**RESEARCH PROTOCOL**

# Healthy Living Diabetes - Long-term Independent National Evaluation (HED-LINE)

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## 2 Study Synopsis

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| **Title** | Healthy Living Diabetes - Long-term Independent National Evaluation (HED-LINE) |
| **Background** | Type 2 diabetes can cause serious health problems. If people with type 2 diabetes make changes to their lifestyle they can reduce their risk of greater health issues. The NHS is introducing a web-based service called 'Healthy-Living' which is being offered to people with type 2 diabetes in England, to help them to change their lifestyle and reduce their health risks. |
| **Aims** | The overall aim is to evaluate the real world implementation of Healthy-Living, a web-based self-management programme for people diagnosed with Type 2 diabetes.<br>Objectives<br>1. To examine the extent to which people with type 2 diabetes start Healthy-Living and continue to use it, and whether engagement varies by patient characteristics (WP1).<br>2. To determine the effectiveness of Healthy-Living in changing clinical outcomes (WP1)<br>3. To assess the barriers and facilitators affecting the implementation of Healthy-Living at clinical and organisational levels (WP2a) |

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| | 4. To assess the fidelity of implementation of healthy-living and its acceptability to patients and the NHS Work (WP2b)<br>5. To establish the cost-effectiveness of Healthy-Living compared to usual care when rolled out across England, from an NHS and personal and social services perspective (WP3) |
| **Design** | We have designed a study to help the NHS understand whether 'Healthy-Living' is a good use of NHS resources. We will analyse information gained from Healthy Living, and general practice records, to see what kind of patients are invited onto the programme, and whether they complete the programme. We will match people referred and not referred to the programme and report on whether referred patients show improved outcomes, such as healthier levels of blood sugar and losing weight, compared to those who were not referred to the programme. We will see if some patients have better outcomes than others and try to find out why. We will interview NHS clinical staff and managers responsible for the Healthy Living programme throughout England. We will ask them how they set up the service and what things they think help or hinder the programme. We will analyse information gained from Healthy Living and interview patients to see how well the Healthy Living programme is delivered to patients and check that they receive all of the self-management materials they need to succeed. We will suggest what might be improved. We will look at whether the programme offers good value for money.<br>This information will be reported back to the people running Healthy Living so they can make improvements as they go along. Our team has the necessary skills and experience to do this research as we have done similar work in the past. |
| **Planned Sample Size** | 138 qualitative interviews<br>We will undertake quantitative analysis of a peudonymised Linked Dataset which we anticipate will include several hundred thousand records. A sample size calculation for this is reported in the protocol. |
| **Analyses** | Our overarching evaluation framework will be *RE-AIM*, which has been applied to a variety of public health and long-term condition programmes.<br>WP1 Participation and Effectiveness: Regression modelling to examine what personal and health characteristics affect participation in the programme. |

People referred to Healthy-Living will be matched to people not invited, using their baseline characteristics. Following matching, various multiple regression models will be used to examine the health outcomes of those who were referred to the programme, compared to those who were not, to test whether the intervention is effective in improving the health of patients. We will also use similar regression methods to consider the effect for those who take up the offer of attending the programme, compared to those who were not referred. We will also use regression methods to examine who the programme is most effective for, with particular attention to health inequalities

WP2 Process evaluation:

Work Package 2a: Interview schedules will be used to guide interviews and are expected to develop as data collection and analysis of early interviews progress. Interviews will be thematically analysed using a modified framework approach. We will initially take an inductive approach to theme generation; subsequent theme refinement will be deductive and informed by Normalisation Process Theory (NPT) and Non-adoption, Abandonment, Scale-up, Spread and Sustainability (NASSS) Framework. Interpretive themes will be refined through discussion at regular analysis meetings.

Work Package 2b (phase 1 and 3): Interview schedules will be used to guide interviews and are expected to develop as data collection and analysis of early interviews progress. Interviews will be thematically analysed using a modified framework approach. The NIH-BCC framework will inform development of a priori thematic codes with additional codes developed inductively from initial coding. The coding framework will then be applied to analysis of subsequent transcripts, with ongoing adaptations until no new themes emerge. Data will then be charted into the matrices with illustrative extracts and interpretive themes refined through discussion at regular analysis meetings.

Work Package 2b (phase 2): data usage patterns will be explored using exploratory statistics such as frequencies and data visualisation, in line with the AMUSED framework for analysing such data.

WP3 Cost Effectiveness: We will carry out an economic evaluation informed by modelling to estimate longer-term benefits and costs, in line with current NICE decision-making. We will use an existing model, UKPDS OM2, which has

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| | been extensively validated and is designed to extrapolate T2DM risk factors to predict long-term outcomes expressed as life expectancy, quality-adjusted life-years (QALYs). |

# 3 Introduction

Type 2 diabetes can cause serious health problems. If people with type 2 diabetes make changes to their lifestyle they can reduce their risk of greater health issues. The NHS is introducing a web-based service called 'Healthy-Living' which is being offered to people with type 2 diabetes in England, to help them to change their lifestyle and reduce their health risks.

We have designed a study to help the NHS understand whether 'Healthy-Living' is a good use of NHS resources. The study is funded by the National Institute of Health Research.

We will analyse information gained from Healthy Living, and general practice records, to see what kind of patients are invited onto the programme, and whether they complete the programme. We will match people referred and not referred to the programme and report on whether referred patients show improved outcomes, such as healthier levels of blood sugar and losing weight, compared to those who were not referred to the programme. We will see if some patients have better outcomes than others and try to find out why. We will also look at whether the programme offers good value for money.

We will interview NHS clinical staff and managers responsible for the Healthy Living programme throughout England. We will ask them how they set up the service and what things they think help or hinder the programme. NHS clinical staff and managers will be interviewed one time, over the telephone and it will last about one hour.

We will analyse information gained from Healthy Living and interview patients to see how well the Healthy Living programme is delivered to patients and check that they receive all of the self-management materials they need to succeed. Patients will be interviewed one time, and it will last about one hour. Interviews with patients will be conducted either face to face or via telephone.

This information we find out will be reported back to the people running Healthy Living so they can make improvements as they go along. Our team has the necessary skills and experience to do this research as we have done similar work in the past.

# 4 Background and Rationale

The health implications of type 2 diabetes are serious (loss of vision, nerve pain, limb amputation, and cardio-vascular complications). Type 2 diabetes costs the NHS £10 billion per year (9% of the total NHS budget).

Appropriate blood glucose and blood pressure control, and changes in lifestyle to reduce weight can reduce these risks, but people often find it difficult to make (and maintain) changes. Structured Type 2 diabetes education programmes are recommended by the National Institute of Health and Care Excellence (NICE), but attending groups is not suitable for everyone.

'HeLP-Diabetes' was developed (by a team at UCL) as a digital alternative to face-to-face support. This is a web-based self-management programme which offers information about type 2 diabetes, content to promote skills and behaviour change and provides support for emotional well-being. In a recent trial, it was found that 'HeLP-Diabetes' was feasible to deliver, acceptable to patients and cost-effective for the NHS.

Now the NHS wants to implement a version of HeLP-Diabetes called 'Healthy-Living' across England and see if there are similar benefits from a large-scale roll-out. Access to Healthy-Living will be by self-referral (with some GP-referral). It will be a self-contained, self-directed service delivered at scale. Type 2 diabetes is more prevalent in people from deprived areas, who may find it more difficult to make lifestyle changes. It will also be important to understand whether Healthy-Living can attract and retain people living in such areas.

Healthy-Living is a significant investment of NHS funds. Although it is based on the evidence from the HeLP-Diabetes trial, we know that translating evidence into practice is challenging.

