treatment type (diet, orals, GLP1 receptor analogues, insulin), BMI, and secondary vs. primary care attendance if data available.

9.1.7: Missing data

The proposed analysis allows for missing data values. However, we may apply multiple imputation methods depending on the extent of missing data.

9.1.8: Analysis of economic outcome data

The economic analysis will calculate the total costs required to deliver the Test Bed, capturing NHS England costs and Test Bed partner costs. Where possible, these costs will be grouped to distinguish between the costs of innovation, set-up and running. This information will be available from NHS England and each Test Bed Partner.

In addition to the direct Test Bed costs the economic analysis will also consider the impact on costs of changes in service utilisation. For example, changes in referral rates for traditional psychological interventions (MyCognition outcome). Changes in the resources used will be costed

using national unit-costs obtained from Personal Social Services Research Unit (PSSRU) unit costs for Health and Social Care [https://www.pssru.ac.uk/project-pages/unit-costs/] and from NHS Reference Costs [https://improvement.nhs.uk/resources/reference-costs/]. A priori it is unknown if these changes in utilisation costs will be positive or negative.

The primary mechanism by which the Test Bed will impact the NHS budget is via the long-term impact the Test Bed has on patients with type 2 diabetes. The hypothesised reduction in HbA1c, bodyweight/BMI, blood pressure, cholesterol and smoking resulting from a successful implementation and adoption of DMW, Oviva and Changing Health has the potential to increase the quality adjusted life expectancy of these patients. Changes in quality-adjusted life expectancy will be modelled using the established UKPDS Outcomes Model [https://www.dtu.ox.ac.uk/outcomesmodel/]. Changes in relevant risk factors (HbA1c, bodyweight/BMI, blood pressure, cholesterol and smoking) will be provided by the effectiveness evaluation and used as model parameter values in the UKPDS Outcomes Model. Forecasted changes in quality adjusted life expectancy will be valued using the NICE threshold and offset against Test Bed costs.

9.2 Sample Size Calculations:

a) DMW, Oviva and Changing Health evaluations: The primary outcome is intervention-related HbA1c change. Assuming an HbA1c SD of 15 mmol/mol,[15] 500 patients provides 80% power to detect an adjusted intervention-related HbA1c difference of 2 mmol/mol ($p<0.05$); 5 mmol/mol is the smallest treatment effect that might be considered clinically significant. Since the study is expected to enrol many more participants, there is adequate power for the main analyses. With ~100 participants ethnicity and deprivation-defined subgroups taking part in DMW and behavioural interventions (600 licences purchased each for Oviva and Changing Health) the study has 80% power to detect an adjusted intervention-related between-group HbA1c difference of 5 mmol/mol ($p<0.05$) and therefore is adequately-powered to detect small clinically significant treatment effects within these subgroups.

Based on prior studies the simple sizes of focus groups and 1:1 qualitative interview cohorts will be sufficient for their purposes (see **Section 9.1.1**).

b) **MyCognition evaluation**: The primary outcome is intervention-related change in 'diabetes distress score (DDS)'. Assuming a SD of 0.92 [16], 140 patients in each group provides 80% power to detect an adjusted intervention-related DDS difference of 0.3 ($p<0.05$); a small clinically significant treatment effect (1/3 of SD).

10. DATA MONITORING AND QUALITY ASSURANCE

The study will be subject to the audit and monitoring regime of the University of Manchester (Sponsor). Since the risks to study participants are low we have no plans to create a data monitoring committee. If any significant safety concerns are raised during the course of the study then this will be communicated to the sponsor along with appropriate intervention as required.

11. SAFETY CONSIDERATIONS AND ADVERSE EVENTS

Low-risk interventions: Clinical risks to study participants are minimal because all of the proposed interventions involve market-ready products in current use with excellent established safety records and no reported safety concerns.

Clinical decisions remain with usual clinical staff: The interventions described are designed to support self-management and enhance routine clinical care. Clinical decisions relating to the prescribing of medication will **not** be made directly by any of the interventions involved in the study. Clinical staff responsible for the routine care the patients will always remain responsible for prescribing decisions.

Adverse events: Since the study is very unlikely to lead to significant levels of clinical risk we will not be recording adverse events including serious adverse events.

