Evaluating the impact of an intervention to increase uptake of self-management education programmes for Type 2 Diabetes in primary care: A wait-list cluster randomised controlled trial

(Embedding Diabetes Education)

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1. AMENDMENT HISTORY

Amendment No.	Protocol Version No.	Date issued	Author(s) of changes	Details of Changes made
N/A	N/A	N/A	N/A	N/A

2. SYNOPSIS

Study Title	Evaluating the impact of an intervention to increase uptake of self-management education programmes for Type 2 Diabetes in primary care: A wait-list cluster randomised controlled trial
Short Title	Embedding Diabetes Education
Trial Design	A wait-list cluster randomised controlled trial (RCT) to evaluate effectiveness of embedding structured education. There will be three steps (baseline: 0-3 months, 1st: 3-12 months, 2nd: 12-21 months). Practices will be randomised in a 1:1 fashion to either 1) immediate group (usual care [control] in baseline step then Embedding Package [intervention] in 1st and 2nd steps) or 2) wait-list group (usual care in baseline and 1st step then Embedding Package in 2nd step). This will be followed by a non-randomised observational follow-up (months 21-33), during which study-staff will no longer actively deliver the intervention, but practices can continue to use it. There will also be integrated Ethnographic and Cost-effectiveness Sub-Studies.
Trial Participants	Randomisation will be at the practice-level; 66 general practices will be recruited. For practical reasons, we will aim to recruit these practices from 4±2 Clinical Commissioning Groups (CCGs; approximately 16-18 practices per CCG). The primary outcome and the majority of the secondary outcomes will be collected and analysed at the patient level. All patients with type 2 diabetes mellitus registered at a participating practice will be assessed for study eligibility. Eligible patients will have the required variables extracted pseudonymously from their practice record.
Planned Sample Size	66 practices will be recruited. Based on a median of 348 eligible patients per practice, data from approximately 22,620 patients will be extracted. A minimum of 1,000 patients will be recruited via return of the completed questionnaire booklet.
Planned Trial Period	33 months maximum (RCT: 21 months; Observational follow-up: 12 months).
Primary Objective	To assess whether the Embedding Package reduces HbA1c in patients with T2DM compared with usual care (RCT).
Secondary Objectives	1. To assess whether the Embedding Package increases referral to and uptake of structured education as well as improving biomedical and psychosocial outcomes (RCT). 2. To assess sustainability of the Embedding Package (Observational follow-up). 3. To contextualise the process of implementation, sustainability of

	the change and the 'fit' of the Embedding Package within routine practice (Ethnographic Sub-Study). 4. To assess cost-effectiveness of the Embedding Package (Cost-effectiveness Sub-Study).
Primary Outcome	Patient-level HbA1c compared between the control (months 0-3 in immediate group and months 0-12 in wait-list group) and intervention (months 3-21 in immediate group and 12-21 in wait-list group) conditions in the RCT.
Secondary Outcomes	The secondary biomedical and process outcomes (including HbA1c) will be extracted for four measurement periods: the baseline step (months 0-3); the 1st step (months 3-12); the 2nd step (months 12-21); observational follow-up (months 21-33). The secondary biomedical outcomes are: 1. Body mass index 2. Weight and height 3. Total, LDL and HDL cholesterol 4. Systolic and diastolic blood pressure 5. Glucose, blood pressure and lipid lowering medications 6. Smoking status 7. Hospital admissions 8. QRisk2 score (a measure of cardiovascular risk). The secondary process outcomes are: 1. Whether or not the patient was referred to and attended (main secondary outcome) SME (patient-level; collected from a combination of primary care records, self-report, and Provider records) 2. Percentage of eligible individuals referred to education (practice-level; estimated from primary care codes showing whether the patient was referred to structured education) 3. Percentage of eligible individuals who attended education (practice-level; estimated from primary care codes showing whether the patient attended structured education) 4. Percentage of eligible individuals who declined education (practice-level; estimated from primary care codes showing whether the patient declined structured education) 5. Number, timing & venue of available education sessions (Provider-level; collected directly from Provider via a

	questionnaire) 6. Number of trained educators (Provider-level; collected directly from Provider via a questionnaire). Secondary psychosocial and process outcomes will also be self-reported by patients at a single time-point during the study. This will be done during the 1st step so that psychosocial outcomes can be compared between those in the intervention and control arms at that point in time. The self-reported outcomes are: 1. Whether or not the patient was referred to and attended SME 2. Where the patient has previously received diabetes information from 3. Patient Activation Measure 4. Well-Being (W-BQ12) 5. Problem Areas in Diabetes (PAID) score.