A high quality study is required to provide ongoing, independent feedback to the programme on the success of roll-out and to provide a longer term assessment of the effectiveness of the Healthy-Living programme in comparison to usual care.

FUNDING: This research is independent research funded by the National Institute for Health Research (Policy Research Programme, Healthy Living Diabetes - Long-term Independent National Evaluation (HED-LINE), NIHR200933). The views expressed in this protocol are those of the author(s) and not necessarily those of the National Institute for Health Research or the Department of Health and Social Care.

# 5 Study objectives

The overall objective is to evaluate the real world implementation of Healthy-Living, a web-based self-management programme for people diagnosed with Type 2 diabetes.

Work Package 1 Uptake and Effectiveness: To examine the extent to which people with type 2 diabetes start Healthy-Living and continue to use it, and whether engagement varies by patient characteristics. To determine the effectiveness of Healthy-Living in changing clinical outcomes.
Work Package 2a Implementation: To assess the barriers and facilitators affecting the implementation of Healthy-Living at clinical and organisational levels
Work Package 2b Delivery and Fidelity: To assess the fidelity of implementation of healthy-living and its acceptability to patients and the NHS
Work package 3 Health Economics: To establish the cost-effectiveness of Healthy-Living compared to usual care when rolled out across England, from an NHS and personal and social services perspective

# 6 Research plan

## 6.1 Evaluation framework

Our overarching evaluation framework will be *RE-AIM*, which has been applied to a variety of public health and long-term condition programmes, including the translation of findings to other settings.[6] Our process evaluation will draw on the *Nonadoption, Abandonment, Scale-up, Spread, and Sustainability* (NASS) Framework[7] and *Normalisation Process Theory* (NPT). [8 9] Both have been used to evaluate implementation of digital interventions for long-term conditions.

We have 3 work packages:

## 6.2 WP1 Uptake and Effectiveness – led by Kontopantelis

### 6.2.1 Population

Two populations will be included in the research: (i) patients living in England, aged over 18, diagnosed with T2DM and referred to Healthy-Living; (ii) patients living in England, aged over 18, diagnosed with T2DM and not referred to Healthy-Living.

### 6.2.2 Data collection, source data and confidentiality

We will negotiate with NHS England and NHS Digital to have access to three datasets: a) 'Minimum dataset': data collected on all people referred to the NHS Healthy Living programme: people are eligible if they live in England and have type 2 diabetes b) 'Usage data': data on usage of various aspects of the programme: people are eligible if they have taken up a place on the Healthy Living programme and c) the National Diabetes Audit ('NDA'): people are eligible if they are adults registered with a GP in England and have a diagnosis of type 2 diabetes. We will not be the data owners of this quantitative data and we will not be involved in its collection. We will sign a data sharing agreement with NHS England and make a DARS application to NHS digital. We have already been promised access to all three datasets by the Department of Health and NHS England, as part of the funding arrangement. The precise details of our access have yet to be negotiated, but we will put in place a data sharing agreement to cover the transfer, management and use of the data, and we will work closely with the UoM information governance and research IT teams on this.

- 'Healthy-Living minimum dataset': A dataset collected by NHS England on people aged over 18, with type 2 diabetes who are referred to the NHS Healthy-Living service. It is a pseudononymised individual level dataset that includes details about participation in the Healthy Living service and is being collected for the purpose of research.
- 'Usage data': data collected by the service provider on usage of various aspects of Health-Living by the people who use the service.
- 'National Diabetes Audit' (NDA). The NDA collects information from primary care practices in England and contains much information for all people with T2DM in England and Wales, including demographics (age, gender, ethnicity, deprivation (from postcode)), clinical measures (HbA1c, BMI, BP and cholesterol), time since diagnosis, treatments, comorbidities and T2DM-related complications. The NDA is a pseudononymised cross-sectional database collected annually: for the proposed evaluation we would need to be provided with a version of NDA that includes patient follow-up data from subsequent years. Primary care participation in NDA increased in 2017-18 to 98.3 per cent in England and Wales.[10] All published NDA data up to and including 2016-17 is now available via the Data Access Request Service (DARS).

- NHS England are implementing an implied consent approach, with an opportunity for opt-out by patients who do not want their pseudonymised data used in research.
- All three databases will be pseudonymised by NHS Digital to allow for linkages and, for each database, the public key (the patient identifier) can theoretically be linked to sensitive information which is available for the data controller and not our research team. We are not fully aware of the data security protocols the data controllers have in place, and it is beyond the remit of this proposal to scrutinise them.
- The three datasets will be matched by processes set by the data controllers, in a way that ensures the resulting dataset is also pseudonymised, with a new public key, and the patients in the resulting dataset are not identifiable for either data controller. Teh pseudonymisation will be performed by a trusted third party (NHS digital). The resulting merged dataset is thus pseudonymised (with the data controller being the third party, in this case NHS Digital) and can be shared to the two original data controllers and, eventually, the research team.

The combined dataset will be utilized by researchers in WPs 1, 2b and 3. We will also use a freely available dataset with practice-level information (formerly known as GMS or General Medical Services database, now known as GP workforce data). This will be matched to the other datasets using the NHS practice identifier. This will allow WPI to examine how participation and health outcomes vary with practice characteristics.

We have deliberately placed the quantitative aspects of the programme towards the end, allowing us up to 2 years to negotiate access to the data we need. Our team is experienced in such discussions and we have successfully negotiated to obtain such databases in the past, so the processes are in place both at the team and organisational level. Prof Evan Kontopantelis (EK) will be the person within the HED-LINE team with specific responsibility for negotiating access to data and overseeing all data processes. He has extensive experience of data access: his research is primarily focussed on analyses of secondary data from the ONS, NHS Digital, NHS England, and the Clinical Practice Research Datalink (CPRD) where he serves as a member of the Independent Scientific Advisory Committee (ISAC).

### 6.2.3 WP1a) Uptake of Healthy-Living

#### *6.2.3.1 WP1a Research Questions*

WP1a addresses objective 1) Examine the extent to which people with T2DM start Healthy-Living and continue to use it, and whether engagement varies by patient characteristics.

Research questions:

- What are the characteristics of service users compared with the target population?
- What is the uptake and level of engagement by service users in different demographic groups?
- Which groups are at higher risk of non-referral or sign up?
- How does uptake and engagement vary by practice characteristics?

#### *6.2.3.2 WP1a Outcomes*

Participation outcomes will include: referral to the intervention; attendance, measured as a binary and as continuous outcomes (total time spent on the website, visits frequency and application views); and completion of the programme.

#### *6.2.3.3 WP1a Statistical Analyses*

Descriptives: Patient demographics, baseline clinical measures, treatments, co-morbidities from the NDA will be reported descriptively in the following four groups: 1) not-referred to Healthy-Living, 2) referred to Healthy-Living, 3) attended Healthy-Living and 4) completing Healthy-Living. This will provide insight into differences in demographic and other characteristics of those who participate at various stages and will allow us to understand whether the programme is contributing to health inequality by failing to engage with the most vulnerable in society. We will map and report these four groups overall, and by Service and Transformation Partnership (STP) and Clinical Commissioning Group (CCG) to visualise variation in implementation and patient participation. The characteristics of patients enrolled to different waves of the programme will be explored.

Modelling referral and retention: Using multiple logistic regressions we will examine what affects participation in the programme at every stage. We will evaluate the association between baseline data (patient demographics, baseline clinical measures, T2DM-treatments, co-morbidities, referral-type) and various measures of participation in Healthy-Living: not-referred/referred; not-referred/attended; not-referred/completed. We will also compare referred/attended and referred/completed to examine inequalities associated with retention. We can report the odds for each characteristic. We will explore the association between engagement and certain key practice characteristics: contract type (PMS, GMS, other), list size (or total GP FTE), proportion of patients

with Type-2 Diabetes, practice location deprivation and urban/rural classification. Due to the large number of models and covariates, we will not focus on statistical significance, but on the estimated sizes of the modelled associations of interest.