12. PEER REVIEW

The application has undergone extensive peer review to assess the scientific quality and patient acceptability including assessment by:

- Professor Michael Grant, University of Manchester (giving MAHSC approval at the time of the grant submission)
- All members of the study steering committee
- Leading staff supporting the digital interventions involved in the application
- The Sponsor (University of Manchester) including Lynne MacRae (Research Practice Governance Manager) and members of her team including Laurence Malbeaux-King (Information Governance) and Mohammed Zubair (Research Governance, Ethics and Integrity including advice on devices)
- Patient groups: locally led by Alan Campbell and Diabetes UK through Yvonne Browne, Improving Care Manager, Diabetes UK Wells Lawrence House, London

13. PATIENT AND PUBLIC INVOLVEMENT

- We have many examples of how PPI has helped shape this project. For example:
    - DMW has had patients involved in every stage of the design, prototyping, development, implementation and review phases of the intervention. The company receives regular feedback from patients by email, secure messaging and online surveys to ensure that the intervention is genuinely patient-centred. The company holds regular steering group meeting including representation by patients. In addition all new product development work involves users - usually through design workshops and through user prototype testing in the field. Early feedback (and ongoing feedback on rollout) continue to drive changes to the DMW product range.
    - *Oviva* Diabetes Support conducts PPI through its continuous patient feedback via surveys which is reviewed monthly and changes to the intervention are made as appropriate.

- *Changing Health* sends out feedback surveys to all users at baseline and subsequently every 3 months. The data from these surveys are used to identify potential issues and to continually refine their programme. In addition to this formal channel, *Changing Health* also has a presence on social media (Facebook and Twitter) through which they share user stories and original content of interest to the public.

14. ETHICAL and REGULATORY CONSIDERATIONS

14.1 Approvals

NHS Research Ethics Committee approval will be obtained before commencing research. The study will be conducted in full conformance with all relevant legal requirements and the principles of the Declaration of Helsinki, Good Clinical Practice (GCP) and the UK Policy Framework for Health and Social Care Research 2017.

The University of Manchester (acting as Sponsor) has approved and endorsed the study along with the local clinical commissioning groups and the local NHS Trusts.

Caldicott guardian approval will be sought by the CI (acting for the University of Manchester) to access and obtain study data from DMW.

14.2 **Risks**

Clinical risks to study participants are minimal because all the proposed interventions involve market-ready products already being used by the public through the NHS Scotland, or through direct personal sales, and these interventions have no reported safety concerns.

Any risks to study participants relate largely to potential data security issues and specifically to the potential release of personal data. However, the risk of a data security breach occurring will be very low because of the following proposed actions described in our *Data Management Plan (attached)*:

- DMW has appropriate policies and procedures in place to manage data on thousands of patients with diabetes within the NHS in Scotland. DMW will store clinical data on an encrypted database within a secure server that complies with ISO27001 and GDPR.
- Any identifying personal data will be removed so that the analysis performed by the University of Manchester will be undertaken using pseudonymised data. The key for unlocking the personal data will be available only to the PI from DMW and this will be stored securely.
- Only summary data will be reported on and shared with collaborators (no personal data will be shared).

15. DEVICE STATUS and NEED FOR MHRA approval

Our study involves *MyCognition* which is CE approved and registered at the MHRA as a class 1a device. *MyCognition* is stand-alone software that does not perform a clinical diagnostic process, and hence is classified as low risk. MyCognition has been reviewed ORCHA (the World's leading

health app evaluation) is posted on their website as a tool for use by healthcare professionals in primary care.
All of other apps/ interventions used in our application are **not** classified as medical devices. Our protocol has been reviewed by the University of Manchester's Research Governance, Ethics and Integrity Team who stated that the research does not meet the criteria of a clinical investigation of a medical device and therefore does not require MHRA input/approval. A copy of this email is provided as an attachment with the application.

16. TERMS AND CONDITIONS

A copy of the terms and conditions and privacy notices related to DMW and the other digital collaborators innovators is available personal attachment to this application.

17. STATEMENT OF INDEMNITY

The University has insurance available in respect of research involving human subjects that provides cover for legal liabilities arising from its actions or those of its staff or supervised students. The University also has insurance available that provides compensation for non-negligent harm to research subjects occasioned in circumstances that are under the control of the University.

18. FUNDING and RESOURCES

This research is part of a £1.2m project. £0.9m is externally funded by Innovate UK with the remainder funded by the innovator SME partners. The University of Manchester element of the funding totals £292,950 and is full funded (100%) by Innovate UK so no additional funding is required for evaluation. The overall grant offer has been received by the lead partner (GMEC SCN) and has been formally accepted, and the research element of the funding has been confirmed. The detailed breakdown of the total grant, including the research element of the award/spend (which will fully fund this study) is as included in the Appendix.