3. ABBREVIATIONS

CCG	Clinical Commissioning Group
CHEERS	Consolidated Health Economic Evaluation Reporting Standards
DESMOND	Diabetes Education and Self-Management for On-going and Newly Diagnosed
DSMC	Data Safety Monitoring Committee
EEPRU	Economic Evaluation of Health and Care Interventions
GCP	Good Clinical Practice
GP	General Practitioner
HCP	Healthcare professional
ITT	Intention-to-treat
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
PAID	Problem Areas in Diabetes score
PID	Participant Identification Number
PIS	Participant/Patient Information Sheet
PPI	Patient and Public Involvement
QALYS	Quality Adjusted Life Years
QOF	Quality and Outcomes Framework
RCT	Randomised Controlled Trial
SME	Self-Management Education
STP	Sustainability and Transformation Plan
T2DM	Type 2 Diabetes
TMF	Trial Master File
TMG	Trial Management Group
TSC	Trial Steering Committee
UK	United Kingdom
UKPDS	United Kingdom Prospective Diabetes Study
W-BQ12	Well-Being Questionnaire
X-PERT	X-PERT Health Diabetes Education Programme

4. BACKGROUND AND RATIONALE

Type 2 Diabetes Mellitus (T2DM) is a serious, progressive chronic disease, affecting approximately 3 million people in the United Kingdom (UK) [1] and leading to poor quality of life and increased prevalence of long term health complications [2, 3]. By 2035, diabetes will account for 17% of National Health Service (NHS) expenditure [4]. Despite advances in pharmacological interventions, management of T2DM remains a challenge. The Quality and Outcomes Framework (QOF) [2] for general practitioners (GPs) and early detection of T2DM may support patients in initially meeting blood glucose control targets. In the long-term, however, it becomes more difficult to sustain targets solely by pharmaceutical interventions, perhaps because of the prevalent limitations of a traditional approach to medical management in long-term conditions.

A substantial body of evidence has demonstrated the benefits of self-management education (SME) in T2DM [5, 6]. In this protocol, we use the term 'self-management education' or SME to include any structured education programme which meets the recommended National Institute for Health and Care Excellence (NICE) criteria [7], regardless of delivery modality. This includes programmes such as DESMOND [5, 6], X-PERT [8] and the Diabetes Manual [9-11]. Studies have shown SME to be cost-effective, and associated with improved biomedical (e.g. HbA1c, lipids, weight, blood pressure), psychosocial (e.g. depression, quality of life, hypoglycaemia rates), behavioural, and medication outcomes [5, 6, 8, 12].

Despite the increase in the quality and quantity of the evidence base since NICE first recommended SME programmes [7], and made SME for T2DM a national priority [13], rates of uptake of SME for those with T2DM have remained largely low. The recent addition of a QOF indicator for referral to SME in those with newly diagnosed T2DM [14] has improved the rate at which education is offered to people with newly diagnosed T2DM, with 71% of those with newly diagnosed diabetes being offered SME in 2015-16 as opposed to 15.9% in 2012-13 [3, 15]. Viewing these figures in isolation however is misleading, as referral does not equate to uptake. The most recent national figures (2015) show that of all people diagnosed with T2DM in the UK, only 5.3% are recorded as having attended SME [3].

Evidence suggests that poor participation is due to multiple patient, healthcare professional (HCP), and organisation factors including: insufficient investment, insufficiently trained educators, lack of staff capacity, absence of public health marketing for diabetes awareness, lack of integration into patient pathways, poor IT systems for tracking the patient, absence of an infrastructure for organisation-wide education, HCPs not advocating or recognising the positive outcomes of self-management education, the misperception that education is expensive, and lack of consideration of patient access issues [16]. Such situations may arise from competing funding priorities, absence of clinical engagement, or lack of knowledge about available programmes [16, 17]. Even when programmes are available and offered, analysis of effectiveness is difficult as data on referral and uptake are poorly recorded [3]. Consequently, SME is often regarded negatively amongst commissioning priorities, due to enduring myths and a lack of information on costs and benefits [18].

There is a burgeoning literature on the ways in which healthcare interventions are implemented in a variety of organisational settings, yet authors have highlighted the absence of studies which focus on the longer term sustainability of such interventions [19-21]. The question of how improvements in healthcare are retained and become embedded or 'routinised' in everyday practice remains poorly understood, and is as much a matter of networks of influence and knowledge of priorities and incentives frameworks as of clinical or cost-effectiveness in themselves

[20]. It is important, therefore, to explore how to ensure that SME can become part of routine care in the new organisational structures of the NHS in ways that are feasible for all stakeholders. This requires a better understanding of the contextual factors and processes which encourage the adoption of SME interventions and what the barriers might be to longer term, sustainable change, and how to overcome these barriers.

The nature of the commissioning of diabetes SME plays a large part in the complexities of ensuring it becomes embedded in routine care. Local Clinical Commissioning Groups (CCGs) must put together a thorough and detailed service specification for Provider services to tender to deliver as part of the local Sustainability and Transformation Plans (STP's). Once awarded, it is the chosen Provider who acts as the central referral and delivery point for all potential referring practices and will continue to report upwards to the CCGs in order to ensure they are fulfilling the agreed service specification. In some cases, multiple CCGs will come together for the tendering process aligned with local STP, with the chosen Provider then delivering SME across a number of neighbouring localities.

We have been awarded a five-year programme grant by the National Institute for Health Research (NIHR) to investigate this problem (grant reference: RP-PG-1212-20004; Chief Investigator: Professor Melanie Davies). The programme has already developed an 'Embedding Package' to increase uptake to structured SME by people with T2DM in primary care, with the overall intention of improving HbA1c levels. The Embedding Package addresses barriers and enablers to uptake at patient, HCP, and organisation levels. This Package has already been piloted and refined in a feasibility study. The study outlined in this protocol is designed to assess the effectiveness, cost-effectiveness, and sustainability of this Embedding Package in comparison with usual care.