In addition, we will use attendance as a continuous outcome to evaluate the association between baseline data (patient demographics, baseline clinical measures, T2DM-treatments, co-morbidities, referral-type) and attendance, through linear regressions. Relevant attendance proxies will include: total time spent on the website, visits frequency and application views. Although linear regression models are quite robust when the outcome variable is not normally distributed, we will examine the distribution of attendance variables and consider alternative approaches, like ordered logistic regression (following categorisation of the outcome variables).

Together these models will allow us to identify and evaluate independent predictors of referral, attendance and completion. Summaries of the findings will be provided, offering a complete picture of potential selection bias in the programme, and its drivers. For example, are more deprived populations, in which age-adjusted T2DM prevalence rates are higher, adequately recruited into the programme, or does the programme inadvertently contribute to a widening of health inequalities?

### 6.2.4 WP1b) Effectiveness of Healthy-Living:

#### *6.2.4.1 Research questions*

WP1b addresses objective **2) Determine the effectiveness of Healthy-Living in changing clinical outcomes**

Research questions:

- What is the real-world clinical effectiveness (e.g. HbA1c change) of Healthy-Living as it rolls-out across England?
- What are the differences in clinical outcomes achieved across different demographic groups?
- How do clinical outcomes vary by practice characteristics?

#### *6.2.4.2 Outcomes measures*

The primary outcome will be change in HbA1c.

Secondary outcomes will include: weight change, BMI, BP (systolic and diastolic), total cholesterol, T2DM-related complications, cardiovascular comorbidities and treatments (e.g. insulin use, as an indication of severity).

We will also consider any outcomes that may be only available for the attending population in a "dose-response" sensitivity analyses (see below).

#### *6.2.4.3 Design*

Matched cohort study. In its simplest form, we will use two years of Linked data (baseline and follow-up) but we can expand if longer-term follow-up is provided. People referred to Healthy-Living will be matched to people not invited, 1 case to 5 controls, using their baseline characteristics. For both groups, we will exclude all people who attended any of the face-to-face self-management programmes, which are recorded in the NDA (but if numbers are very large, we will include each programme as a matching variable in the process described below). We will consider exact matching on age, sex, HbA1c (+/-0.1%), BMI (+/-1 kg/$m^2$), systolic BP (+/-5mmHg) and total cholesterol (+/-0.5 mmol/l). If not enough controls are available through such an approach we will consider relaxing the criteria. If the criteria need to be severely relaxed we will employ propensity scores to perform the matching. The follow-up (following year) data will provide outcome measures.

#### *6.2.4.4 Sample size*

By the analysis in 2022, the national roll-out will have completed. NHS England plan that 10% of people on the diabetes register (around 2.5m) will be referred in the first year in each STP. If we assume conservatively that 5% on the registers are referred, we will have approximately 125,000 people. The HeLP-Diabetes RCT found a reduction of 0.24% (95% CI −0.44 to −0.049; p=0.014) in HbA1c. Assuming a baseline HbA1c level of 7.3%, a standard deviation of 1.5,[11] 90% power, alpha 5% and 5-to-1 allocation of controls to cases, to observe a reduction of 0.2% in HbA1c levels we would need a total of 3,470 people (578 invited 2,892 not invited). To observe a reduction of 0.1% in HbA1c levels, under the same assumptions, we would need 13,876 people (2,313 invited; 11,563 not invited). In 2011, the NGSP (National Glycomoglobin Standardization Program) considered a 0.5% reduction in HbA1c to be clinically significant, but we have based the sample size calculation on the trial results, because policy makers want to know whether Healthy-Living achieves similar results.

#### *6.2.4.5 Statistical analyses*

1. Following matching, multiple regression models will be used to evaluate the association between being referred to Healthy-Living and clinical outcomes, compared to people not referred, controlling for all NDA covariates at baseline (including other outcomes). We designed the treatment group to include those referred to approach an intention-to-treat analysis as closely as possible, and minimise bias from noncompliance or withdrawal. Linear and logistic regressions will be used for continuous (e.g. HbA1c) and binary (e.g. insulin use) outcomes respectively. We will consider a conditional approach in the logistic regression models, which potentially better accounts for the matched design.
2. A first set of subgroup analyses will explore subgroups that potentially benefit most or least from the intervention (assuming we have identified an association between the intervention and outcome). We will model the relationship between the intervention and a population characteristic (e.g. age, sex, ethnicity, SES, referral-type) as an interaction term in a multiple regression model. Due to the large number of models this will be an exploratory analysis and will not focus on statistical significance.
3. A second set of subgroup analyses will focus on those attending Healthy-Living at least once or completing the programme, compared to people not referred. In addition, for the population attending Healthy-Living, we will use a "dose-response" approach to model exposure to the intervention and its association with outcomes (non-linearly). Assuming, an overall effect exists in completing the programme, this will allow us to quantify the benefits at various levels of engagement. We will use splines to allow for a non-linear association. We will use the total time spent on the website as a proxy for engagement, but we will consider alternatives like visit-frequency or application-views. This more advanced analysis will allow us to reliably model attendance and provide insight into its role on outcomes.

We will explore the association between outcomes and certain key practice characteristics: contract type (PMS, GMS, other), list size (or total GP FTE), proportion of patients with Type-2 Diabetes, practice location deprivation and urban/rural classification.

We expect levels of data missingness to be low in the Linked Data; we will use a multiple imputation framework. We will use Stata (v.15) for data management and analysis.

## 6.3 WP2 Process Evaluation

The process evaluation will determine the barriers, challenges and enablers concerning:

- How to improve uptake, acceptability, usability, satisfaction, and equity of access for service users
- How to improve reach, effectiveness, adoption, implementation and maintenance
- How to integrate Healthy-Living within existing NHS T2DM management care pathways

Our process evaluation includes 2 elements: *WP2a Implementation* and *WP2b Service Delivery and Fidelity*.

## 6.4 WP2a Process Evaluation – Implementation –led by Wilson

This work package will contribute to objective 3: To assess the barriers and facilitators affecting the implementation of Healthy-Living at clinical and organisational levels.

### 6.4.1 Research Questions

- What are the barriers, challenges and enablers to adoption and implementation of Healthy-Living?
- What are the barriers, challenges and enablers to integrating Healthy-Living within existing NHS T2DM management care pathways?

NHS England has an ambitious plan to roll out Healthy-Living nationally. Using an incremental strategy, roll out will start with 10 STPs ('Early Engagement areas') (https://www.england.nhs.uk/2019/05/online-diabetes-support/) followed by roll-out to all other STPs in waves. Results from the original implementation study[4] suggest that Healthy-Living can be implemented into routine care with support from health-care professionals, but this requires resources that are not practical during England-wide implementation. We will explore how implementation lessons from the original research programme and other sources[12] are put into practice when Healthy-Living is implemented nationally. This will include exploring how COVID-19 has impacted on plans for implementation.

### 6.4.2 Phase 1a: Understanding the policy context for roll out

#### *6.4.2.1 Design and setting*

We will conduct semi-structured telephone interviews with individuals with national responsibility for the implementation of the Healthy-Living service in England. These interviews will seek to understand the strategic vision for and selection of guidance and strategies to promote and support the national roll-out of the Healthy-Living service.