19. PUBLICATION POLICY

Should the expected outcomes be demonstrated then we will take the following steps to ensure that results are useful to the NHS and the global clinical community: a) *Ensure effective dissemination of results:* i) Deliver conference presentations; ii) Peer-review publications; iii) Run a engagement workshop on *'Digital solutions to improve diabetes self-management'* which will involve senior clinicians, NHS England, public health staff, diabetes charities, academics, patients and the general public; iv) Social media postings; v) Give radio and TV interviews; and *b) Present the results in ways that create maximum utility for clinical users* e.g. Clearly describe the practical steps necessary to introduce the system. Participants be provided with a summary of the main study findings through the DMW website.

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21) APPENEDIX

a) List of additional documents: Introductory letters, text and emails, Patient information sheets, GP letters, usability questionnaires, diabetes distress questionnaire and other documents

Communication with patients

- Introductory letter DMW 22March19 (by post)
- Introductory text DMW 22March19
- Introductory email DMW 22March19

- Patient information Sheet DMW 22March19 (provided online)
- Patient information Sheet Oviva 22March19 (provided online)
- Patient information Sheet Changing health 22March19 (provided online)
- Patient information Sheet MyCognition 22March19 (provided online)

Communication clinical staff

- GP information letter DMW via email 22March19 (emailed)
- GP information letter Oviva via email 22March19 (emailed)
- GP information letter Changing Health via email 22March19 (emailed)
- GP information letter MyCognition via email 22March19 (emailed)

Usability questionnaires

- Usability questionnaire DMW 22March19 (to be completed online)
- Usability questionnaire Oviva 22March19 (to be completed online)
- Usability questionnaire Changing health 22March19 (to be completed online)
- Usability questionnaire MyCognition 22March19 (to be completed online)

Other questionnaires

- Diabetes Distress Score questionnaire (to be completed online)

Other documents

- IRAS form
- Data management plan
- Terms and conditions in relation to DMW and other digital interventions
- Privacy notices in relation to DMW and other digital interventions
- Insurance assessment form
- Schedule of events
- Statement of activities
- UoM Research Governance advice on Device and MHRA status

b) Details of funding

Eligible costs and grant allocations
File reference: 104658
Application number: 15790

Competition: NHS Test Beds: testing innovations to address health and care challenges - Full stage
Project title: DiabetesMyWay (formally GM DiabetesMyWay)

Industry costs	**Greater Manchester Strategic Clinical Networks**	**Changing Health Ltd**	**Myway Digital Health Ltd**	**Oviva UK Ltd**	**The Smart Care Doc Company Ltd ***	**Total (industry)**
Labour	£126,121	£52,579	£352,172	£90,575	£33,793	£655,240
Overheads	£25,224	£10,516	£70,434	£18,115	£6,759	£131,048
Materials	£0	£0	£7,044	£1,545	£34,600	£43,189
Capital usage	£0	£0	£1,761	£973	£538	£3,272
Subcontract	£0	£0	£55,318	£0	£0	£55,318
Travel and subsistence	£0	£0	£3,520	£4,394	£10,332	£18,246
Total eligible costs	£151,345	£63,095	£490,249	£115,602	£90,022	£910,313
Rate of grant (%)	100.00%	70.00%	70.00%	70.00%	70.00%	74.99%
Total grant	£151,345	£44,166	£343,175	£80,921	£63,015	£682,622

Academic costs		**University of Manchester**
Directly incurred	Staff	£123,638
	Travel and subsistence	£0
	Equipment	£0
	Other costs	£3,200
Directly allocated	Investigators	£24,415
	Estates	£23,071
	Other DA	£0
Indirect costs	Indirect costs	£118,626
Exceptions	Staff	£0
	Travel and subsistence	£0
	Equipment	£0
	Other costs	£0
	Total eligible costs	£292,950
	Rate of grant (%)	100.00%
	Total grant	£292,950

**SmartCareDoc* was planning to provide videoconferencing facilities as part of this study. Unfortunately, since the award was given, the company has ceased to operate in England and therefore the funds will either be reallocated to other parts of the study or will be withdrawn by NHS England. Discussions are underway make decisions on this funding.

Summary	**Totals (£)**
Total project costs	£1,203,263

Total project grant	£975,572
Rate of grant (%)	81.08%