5. OBJECTIVES

5.1 Primary Objectives

The Embedding Package is designed to increase uptake in primary care to structured SME by people with T2DM by addressing barriers and enablers to uptake at patient, HCP, and organisation levels, with the ultimate aim being to improve glycaemic control in these patients. Therefore, the primary objective of this study is:

To assess whether the Embedding Package, through increasing uptake and attendance at structured education, reduces HbA1c (a measure of glycaemic control) in patients with T2DM compared with usual care.

This objective will be addressed through a randomised controlled trial (RCT).

5.2 Secondary Objectives

1. To assess whether the Embedding Package increases referral to and uptake of structured education as well as improving biomedical and psychosocial outcomes (RCT).
2. To assess sustainability of the Embedding Package (Observational follow-up).
3. To contextualise the process of implementation, sustainability of the change and the 'fit' of the Embedding Package within routine practice (Ethnographic Sub-Study).
4. To assess cost-effectiveness of the Embedding Package (Cost-effectiveness Sub-Study).

6. STUDY DESIGN

6.1 Summary of Study Design

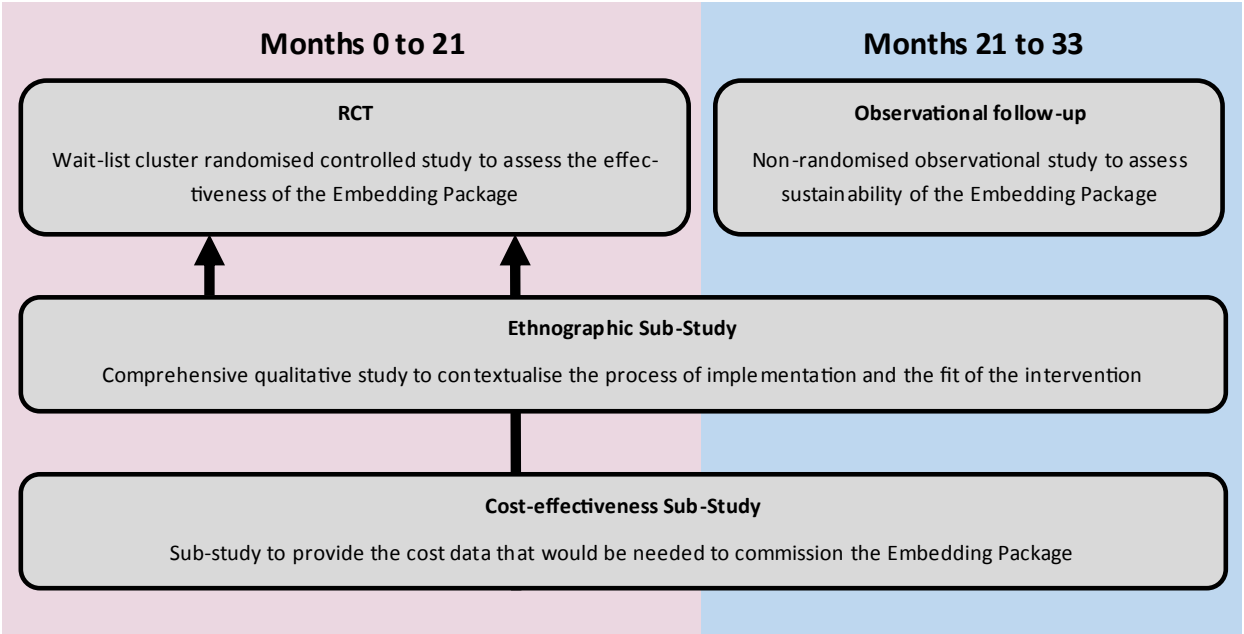
This open-label study is testing a complex intervention that is aimed at increasing SME uptake and subsequent improvements in health outcomes by creating changes in views, attitudes, processes, and behaviours at various stakeholder levels (Provider organisations, CCGs, STP's, practices, and patients) through a clear marketing strategy, user friendly and effective referral pathways, a local clinical champion, an 'Embedder' role, and a toolkit of resources for patients, HCPs and other key stakeholders.

The study has been designed in line with best practice guidelines to provide a comprehensive understanding of whether and how the intervention works, as well as providing cost data to inform its potential roll-out in the future. Accordingly, the study comprises a wait-list cluster RCT to ascertain the effectiveness of the intervention, followed by an observational study to ascertain whether changes are maintained after study support is withdrawn. Running alongside this will be two complementary and integrated sub-studies designed to better understand and evaluate the process of implementation; namely, an Ethnographic Sub-Study and a Cost-effectiveness Sub-Study (Figure 1). This protocol describes all of these complementary aspects of the project and forms part of their ethics submission.

This study will compare the Embedding Package (intervention to be tested) with usual care. In this study, 'usual care' means the study team will not be delivering the Embedding Package at that time, thus the practices will continue to refer their patients to diabetes education in line with their current procedures and practice. Usual care is likely to vary, but baseline data will allow us to quantify this variation. The variation will not affect the evaluation because the baseline level of education provision will be taken into account by the study design in which each practice acts as its own control.