#### *6.4.2.2 Sampling and recruitment*

We are already in contact with the representatives that we seek to recruit, and we will send them an email inviting them to take part in the study (with participant sheet attached). A process of snowball recruitment may be employed if additional names are provided by representatives from the National Delivery Team. We will seek to recruit 5-10 representatives from the National Delivery Team and NHS England.

#### *6.4.2.3 Data collection and storage*

Telephone interviews will be arranged at a day/time suitable for the respondent. An interview topic guide has been developed to guide the interviews. With the respondents' permission, telephone interviews will be digitally audio-recorded on a university provided encrypted audio device. The researcher will write field notes (immediately following a telephone interview) to provide context to the transcribed interview data. With permission, we will also seek to obtain any relevant documents such as plans or guidance issued to support the dissemination and implementation of the Healthy-Living service from the national delivery team. We will use University of Manchester provided encrypted audio recording devices to record the consent process and interviews.
Where University of Manchester laptop computers are used, these are encrypted. Storage of personal data will be on secure university servers (and not on the hard drives of laptops) and can only be accessed by the research team.

#### *6.4.2.4 Analysis*

Audio recordings will be transcribed. We will use NVivo software to manage the data. We will analyse the interviews and any relevant documents using thematic analysis to understand:

- Overall aims and objectives of the strategic implementation plan
- Roll out strategies as intended
- Key performance indicators to measure 'success'
- Details of any incentive structures
- Targeted patient groups

### 6.4.3 Phase 1b Early Engagement Areas context and experience.

#### *6.4.3.1 Design and setting*

We will conduct semi-structured telephone interviews with the local area leads responsible for the implementation of Healthy-Living in each Early Engagement area in England.

#### *6.4.3.2 Sampling and recruitment*

Purposive sampling techniques will be used to recruit respondents; we will seek work-email contact details of Early Engagement sites' leads from the national delivery team at NHS England and we will send them an email inviting them to take part in the study (with the participant information sheet attached). After 2 weeks, a reminder email will be sent to non-responders. Our previous research on diabetes suggests that there are 1 or 2 leads per STP, and they are responsive to research requests. [13] A process of snowball recruitment may also be employed if additional names are provided by local leads. We expect to conduct between 11-20 interviews in this phase.

#### *6.4.3.3 Data collection and storage*

Telephone interviews will be arranged at a day/time suitable for the respondent. Interview topic guides have been developed to guide the interviews. For development of the topic guides, we draw upon *Normalisation Process Theory* (NPT) [8 9] to understand how new processes become routine practice. NPT comprises four constructs that represent individual and collective levels of work involved in the implementation of new practice (coherence, cognitive participation collective action and reflexive monitoring). These constructs will be framed as a set of propositions to identify factors impacting on implementation of Healthy-Living. Interviews will explore perceptions, expectations and attitudes towards Healthy-Living, experiences of implementation in existing T2DM care pathways, and challenges and unintended consequences during local implementation. As data collection progresses, the topic guide will be iteratively reviewed to incorporate issues not previously included, but which are relevant to the study. With the respondents' permission, telephone interviews will be digitally audio-recorded on a university provided encrypted audio device. The researcher will write field notes (immediately following a telephone interview) to provide context to the transcribed interview data. We will also request, where it exists, any locality

generated guidance documents to support practice level implementation. We will use University of Manchester provided encrypted audio recording devices to record the consent process and interviews. Where University of Manchester laptop computers are used, these are encrypted. Storage of personal data will be on secure university servers (and not on the hard drives of laptops) and can only be accessed by the research team.

#### *6.4.3.4 Analysis*

A common analysis approach will be adopted for WP2a process evaluation – implementation. Interviews will be transcribed and thematically analysed using a modified framework approach and using NVivo software to manage the data.[14] This produces a matrix of summarised data providing a structure for analysis and interpretation which is useful for policy research.[15] By 'modified Framework approach' we mean that we will initially use the Framework approach to take an inductive approach to theme generation. Subsequent theme refinement will be deductive and guided by Normalisation Process Theory (NPT) and the Nonadoption, Abandonment, Scale-up, Spread, and Sustainability (NASSS) framework. This approach will allow us to: (a) answer the specific research questions we have set, whilst (b) allowing important insights to be produced inductively. The use of this modified framework approach will also utilize the strengths of Framework analysis in providing structure to the analysis of large datasets, especially allowing comparisons between different participant groups on key issues. As stated in the application and as per Gale (2013), we also intend to engage the wider research team, our PPI group and clinical stakeholders in the analysis process.

A detailed analysis (combining interviews and documents) will be guided by NPT and the NASSS framework.[7] The NASSS has 7 domains (the condition, the technology, the value proposition, the adopter system, the health or care organisation, the wider context, and interactions and adaptations over time) and provides a lens through which implementation in 'Early Engagement Areas' can be understood and plans for further roll-out refined.

The implementation analysis will:

- Explore professional perceptions and attitudes towards Healthy-Living
- Consider initial and enduring challenges to adoption, and unintended consequences arising from implementation

- Surface "core enabling ingredients" that must be replicated at other sites, as well as any capacity for adaptation in context.
- Compare places with high and low uptake in order to recommend implementation strategies to improve future roll-out

The NASSS and NPT will inform a priori thematic codes with additional codes developed inductively. The coding framework will then be applied to subsequent transcripts, with ongoing adaptations until no new themes emerge. Data will then be charted into matrices with illustrative extracts and interpretive themes refined through regular analysis meetings. The results will be discussed with the PPI group and the clinical members of the management group. The learning will be shared with the national delivery team to refine future phased roll-out, and we would welcome the opportunity to contribute to future re-commissioning.

### 6.4.4 Phase 2: Barriers and facilitators to implementation of Healthy-Living within practices.

#### *6.4.4.1 Design and setting*

We will conduct telephone interviews with respondents in general practice (Practice Managers, GPs, Practice Nurses, Diabetes Specialist Nurses etc.) to explore the implementation of Healthy-Living in general practice, examining the processes implemented to promote patient awareness, referral and uptake and to explore the extent to which Healthy-Living has become embedded into routine practice.

#### *6.4.4.2 Sampling and recruitment*

Data from Phase 1 will help us to identify a purposive sample of 8 general practices in up to 4 of the 'Early Engagement areas' to explore the implementation of local practice-level processes. Using a the sampling framework similar to that employed in other similar research[16], we aim to recruit a mix of sites varying by rural and urban locations, socio-economic and ethnicity characteristics, as well as levels of adoption and approaches taken to implementation.

Once we have identified the general practices we wish to sample, we will use snowball sampling techniques to recruit respondents. We will gain names and work-email addresses of general practice staff from the local leads that we have interviewed in phase 1. We will send potential respondents an email inviting them to take part in the study (with the participant information sheet attached).

Again, we may use a process of snowball recruitment if additional names are provided by GP practice staff. In each practice, we aim to conduct 2-4 semi-structured telephone interviews with the practice manager and health professionals with varying levels of engagement with the Healthy-Living service[17]. We anticipate recruiting a sample between 20-30 participants.

#### *6.4.4.3 Data collection*

Telephone interviews will be arranged for a time/day to suit the respondent. For the development of topic guides, we have again drawn upon NPT, exploring perceptions and attitudes towards Healthy-Living, levels of contact and experience, identify practice-level support or implementation challenges and any intended or unintended consequences of integrating Healthy-Living into existing NHS T2DM management care pathways at the practice-level. As previously explained, topic guides are expected to develop as data collection and analysis of early interviews progress. With the respondents' permission, telephone interviews will be digitally audio-recorded on a university provided encrypted audio device. The researcher will write field notes (immediately following a telephone interview) to provide context to the transcribed interview data. We will use University of Manchester provided encrypted audio recording devices to record the consent process and interviews. Where University of Manchester laptop computers are used, these are encrypted. Storage of personal data will be on secure university servers (and not on the hard drives of laptops) and can only be accessed by the research team.