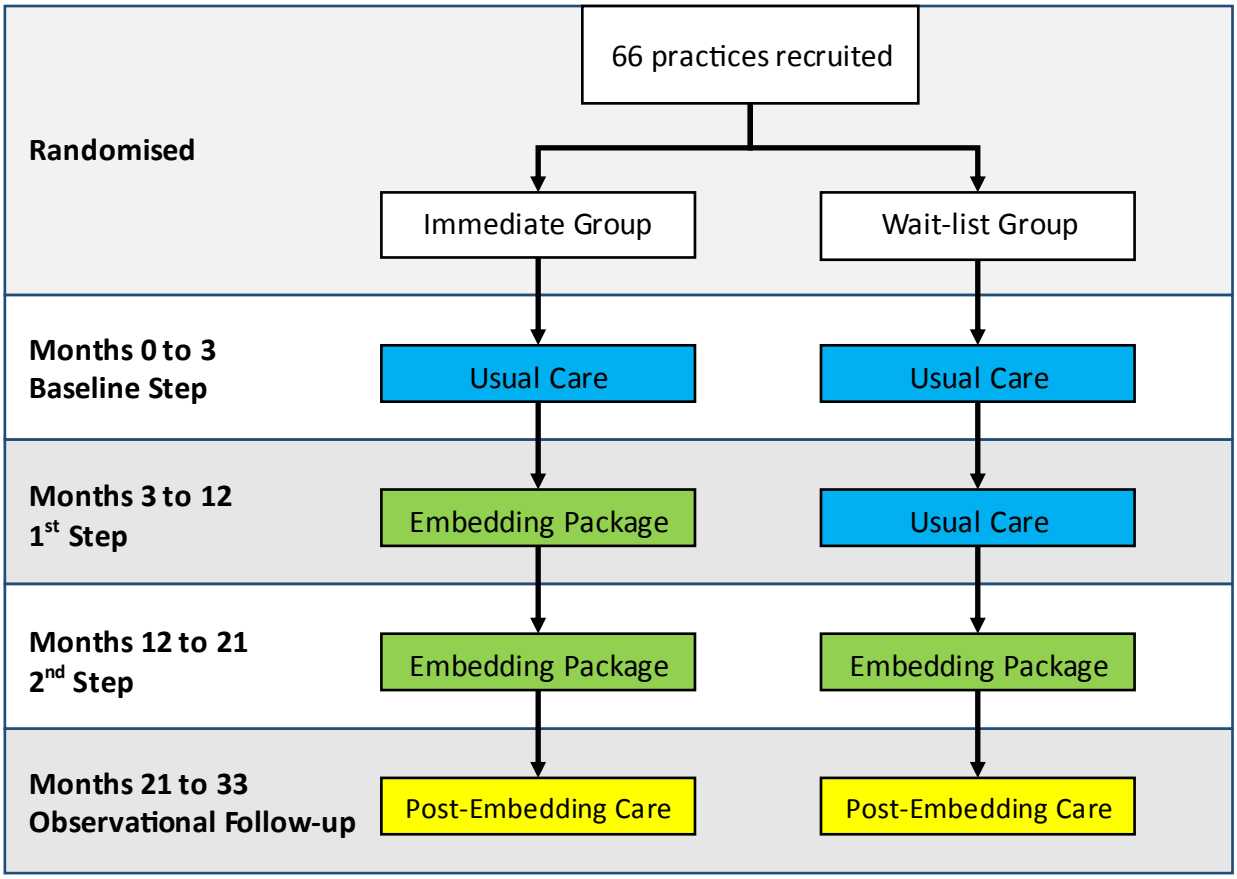
The practices will be in the RCT for 21 months and in the observational follow-up for 12 months, thus the total time in the study for practices is 33 months.

Figure 1. Outline of the study design.



The RCT is designed to assess the effectiveness of the intervention. It has a wait-list cluster RCT design. This means all practices will initially provide usual care for three months while baseline data are collected (months 0-3). Practices are then 1:1 randomised to 1) the immediate group who receive the Embedding Package from months 3 to 21, or 2) the wait-list group who provide usual care for months 0-12 and receive the Embedding Package for months 12-21 (Figure 2). Since data are collected from each step, each practice has both control and intervention data available and so acts as its own control, similar to a standard cross-over design. The main benefit of this design are that every practice will eventually receive the Embedding Package, which is likely to improve practice recruitment and retention. To limit potential contamination, for the aspects of the intervention that are targeted at CCG/locality/Provider level (e.g. social marketing initiatives), we will request that as far as possible, these are first targeted at practices participating in the Embedding Package, and only aimed at wait-list practices when these have crossed over to receive the Embedding Package. The cluster element of this design arises because randomisation is at the practice level, but the primary outcome is collected and analysed at the patient level.

Figure 2. Outline of the design of the main study.



Notes: The primary outcome will be a comparison of HbA1c between the control (usual care; blue) and intervention (Embedding Package; green) conditions. 'Post-Embedding Care' refers to the period where the study team will no longer actively deliver the intervention and so the practices will revert to providing their usual care, however if the intervention package is successful then this level of care will be higher than that provided during the baseline data capture period.

The observational follow-up is designed to investigate whether any improvements observed in the RCT are maintained beyond the trial as recommended by the MRC complex interventions framework [22]. This will be achieved through a 12-month follow-up period during which the study team will no longer actively reinforce the Embedding Package, but practices can continue using the solutions put in place during the RCT, if they choose to do so. This will apply to both arms and therefore will be a non-randomised observational period.

Data for the RCT and observational follow-up will be measured at the patient, practice, and Provider level. The patient level outcomes listed in Section 6.2 (including HbA1c) will be collected through data extraction of one line per patient primary care data by a third party provider (PRIMIS). The Caldicott guardian provides consent for this data extraction, rather than individual patients, as the extracted data will be pseudonymised (i.e. scrambled NHS numbers will be used). However, patients will optionally be able to opt-in to self-reporting information regarding previous SME attendance and psychosocial outcomes as well as consenting to have these self-reported data linked with their primary care data extracted by PRIMIS and their attendance data recorded by the SME Provider. These attendance data from three different sources will be used to validate, compare and contrast the sources as well as identifying weak reporting feedback mechanisms (i.e. it might be identified for example that Provider records are reasonably accurate, but primary care ones are not) so that these mechanisms can be targeted in the Embedding Package. The questionnaire booklet containing optional self-report questionnaire and consent form and the patient information sheet (PIS) will be mailed out to patients. This will include an optional expression of interest for participants invited to take part in the Ethnographic Sub-Study. Participants completing the self–report questionnaire will be asked to complete an additional study questionnaire (postal). The secondary process outcomes listed in Section 6.2 will be measured at the practice or Provider level as appropriate. These will be collected by aggregating the pseudonymous data extraction of patient-level primary care data by PRIMIS (practice level outcomes) and a brief questionnaire (Provider level outcomes).

The Ethnographic Sub-Study is designed to provide comprehensive data on the process of implementation and the fit of the intervention. Informed by Normalisation Process Theory [23, 24] and the findings of development work for this study, it focuses on different levels of implementation (patient, practice, CCG, Provider). Qualitative data will be gathered from observations and interviews, and will:

1. Use the formative findings from the immediate group to refine, tailor and enhance the Embedding Package and its implementation in the 2nd step.
2. Provide additional evidence about the context of implementation and sustainability of change in primary care
3. Investigate the degree to which active work to embed SME has continued in the observational follow-up
4. Examine the extent to which changes are perceived to have been sustained
5. Identify any external or internal changes with a bearing on sustainability.

Observations and semi-structured interviews will be the main two complementary methods of data collection used throughout the Ethnographic Sub-Study; interviews will ascertain the perceptions and experiences of key stakeholders; observations will provide evidence of how activity is

undertaken, reducing reliance on post-hoc accounts, and informing the focus of subsequent interviews with key stakeholders. Documentary evidence, including publically available information, will also be collected.

The Cost-effectiveness Sub-Study is designed to provide cost estimates of the implementation of the Embedding Package together with an estimate of the overall value for money of the Package. Cost estimates will be generated from structured interviews with staff in a sample of practices and across the CCGs and SME Providers, plus a survey of all practices not interviewed. The interview structure and the survey have been developed and tested in the preceding feasibility study. The cost-effectiveness estimates will be based on modelling the HbA1c data from the RCT using the Sheffield Type 2 Diabetes Policy Model, together with the costs associated with increasing uptake of SME via the Embedding Package.

6.2 Primary and Secondary Outcome Measures

All outcomes will be measured over the baseline (0-3 months), first (3-12 months), and second (12-21 months) steps, as well as over the observational follow-up (21-33 months), except for the self-report data which will only be measured once (during the 1st step). For most variables extracted from primary care records, the most recent measurement over that time period will be used. For example, baseline HbA1c will be defined as the most recent HbA1c measurement between months 0 and 3. If the variable has not been measured over that time period then it will be deemed missing.

Primary outcome

The primary outcome is patient-level HbA1c compared between the control (baseline step in immediate group and baseline and 1st steps in wait-list group) and intervention (1st and 2nd steps in immediate group and 2nd step in wait-list group) conditions in the RCT.

Secondary outcomes

Biomedical outcomes associated with increased risk of T2DM complications and routinely measured in primary care will be collected at the patient-level. These will provide further evidence as to whether the Embedding Package ultimately results in improved health outcomes. The secondary biomedical outcomes to be collected are:

1. BMI
2. Weight and height
3. Total, LDL and HDL cholesterol
4. Systolic and diastolic blood pressure
5. Glucose, blood pressure and lipid lowering medications
6. Smoking status
7. Hospital admissions

8. QRisk2 score (a measure of cardiovascular risk).

Process outcomes reflect how the intervention is implemented and aid understanding of effectiveness. They will be measured at the patient, practice, or Provider level as appropriate, and will include the following:

1. Whether or not the patient was referred to and attended (main secondary outcome) SME (patient-level; collected from a combination of primary care records, self-report, and Provider records)
2. Percentage of eligible individuals referred to education (practice-level; estimated from primary care codes showing whether the patient was referred to structured education with those with a code showing they are not suitable for SME removed from the denominator and numerator)
3. Percentage of eligible individuals who attended education (practice-level; estimated from primary care codes showing whether the patient attended structured education with those with a code showing they are not suitable for SME removed from the denominator and numerator)
4. Percentage of eligible individuals who declined education (practice-level; estimated from primary care codes showing whether the patient declined structured education with those with a code showing they are not suitable for SME removed from the denominator and numerator)
5. Number, timing & venue of available education sessions (Provider-level; collected directly from Provider via a questionnaire)
6. Number of trained educators (Provider-level; collected directly from Provider via a questionnaire).