#### *6.4.4.4 Analysis*

As with Phase 1 interviews will be audio-recorded with consent, transcribed and thematically analysed, using a modified framework approach as outlined in section 6.4.3.4 above. Deductive coding will be informed by NPT, enabling cross-comparison with the original implementation study.[4]

### 6.4.5 Phase 3: Understanding national roll out

#### *6.4.5.1 Design and setting*

After sharing learning from phase 1 to inform future phased roll-out, we intend to explore the extent to which later waves of implementation are informed by the experience of the 'Early Engagement' areas. We will conduct semi-structured telephone interviews with all remaining designated STP site

implementation local leads (that we did not interview in phase 1) for one later wave of the national rollout. The approach taken will mirror Phase 1 and be informed by the earlier analysis.

#### *6.4.5.2 Sampling and recruitment*

As in phase 1, a mix of purposive and snowball sampling techniques will be used to recruit respondents. In the first instance, we will seek work-email contact details of designated local leads from the national delivery team at NHS England and we will send them an email inviting them to take part in the study (with the participant information sheet attached). After 2 weeks, a reminder email will be sent to non-responders. Snowball recruitment may then be employed if additional names are provided by local leads. We expect to recruit between 35 - 50 respondents in this phase.

#### *6.4.5.3 Data collection*

We will follow the data collection plan as outlined in section 6.4.3.3 (phase 1b data collection).

#### *6.4.5.4 Data analysis*

We will follow the analysis plan as outlined in in section 6.4.3.4 (phase 1b data analysis).

### 6.5 WP2b – Process Evaluation: Service Delivery and Fidelity - led by French

This WP will contribute to Objective 3): Assess the barriers and facilitators affecting the implementation of Healthy-Living at clinical and organisational levels, the fidelity of implementation and acceptability to patients and the NHS, and Objective 1) by examining engagement with Healthy-Living components by patients' characteristics.

#### 6.5.1 Research Questions:

- Assessment of fidelity between what people who are enrolled on the Healthy-Living programme receive from the intervention, and what was intended.

- How does exposure to Healthy-Living content vary by sub-groups: age, gender, ethnicity, deprivation, time since diagnosis, co-morbidity
- How to improve uptake, acceptability, usability, and satisfaction for users?

### 6.5.2 Phase 1: Fidelity

#### *6.5.2.1 Documentary analysis of web content – BCT coding*

We will capture online content (by looking at programme specifications) and code for (a) behaviour change technique (BCT) content, and (b) self-management tasks.[18] BCTs have been defined as the "active ingredients" that bring about behaviour change in an intervention.[19] Self-management tasks are those "that are relating to emotional and role management, as well as those pertaining to medical management"[4], e.g. having less time to look after others. The BCT content and self-management tasks of HeLP-Diabetes have previously been described for each intervention component[4] – so we will aim to assess the extent to which material has retained fidelity to the original BCTs.

The web content of Healthy-Living includes a number of different components (over 500 webpages across 8 sections). We will check whether intervention components that are rolled-out are similar to those specified in the HeLP-Diabetes trial, using published descriptions of the HeLP-Diabetes trial intervention (including appendices and supplementary materials from the team). We will then examine the rolled-out Healthy-Living webpages and code these for the presence of BCTs and self-management tasks. We anticipate that the majority of BCTs will appear in the 107 webpages relating to "staying healthy".

#### *6.5.2.2 Qualitative interviews*

We will conduct semi-structured telephone interviews with ALL credible key informants who can look for evidence of discrepancies in the presence or absence of BCTs between the original trial specification and the webpages of the intervention as implemented. Where these are detected, we will conduct interviews to document precisely how and why components have been adapted. We will interview ALL credible key informants who can tell us about the design of the intervention and how/why the components may have changed from the original version that was tested in the trial. This is likely to include managers, commissioners and policy makers responsible for the national roll-out, and the team who led the original trial.

#### 6.5.2.2.1 Sampling and recruitment

We will identify key informants from discussions with the provider about who could usefully provide information on interview contents, and via snowballing with these initial informants. We have already had initial conversations with the provider about this. We expect the number of key informants to be quite low (n=8) and we want to interview all of them, rather than a sample. If it becomes apparent that there are more (or less) credible informants than 8 people, we will revise our number of interviews upwards (or downwards).

#### 6.5.2.2.2 Data collection and storage

Telephone interviews will be arranged at a time/day suitable for the respondent. With the respondents' permission, interviews will be digitally audio-recorded on a university provided encrypted audio device. We anticipate conducting up to 8 interviews, to investigate the process of changes being made over time, and the decisions that were made. We have developed a topic guide to guide the interviews. We will use University of Manchester provided encrypted audio recording devices to record the consent process and interviews. Where University of Manchester laptop computers are used, these are encrypted. Storage of personal data will be on secure university servers (and not on the hard drives of laptops) and can only be accessed by the research team.

#### 6.5.2.2.3 Analysis

Audio recordings will be transcribed. We will use Nvivo software to manage the data. We will refer to the materials and theories used in the development of the published descriptions of the original HeLP-Diabetes intervention, to assess the principles originally used, to investigate whether these principles are used in any intervention refinements.

### 6.5.3 Phase 2: Exposure

#### *6.5.3.1 Data*

We will extract information from the Usage data, to quantify how much each component is used by patients. Given that we will know (from the previous phase) what is contained within each

intervention component, we will be able to quantify how much exposure to each BCT/self-management task any participant receives.

#### *6.5.3.2 Analysis*

We will report this information as follows:

- Overall exposure to BCT/self-management content, in terms of frequencies of use of each component, and median/ range of engagement with each component.[20] We will calculate survival curves, where appropriate, to ascertain when people disengage with key components. We will compare this with published information for participants in the HeLP-Diabetes trial, as reported in the trial outputs – to assess whether the roll-out sample experiences content differently from the trial sample.
- We will also quantify exposure to BCT/self-management content according to each of the following variables in the Linked Dataset: age, gender, ethnicity, deprivation, time since diagnosis, co-morbidity, severe mental impairment or learning disability, to assess whether there are inequalities in access.
- We will also examine how these exposures change over time, to assess if those users who take up the intervention earlier have similar demographic characteristics those who take it up later, and how usage of different parts of the content differs from the earlier stages of intervention use (in first 3 months) from later intervention use (between 6 months and one year).

### 6.5.4 Phase 3: Patient Experience

#### *6.5.4.1 Design and setting*

To assess how the intervention is experienced, we will interview participants who have undertaken the Healthy-Living programme. These will conducted either face to face or via telephone.

#### *6.5.4.2 Sampling and recruitment*

We will interview a subsample of 20-30 participants who have undertaken the programme. This number should allow some scope to examine how experience varies across different demographic and clinical groups. This is based on our previous experience with sampling for qualitative evaluation studies. We have found in past studies that 20-30 generally allows for a sample that reflects

sufficient diversity and depth regarding interview data. In reality the final sample size will be contingent upon iterative analysis until we have developed robust and recurring themes. If further sampling is required based on initial analysis, we will adjust the sample accordingly.

Patients will be identified via the provider of the Healthy Living service, an organization called Changing Health, who are commissioned to provide this NHS service, and are the direct care team. Healthy Living has NHS branding, and communications about recruitment give the clear impression to patients of an NHS service. The provider will identify participants by reviewing their records against the inclusion/ exclusion criteria we have provided. We will explore with providers how they can assist us in facilitating the identification of potential participants to ensure we purposively sample diverse groups to ensure that the final sample reflects maximum diversity. We will specify the geographical, demographic and clinical characteristics by which we want to sample, but we will not have access to patient records at any point. We have already had initial conversations with the provider about this.