Secondary psychosocial and process outcomes will also be self-reported by patients at a single time-point during the study. This will be done during the 1st step so that psychosocial outcomes can be compared between those in the intervention and control arms at that point in time. The self-reported outcomes are:

1. Whether or not the patient was referred to and attended SME
2. Where the patient has previously received diabetes information from
3. Patient Activation Measure
4. Well-Being (W-BQ12)
5. Problem Areas in Diabetes (PAID) score.

Additionally, back end website data on the extent of user engagement (e.g. length of time for which individual pages were viewed and the number of occasions etc) with specific tools in the online toolkit (see Section 9.1) and with MyDesmond (online version of the DESMOND SME programme) will be collected. For the cost-effectiveness analyses, cost estimates will be measured at the practice, SME Provider and CCG level.

7. TRIAL PARTICIPANTS

7.1 Overall Description of Trial Participants

CCGs (4±2) and the associated SME Providers will be approached regarding the study. This decision was based on practical grounds (it will be more feasible to deliver the intervention if the geographical spread of practices is relatively small, and easier to recruit practices if this is aided by CCGs), and because CCGs and Providers will need to support the study by implementing the aspects of the Embedding Package aimed at CCGs and Providers themselves, therefore it is vital that recruited practices are part of a locality that is amenable to the study. Participating CCGs and Providers will contribute data on activities relating to the Embedding Package for use in the cost-effectiveness study, on the availability of education sessions and on the number of educators.

Eligible practices (n = 66) within these CCGs will be recruited (i.e. approximately 16-18 practices per CCG if 4 CCGs are recruited). Participating practices will contribute data through extraction of patient-level data from their computing system and by recording activities relating to the Embedding Package for use in the cost-effectiveness study.

All patients diagnosed with T2DM (including those newly diagnosed during the study period), registered at one of the 66 participating practices, and meeting the eligibility criteria in Section 7.2 will have their pseudonymised data extracted for the variables listed in Section 6.2 and will be invited to complete a consent form to connect extracted data with self-reported information (as well as optional expression of interest for the Ethnographic Sub-Study).

The Ethnographic Sub-Study will be conducted within a sub-sample of approximately 12 out of the 66 practices and related contexts (e.g. CCGs and Providers). Purposive sampling of practices will take place in the 1st and 2nd steps of the RCT to ensure a representative sample [25]; we will likely sample around 6 practices in the 1st step and around 6 practices in the 2nd step. In the 1st step, this will be informed by demographic profile and discussions with the trial co-ordinators, and will aim to generate a maximum variation sample [26]. Sampling during the 2nd step will be theoretically informed by mid-term progress data to explore the challenges involved in implementing and sustaining the Embedding Package in a variety of circumstances. We will also collect data in organisations associated with the delivery of the Embedding Package in these 12 practices, e.g. CCGs, Providers, NHS England regional offices and area teams, commissioning support units. Practices and associated organisations sampled in the 1st step will continue to be included in data collection in the 2nd step.

The same sub-sample of 12 practices and all of the participating CCGs and SME Providers will also provide more detailed information on the costs of the individual activities, via interviews with a designated staff member (such as the practice manager).

7.2 Eligibility Criteria

Practices, patients and stakeholders will be recruited and take part in relevant study activities if they meet all of the relevant inclusion criteria and none of the relevant exclusion criteria, as detailed below.

Practices

Practice inclusion criteria:

- Located within a participating CCG
- Use either EMIS Web or TPP System One (required for data extraction)
- Able to refer patients with T2DM to an evidence-based, nationally recognised structured education programme which meets NICE criteria
- Willing to sign a data sharing and data collection agreement with PRIMIS allowing the collection of one line per patient pseudonymised and, where patient consent is given, identifiable data, as required for analysis
- Willing to have a sample of meetings and consultations observed or to be interviewed, where appropriate, for the Ethnographic and Cost-effectiveness Sub-Studies.

Practice exclusion criteria:

- Unable to make contact with practice manager or equivalent.

Patients – Data Extraction and Mail-out

All patients registered at a participating practice and meeting the following eligibility criteria will have pseudonymised one line per patient data extracted, and will be mailed an invitation pack which includes an invitation letter, PIS and questionnaire booklet. The questionnaire booklet contains a self-report questionnaire and a consent form which gives patients the option to have their questionnaire responses linked to their attendance data in their practice and Provider records. Ethnographic Sub-Study information and expression of interest forms will also be included in these documents when mailed to patients invited to take part in the Ethnographic Sub-Study.

Patient inclusion criteria:

- Registered at a participating practice
- Aged ≥18 years old
- Coded in their primary care medical record as diagnosed with T2DM before or during the study period (to be re-assessed at each data extraction point)
- Willing and able to provide informed consent (Applicable to optional consent form and questionnaire booklet only)
- Able to understand written English to a level sufficient to enable an understanding of the research and their participation within it (Applicable to optional consent form and questionnaire booklet only).

Patient exclusion criteria:

- Coded in their primary care medical records as having a terminal illness
- Coded in their primary care medical records as housebound or in residential care

- A dissent code in their primary care medical records for researcher to access clinical data.

Patients – Ethnographic Sub-Study

Patients who express an interest to participate in the Ethnographic Sub-Study and meet the following eligibility criteria will be eligible for the Ethnographic Sub-Study.

Patient inclusion criteria:

- Meet all of the above patient eligibility criteria
- Is able to attend the practice unaided or with a carer or support (Applicable to observations of consultations only).

Patient exclusion criteria:

- Unable to understand spoken English to a level sufficient to enable an understanding of the research and their participation within it.

Stakeholders

Stakeholders are individuals who work at participating practices, are members of CCGs, are education Providers, or are in attendance at meetings in a PPI capacity, who may be approached to participate in a number of activities. Stakeholders will be eligible for inclusion in the Ethnographic Sub-Study if they meet all of the following inclusion criteria and none of the following exclusion criteria.

Stakeholder inclusion criteria:

- Employed by a participating practice/CCG/Provider Organisation, or involved in the delivery of or commissioning of any aspect of the Embedding Package in a participating practice/CCG/Provider Organisation
- Willing and able to give informed consent (written or verbal).

Stakeholder exclusion criteria:

- Unable to understand written and spoken English to a level sufficient to enable an understanding of the research and their participation within it.

8. STUDY PROCEDURES

8.1 Informed Consent

Informed consent will not be required for the data extraction element of the study as patients will not be directly approached and their data will be extracted pseudonymously. However, the Caldicott guardian of each participating practice will be required to consent to these data being extracted before extraction will take place.

Informed consent will be required for 1) the linkage of self-reported questionnaire data with attendance data from primary care and Provider records, 2) the Ethnographic Sub-Study, and 3) the Cost-effectiveness Sub-Study. The method of taking consent will depend on who is giving consent and what they are being asked to do; a summary is provided in Table 1 and further information on the documents to be used in each situation can be found in the study training document 'study document procedures', this will be maintained and stored in the Trial Master File (TMF). A more detailed description follows.

Table 1. Summary of method of consent per study element

Study Element	**Method of Consent**
Complete questionnaire booklet and link with routine clinical data	Written via mail-out
Interviews - Face-to-Face	Written
Interviews - Telephone	Verbal
Observations – SME Session	Written
Observations – Consultations/Meetings	Verbal

All members of the research team taking informed consent for the Sub-Studies will be ICH Good Clinical Practice (GCP) certificated, and authorised to do so by the Chief Investigator. Where written consent is taken the original signed consent forms will be retained within the TMF and participants will be given or sent a copy. The PIS will detail no less than the exact nature of the study, the implications and constraints of the protocol, and any risks involved in taking part.

Consent to complete questionnaire booklet and link with routine clinical data

Patients will be approached about this by postal invitation sent from the practice to include information about the study in a PIS (including the Ethnographic Sub-Study in participating practices) and a questionnaire booklet containing a short questionnaire and consent form. The questionnaire booklet will allow patients to provide simple information about whether they have had a previous referral to a SME programme and, if so, whether and which SME programme they attended. It also includes an invitation to complete a further additional study questionnaire which consists of validated psychosocial questionnaires, Patient Activation Measure, W-BQ12 and PAID. This additional questionnaire will be posted to all participants indicating they are willing to complete it.. Patients will also be asked to provide consent for the research team to link their responses to the data extracted from GP practices and their record held by the local SME Provider, if such a

record exists. Additionally, if the patient is registered at a practice that is one of the 12 taking part in the Ethnographic Sub-Study, the patient may be given the option of indicating their willingness to participate in an interview with the research team and/or to participate in an observation of a consultation that may lead to a referral to a SME programme. Patients will be able to decline participation, or to indicate willingness to participate in either the self-report and data linkage or any activity in the Ethnographic Sub-Study (participation in one of these does not necessitate participation in any other activity).

Consent to interviews (Ethnographic and Cost-effectiveness Sub-Studies)

Individual consent will be taken by a member of the research team when a patient or stakeholder participant is taking part in an interview. All participants will have the opportunity to discuss the purpose of the interview and the PIS, ask any questions they have, and then to decide whether they will participate. Patient participants will have been provided with a patient PIS in their invitation pack and those who indicate an expression of interest on their questionnaire response will be contacted by a member of the research team. Stakeholder participants will be given a stakeholder PIS. For face-to-face interviews, written informed consent will be obtained by means of participant dated signature and dated signature of the interviewer immediately prior to the interview. For telephone interviews, the interviewer will audio record the reading of the latest approved version of the consent form and sign and date the form. The original signed form and a note of the audio file of recorded consent will be retained in the TMF. A copy of the signed form will be sent to the participant.