Patients will be contacted by the intervention provider via email and be provided with an information sheet. They will be asked to contact the research team if they are willing to be interviewed and provide an information sheet. The research team will ask the provider to identify a sample of people who are diverse in terms of relevant demographic and clinical criteria – but data on any of these will not be passed to the research team. The researcher will then reply to the patient, to arrange a time to discuss further. At this initial appointment, the researcher will explain the research and what will be involved, respond to any questions or other issues that the patient has about the research, and arrange a time and place for the interview, if the patient is willing. The researcher will take consent verbally over the telephone or written consent if interviews are face-to-face.

We will purposively sample participants in multiple rounds of approximately 5 participants to allow for iterative analysis to inform further sampling. We will ensure diversity in age, gender, ethnicity, deprivation, time since diagnosis, co-morbidity, severe mental impairment or learning disability. We have had successful experience other studies of focusing recruitment of people at risk of diabetes in certain geographical areas in order to target particular groups, and we can work with providers to take a similar geographical approach in HED-LINE. Our previous experience of recruiting diverse groups suggests that having a diverse PPI group is key. Such a group will then be well positioned to advise us on how best to recruit a diverse sample. For example, in previous studies PPI groups have

helped us to devise effective study information for potential participants that is culturally appropriate and sensitive to the views and perspectives of specific groups. We have also frequently worked with community networks and charities and used translation where necessary. CS leads a Greater Manchester PPIE forum with membership from local community groups and national charities and networks who we can link with for advice on format and dissemination of recruitment materials.

We have experience of successfully recruiting a diverse sample of participants. For instance, we recently published a study where we recruited 19 British-Pakistani women and interviewed them for their views on screening for breast cancer. Of the 19 interviews, 14 were interviewed using an interpreter. (see https://journals.sagepub.com/doi/full/10.1177/0969141319887405) In a study of people at risk of diabetes we targeted our research in geographical areas and were successful in recruiting a sample including ethnic minorities and people from areas of high deprivation. Thus, our experience of working with "hard to reach" groups is that they are not hard to reach if one goes about it the right way (and has appropriate financial incentives that do not financially disadvantage them).

We have extensive recruitment expertise in our team, having been centrally involved in the MRC Hubs for Trials Methodology and the new Trials Methodology Research Programme (https://www.methodologyhubs.mrc.ac.uk/about/tmrp/). We will draw on the most up-to-date knowledge on recruitment, available at http://www.orrca.org.uk/. We will work closely with the NIHR Clinical Research Network, to learn from their experience on recruitment. The CRN has an initiative to ensure underrepresented groups have equal access to research, which we can engage with to define best practice: (https://www.ncl.ac.uk/medicalsciences/research/crn/newsitems/innovationsinclinicaltrialdesignanddeliveryfortheunderserved.html).

Participants will be paid £50 each to facilitate recruitment. Our previous experience of recruiting "hard to reach" groups, especially those with low incomes is that financial incentives are necessary. Therefore to not have such incentives would result in a sample lacking diversity. We will discuss this issue with PPI group before making a final commitment about payment. Again, our experience with previous PPI groups where we are seeking to include people with low incomes suggests that not to do this is seen as lacking credibility. This may be particularly important in the present context, given the anticipated length of interviews. HRA guidance (2014) on this point suggests that the two main

considerations regarding payments relate to coercion or undue inducements. Coercion is not appropriate here as financial inducements expand rather than restrict people's options. "Undue inducements" are offers that lead people to do something to which they would normally have real objections based on risk or other fundamental values. Again, we do not believe that either of these applies to an interview about using a digital intervention. Instead, we are removing barriers to participation from groups that have limited time due to financial hardship.

The focus of our interviews will be on how the digital intervention is experienced by people with type 2 diabetes, so we expect that carers will generally be less able to contribute to this. However, we accept that carers may have a role in translating the components of the course into action (e.g. family food practices, encouragement and support to be more physically active). If this is the case, we will seek further ethical clearance to allow us to potentially do joint or separate interviews, which we have done before.[23] This may be particularly appropriate where the person with type 2 diabetes who is offered the interview also has learning disabilities or severe mental illness.

#### *6.5.4.3 Data collection and storage*

Interviews will be arranged for a day/time and place suitable for the participant. Interviews will either be conducted face to face or via telephone. With permission, interviews will be audio-recorded on a university provided encrypted audio device.

Face to face interviews may be conducted in the patients' homes; in such cases, researchers will follow the University of Manchester's standard lone worker policy, with full details of researcher visits documented in secure systems where all members of the research team can access them. In all cases, there will be a nominated contact person who will be contacted before and after interviews, who will have interviewer phone numbers (on both study phones and personal phones). The contact person will attempt to contact the interviewer after 90 minutes has elapsed if they have not been contacted. If they are unable to contact, they will escalate to first, senior member of research team and subsequently the policy. Occasionally, patients may request interviews out of hours, and we will ensure that all researchers retain an appropriate contact person in such circumstances where visits cannot be arranged in working hours.

The focus of our interviews will be on how the digital intervention is experienced by people with type 2 diabetes. Interviews will cover the following, with input from the PPI group and Research Advisory Group:

- What content users engaged with.
- Barriers to participation/engagement.[21-24]
- In line with the NIH-BCC framework, we will investigate how the material is understood (i.e. intervention receipt), and how this impacts on usage of intervention materials (i.e. intervention enactment).
- How acceptable (enjoyable, usable, and satisfying) they found different elements of the intervention

Topic guides are expected to develop as data collection and analysis of early interviews progress.

Demographic and clinical information will be collected on the same occasion as the main interview, but that part of the conversation will be collected via a separate digital recording, with responses being noted in a study spreadsheet shortly after recording. Recordings in relations to demographic and clinical information will be deleted as soon as they have been transcribed. Where University of Manchester laptop computers are used, these are encrypted. Storage of personal data will be on secure university servers (and not on the hard drives of laptops) and can only be accessed by the research team.

#### *6.5.4.4 Analysis*

Audio-recordings will be transcribed and we will use Nvivo software to manage the data. Analysis will follow a similar approach to the implementation interviews (see section 6.4.3.4). We will use thematic analysis, structured using the framework approach,[14] which is well suited to managing large datasets such as this. The NIH-BCC framework will inform development of a priori thematic codes with additional codes developed inductively from initial coding. The coding framework will then be applied to analysis of subsequent transcripts, with ongoing adaptations until no new themes emerge. Data will then be charted into the matrices with illustrative extracts and interpretive themes refined through discussion at regular analysis meetings.

The results of will be discussed with the PPI group and the clinical members of the management group to ensure we incorporate patient and clinical perspectives into what improvements to suggest to the national delivery team to improve acceptability, participation and engagement. We would welcome the opportunity to contribute to any future re-commissioning processes.

### 6.5.5 Ethical considerations

The main ethical considerations for WP2 Process Evaluation: are informed consent; confidentiality, anonymity and data protection; and risks and burdens.

#### *6.5.5.1 Informed consent*

All potential research respondents who are recruited for interviews will receive verbal and written information (participant information sheet) regarding the study and will be encouraged to ask questions prior to taking part. It will be made clear that participation is purely voluntary and respondents are able to withdraw from the study at any time, without giving a reason. We will obtain verbal consent before undertaking the telephone interview which we will audio-record separately to the interview audio-recording. We will obtain written consent before undertaking face to face interviews (WP2b: phase 3 patient experience).

#### *6.5.5.2 Confidentiality, anonymity and data protection*

With consent, all interviews will be audio-recorded using a secure University provided encrypted audio device. We will follow the University of Manchester's standard operating procedure for taking recordings of participants for research purposes: http://documents.manchester.ac.uk/display.aspx?DocID=38446). Recordings of the consent process and interviews will be transferred from the device as soon as possible to separate, secure university servers (so that de-identified data is stored separately to consent data) and then deleted from the device. Transcription of audio-recordings will be undertaken by a University of Manchester approved external transcription company. Audio recordings will be uploaded to the transcription company via a secure server. We will remove any personal identifying information (such as names, places) from transcriptions once they are returned. We will securely destroy the audio-recording of each interview, once an interview has been transcribed and the research team has checked the transcription for accuracy.

Once a respondent enters the study, they will be provided with a unique identifier. This means that data including field notes, audio recordings, transcriptions and demographic data will be identified only by their unique identifier and not the name of the respondent. The 'pseudonymisation key' to

the unique identifier and respondent's details (name, contact details, site and job title), will only be accessible to members of the research team and stored electronically on a University of Manchester secure server, separate to the de-identified data. Where University of Manchester laptop computers are used, these are encrypted. Electronic data (such as digital audio-recordings, transcriptions, field notes, and demographic data) will be stored on a University of Manchester secure server. Hard copies of consent forms and demographic data will be kept in a locked cabinet in a locked room on University of Manchester premises. Once the study is finished, data will be archived securely for 10 years, after which time it will be securely destroyed.

The interviews will be with people who are receiving a web-based service, about their experience of using that service: we cannot envisage any issues of safety or identification of bad practice that would require us to break confidentiality

#### *6.5.5.3 Risks and burdens*

There is a small chance that may become upset during patient interviews. The researchers conducting the study will receive support and training in managing this and interviews will be sensitive towards patients throughout. Should a patient become distressed during the interview, the interviewer will ask the patient if they want to take a break. If they continue to be distressed, they will be asked if they want to stop the interview or continue at a later date. They will also be reminded that their participation is voluntary and that they are free to withdraw from the study at any time and they do not need to give a reason.

## 6.6 WP3 Health Economics – led by Elliott

Objective: 4) Establish the cost-effectiveness of Healthy-Living compared with usual care when rolled out across England, from an NHS and personal and social services perspective.

### 6.6.1 Research questions

- What are the consequences, e.g. impact on prescribing, healthcare utilisation (both positive and negative)?
- What are the predicted net financial benefits and costs to the health system over the next 3 years, using at least 24 months financial data collected during this research?

### 6.6.2 Design

NICE has produced guidance on the type of economic analysis needed for digital health technologies (DHTs), depending on the level of NHS financial risk.[25, 26] For a nationally-commissioned DHT like Healthy-Living, that has significant implementation costs, but the potential to be cost-saving the economic analysis level could be defined as 'low financial commitment', requiring at least a cost-consequence analysis (CCA) and a budget impact analysis (BIA). Given the potentially wide impact and the uncertainty about whether Healthy-Living will lead to cost-savings we suggest being more cautious, defining the level as 'high financial commitment', and accordingly we will carry out a cost-utility analysis to provide estimates of overall impact of Healthy-Living.

The original evaluation demonstrated HeLP–Diabetes was cost-effective according to NHS England thresholds.[4, 27] This analysis did not extrapolate the effect of HeLP–Diabetes on costs and outcomes beyond the trial. As the potential benefits of Healthy-Living are likely to be seen after the observed follow-up, we will carry out an economic evaluation informed by modelling to estimate longer-term benefits and costs, in line with current NICE decision-making.[28]

#### *6.6.2.1 Costs*

<u>Intervention costs</u>

Original development costs will not be included as they relate to research funding rather than NHS and PSS resources.

Costs will consist of: delivery, maintenance and updating; facilitating activities (including referral), and training NHS staff. Costs will be obtained from digital developers, NHS England Healthy-Living team, implementation leads and the companies involved in Healthy-Living.

Delivering, maintaining, and updating Healthy-Living: Staff costs relate to activities for engagement, and revising website content. Costs incurred by the third-party service provider responsible for hosting and maintaining Healthy-Living, making improvements to functionality and interface, making

Healthy-Living accessible from mobile devices; scalability for national rollout and adherence to NHS technical standards will be included.

Total costs of promotion, referral and facilitated access (if any) include staff training, practice staff time and printed materials to support staff and patients.

Data from WP2b – Service Delivery and Fidelity will be used to inform intervention costs. Identifying engagement with each intervention element using usage data will allow us to estimate real costs of the intervention at an individual patient level.

Comparator costs

The comparator is usual care, which includes access to self-management and lifestyle information on the websites of Diabetes UK and NHS Choices, as well as referral to face-to-face self-management programmes. No costs will be apportioned to usual care.

Downstream costs

Direct downstream costs are for management (for primary prevention of complications); and T2D-related complications. The core (NDA) data will allow quantification of antihypertensive and statin prescribing and eight T2D-related primary care costs (BP, BMI, renal function (serum creatinine), urinary albumin, cholesterol, foot check, smoking status and HbA1c) for 1-year follow-up at patient-level, and 2 years at national level. These data will allow analysis of impact on prescribing and T2D-related primary care healthcare utilisation. We will use published UK costs for T2D-related complications.[29]

These data will be combined with BNF[30], NHS reference[31] and PSSRU[32] unit costs to derive prescribing and primary care costs.

Costs (NHS/PSS) over a life-time horizon will be generated using the UKPDS OM2 model (see below).[33, 34]

### 6.6.3 Outcomes

Clinical indicators collected as part of the NDA (HbA1c, BP, total cholesterol, BMI) will be used to generate patient outcomes, expressed as quality-adjusted life-years (QALYs) using the UKPDS OM2 model (see below).[33, 34]

### 6.6.4 Analyses - Economic evaluation and BIA

We will use an existing model, the UKPDS OM2 model.[33, 34] This extensively validated[29, 34] simulation model is designed to extrapolate T2DM risk factors to predict long-term outcomes expressed as life expectancy, quality-adjusted life-years (QALYs), and NHS/PSS costs, is based on UK data, and has supported NICE guidelines.

We will use input parameters based on the study cohort available from the NDA to properly reflect the population of people with T2DM and their specific risk factors, including age, sex, duration of T2DM and baseline HbA1c, SBP, total cholesterol, BMI. We will use the results of observed comparisons of change in HbA1c, SBP, total cholesterol levels and BMI (generated in WP1) to estimate effects of Healthy-Living on patient outcomes, expressed as QALYs, and NHS/PSS costs.

Incremental cost-effectiveness ratios will be calculated in the event of Healthy-Living having higher costs and better outcomes than usual care and will express costs incurred in terms of QALY gain. Uncertainty will be addressed by cost-effectiveness planes from bootstrapped resamples. Cost-effectiveness acceptability curves (CEACs) will show the probability that the intervention is cost-effective for different QALY thresholds, along with net benefit estimation. The time horizon will be lifetime. Costs and effects will be discounted by 3.5%.

BIA will be carried out to estimate of the impact of Healthy-Living on decision-makers' budgets, where both costs and benefits are monetised over at least 2 years (preferably 3, depending on follow-up available). We will develop CCG-specific impact estimates based on local population and uptake characteristics.

Sensitivity analyses will focus on the effect of time horizon, missing data imputation on effectiveness estimates, wave, patient attendance and engagement, dose-response effects for attenders (if available), 5-year BIA extrapolation.

Cost per overall PAID score levels at one-year follow-up will be generated to compare results with the original trial CEA.

## 6.7 Peer Review

The scientific quality of the proposal was assessed by an NIHR funding panel and anonymous independent expert peer reviewers identified by the funder.

## 6.8 Ethical and Regulatory Considerations

### 6.8.1 Approvals

The HED-LINE study have been reviewed and approved by the Leeds West NHS Research Ethics Committee (Reference: 20/YH/0250, 29 September 2020). 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.

### 6.8.2 Risks

Work package 1: although we will approach data security issues very carefully, it needs to be made clear that the risk of identifying patients from the pseudonymised dataset we will receive is extremely low if not zero. This is because we do not have access to the de-anonymising key, which will stay with the data controller.

Work Package 2b (phase 3) patient interviews - there is a small chance that patients may become upset during patient interviews; however we view this as very low risk. The researchers conducting the study will receive support and training in managing this, and interviews will be sensitive towards patients and carers throughout.

Work Package 2b (phase 3) patient interviews - Researchers may visit patients' homes to conduct interviews. In such cases, researchers will follow the University's standard lone worker policy, with full details of researcher visits documented in secure systems where all members of the team can access them. In all cases, there will be a nominated contact person who will be contacted both before and after interviews, who will have interviewer phone numbers (on both study phones and

personal phones). The contact person will attempt to contact the interviewer after 90 minutes has elapsed if they have not been contacted. If they are unable to contact, they will escalate to first, senior member of research team, and subsequently, police. Occasionally, patients may request interviews out of hours, and we will ensure that all researchers retain an appropriate contact person in such circumstances where meetings cannot be arranged in working hours.

## 6.9 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.

## 6.10 Funding and resources

This research is independent research funded by the National Institute for Health Research (Policy Research Programme, Healthy Living Diabetes - Long-term Independent National Evaluation (HED-LINE), NIHR200933). The views expressed in this protocol are those of the author(s) and not necessarily those of the National Institute for Health Research or the Department of Health and Social Care.

## 6.11 Publication policy

The audience for HED-LINE includes NHSE, PHE, Diabetes UK, NHS managers and clinicians, patients and researchers. Our team already has substantial links that can facilitate wider dissemination and implementation: Manchester affords us with excellent opportunities through the Health and Care Systems and Commissioning Policy Research Unit (PRU), Older People and Frailty Policy Research Unit, policy@manchester, Health Innovation Manchester, ARC Greater Manchester (where Wilson leads implementation and other HED-LINE team members have leadership roles), ensuring our longer term dissemination draws on local expertise. In turn these local opportunities open up wider dissemination routes via the national ARC, AHSN and PRU networks.

Our dissemination strategy includes wider dissemination, beyond the immediate programme, to patients, health professionals, CCGs and practices. The Research Advisory Group will have a key role to play in keeping an eye on the bigger picture to ensure the research has long-term impact. We will

speak at conferences and write articles to inform national and international audiences interested in diabetes self-management and web-based delivery of services. We will also communicate our findings through the UoM communications team and engage with media outlets, in which we have considerable experience https://www.youtube.com/watch?v=W8qI4zQ2F9E&t=5s

We will disseminate the findings in three ways:

I. Shaping implementation of Healthy-Living. We would be in regular contact with the Healthy-Living team through workshops, short written briefings, phone and email contact to share our early findings and ensure our research takes account of any changes in planned delivery. We are open to exploring ways for us to shape implementation.
II. Patients and health professionals. We will seek opportunities for wider dissemination e.g. attending events by Diabetes UK and others, publishing regular blogs, tweets or webinars for CCGs and practices (e.g. https://www.clahrc-gm.nihr.ac.uk/projects/diploma-evaluation-national-nhs-diabetes-prevention-programme). We will involve patients to ensure the most important findings are disseminated clearly.
III. Researchers. Findings will be presented at academic conferences and in open access journals.

2) Outputs and deliverables

- Presentations and short reports of our plans, findings and recommendations,
- Logic model for the evaluation
- Evaluation plan
- Statistical analysis plan
- Interim reports and a publishable final report (including a draft report, executive and lay summaries); timetable to be agreed
- Slide set and toolkit
- Presentations to stakeholders
- Raw data (if suitable for sharing)
- Blogs and tweets by members of the research teamConference presentations (e.g. Diabetes UK, UK Society for Behavioural Medicine, HSR-UK).Open access articles
- We will explore opportunities to present at some of the events that attract policy makers, decision-makers or commissioners, such as the NHS Expo. Within our team we have contacts

at the NHS Primary Care Digital Transformation team and we can approach them about the potential to present our findings at one of their team meetings or conferences.

3) Impact

Our dissemination of this research to stakeholders will have an immediate impact on the delivery of Healthy-Living. We will feedback early findings on the Early Engagement Areas to inform future roll-out. Lessons from the fidelity work will be reported in sufficient detail to enable changes to be made to the specification for later implementation within the lifetime of the evaluation. The statistical and health economics analysis will be undertaken later in the programme, to make use of the maximum amount of data, so the impact of those analyses will be felt later.

## 6.12 Patient and Public Involvement

We are evaluating a digital intervention, which will become a fixture in their homes and / or be carried around by them, and therefore it is particularly important to have patients involved in the study.

- For the PPI group we will recruit six people with experience of type 2 diabetes (T2DM), including some who have taken part in a T2DM education programme. We will advertise via relevant channels, including HelpBEAT Diabetes https://www.researchforthefuture.org/diabetes/ to bring a diverse patient view to the forefront of the research.
- Eric Lowndes is a co-applicant and will be part of the research team, providing a lay perspective to the study.
- The PPI group will meet up to 10 times during the project, more frequently at the start, while members establish their role.
- Members of the group will be involved in:
    - discussing research plans of each work package to ensure that what we do is relevant to patients with T2DM; contributing to research tools such as interview topic guides;
    - advising on suitable methods and places to recruit patients;
    - contributing to research documents which will be given to patients to ensure plain English, readability and appropriateness for people with T2DM;

  - checking that the main messages from the research are the ones that patients and the public care most about, and identifying appropriate ways of disseminating the messages to patients and others;
  - involvement in dissemination, for example writing short summaries, newsletters or blogs, attending a conference such as Health Services Research UK or INVOLVE, or presenting at an event.

- Lay people can be helpful in many aspects of the research and we will discuss with the PPI group the specifics of the PPI plans. We intend to be responsive to the group about what they would like to be involved in and we will explore whether members of the PPI team are interested in contributing to the analyses once the project is underway.
- Meetings will be face-to-face, but we will also allow members to contribute by email/phone/post, depending on individual circumstances.
- As well as providing a lay perspective on study processes, members of the group will contribute to decision-making. Two members of the PPIE group (Eric Lowndes and another) will attend the Research Team, which manages the research, and meets every two months. Two of the PPIE group will be full members of the Research Advisory Group (which provides a link with policy makers). They will have equal decision-making rights at these meetings. This will ensure the overall management and priorities of the project benefit from a lay perspective and will allow them to feed in the views of the PPI group, of which they will also be members. They will be supported by SG.
- We will apply the National Standards for Public Involvement in Research https://sites.google.com/nihr.ac.uk/pi-standards/standards and pay £20 ph/£150 per day (INVOLVE rates) plus travel and caring expenses.
- Sally Giles will organise the PPI group and provide expert support to public contributors and the project researchers. The Researchers will facilitate the PPI with support from SG and any experienced public contributors on the project.

Sally Giles can provide informal support and coaching to the group if needed. UoM Faculty of Biology Medicine and Health runs an induction course for PPIE contributors, which will be available for the members of the PPI group. There are also UoM training courses on aspects of PPI for researchers (Introduction to PPI workshop; Masterclass: Communication Skills in PPI; Masterclass: Setting up a PPI Group) and we will ensure that all researchers attend.

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