Consent to observation of SME sessions (Ethnographic Sub-Study)

A sample of one-to-one or group based SME sessions will be identified for observation. After identifying a session to be observed, individual written consent will be taken from all those who will be present (i.e. the educator and all participants attending the session). First the educator(s) will be given a copy of the stakeholder PIS and will have the opportunity to consider this information and ask any questions. They will then be asked to provide written consent (via dated signatures of the educator(s) and the researcher who presented and obtained the informed consent) and confirm the dates of the sessions they would be happy to have observed. If the educator(s) does not consent then no participants will be approached. After educator consent has been received, when booking participants onto one of these sessions, the SME administrator will inform each participant verbally about the study and the presence of an observer. If a participant does not want to attend a session that is being observed, they will be booked onto a session on an alternative date. Participants who give verbal consent (when booking) to be observed will be sent a PIS. Immediately prior to the session, a verbal delivery of the PIS will be given by the researcher. This presentation may be delivered on a one-to-one or group basis. Prior to requesting written consent, potential participants will be given the opportunity to have any questions related to the study or their participation within it addressed. Written informed consent will be obtained via dated signatures of the participants and the researcher who presented and obtained the informed consent.

Consent to observation of healthcare consultations (Ethnographic Sub-Study)

The ethnographic team will attend clinics in order to observe consultations where discussions about SME may take place between patient and HCP. Potential consultations for observation will be identified from completion of a patient expression of interest section on the mailed out consent form, and the ethnographic team will carry an expression of interest form with them while present in a practice to allow a more *ad hoc* recruitment method. After identifying a consultation for observation, verbal consent will be taken by a member of the research team from all those who will be present. It will not be practical or appropriate to obtain written consent from the HCP or the patient on the day as this would present a burden to the practice and introduce delays in the clinic/appointment schedule. Therefore, we plan to use an approach we have previously used successfully, which relies on obtaining verbal permission from the patient and the HCP ensuring that those who wish to opt out can easily make this known and recording only completely anonymised data. Written and verbal versions of the PIS will be provided and all participants will be given time to consider the information and ask questions. Patients will be informed of the possible presence of an observer by the practice receptionist when they arrive for their appointment. It will be made clear that they are free to ask that their consultation is not observed. The observer will offer to withdraw without any reason having to be given by either the patient or the health care practitioner, and in any event will withdraw if there is any doubt about the appropriateness of their presence.

Consent to observation of meetings (Ethnographic Sub-Study)

A sample of meetings where SME is discussed may be observed. Verbal consent will be sought from the appropriate person in the organisation and/or the Chair of the meeting. When possible, those due to attend the meeting will be informed about the study by the observer prior to the meeting, by providing them with a copy of the stakeholder PIS. If the Chair is willing, at the start of the meeting the observer will explain their role, that anonymity is guaranteed and that they will absent themselves at any time if anyone would rather they were not there; they will then take verbal consent from all those present. In some situations, participants may have a limited amount of time to ask the researcher questions or consider their consent to the study. If any individual does not wish to give consent, the observer will withdraw from the meeting. Participants may also request that the observer withdraws temporarily, for example if part of the meeting relates to issues that are confidential, or are not pertinent to the focus of the study. The researcher will respect all such requests.

8.2 Recruitment

Practices will be recruited to the RCT and observational follow-up. Practices within the 4±2 participating CCGs will be contacted and asked to take part in the study. The study team may also attend established events for local practice staff in order to distribute promotional material. Practices interested in taking part will be able to contact the research team to discuss their possible participation.

Patients meeting the eligibility criteria (Section 7.2) will be invited to join the self-report and consent to link data part of the study via a mail-out from the practice. They will be sent the study documents (Invitation letter, PIS, questionnaire booklet, and prepaid envelope) and asked to complete and return the questionnaire booklet in the prepaid envelope. Patients who complete the expression of

interest section for the Ethnographic Sub-Study may be contacted by the research team via telephone or email to discuss their possible participation in these activities and arrange an interview and/or observation if appropriate. Additionally, *ad hoc* recruitment of patients to the ethnographic study will occur in participating practices via researchers approaching patients, where the practice has given permission for this to take place. Study information posters will be displayed in participating practices; these will include research team contact details.

Additional relevant stakeholders involved in commissioning, providing, or delivering SME, and implementing and conducting training related to the Embedding Package will be identified for inclusion in the Ethnographic Sub-Study because of their professional role and involvement in SME; many of these people will be identified from the observational work and from other individuals' suggestions (a form of strategic snowball sampling). Relevant meetings, training events and SME sessions will be identified for observation via discussions with the practice staff, interviews, and earlier observations. The member of the research team conducting the observation will be responsible for checking eligibility of meeting attendees/interview participants prior to consent or any study data collection.

8.3 Data Collection

Provider-level process outcome data (Section 6.2) will be collected from the Provider using a brief questionnaire at months 3, 12, 21, and 33.

Patient-level biomedical and process outcome data (Section 6.2) will be collected through pseudonymous extraction from primary care data using Read codes. These data will be aggregated where appropriate to calculate the practice-level process outcomes. Data will be extracted at four time-points (Month 3, 12, 21, and 33) facilitated by PRIMIS with the consent of the Caldicott guardian of participating practices via a data collection agreement and data extraction agreement, signed as part of enrolment onto the study. Data extraction procedures are based on those used previously in similar studies [27], and used in the preceding feasibility study. Essentially, practices will extract their own data, pseudonymise it and then transfer it electronically to the study team at the University of Leicester. PRIMIS will provide help desk support for practices who would like it. Furthermore, PRIMIS will dial in and perform this operation remotely for those practices that wish for them to do so.

Data extraction will be performed using MIQUEST software that is widely used throughout primary care and has inbuilt security features to ensure that only appropriate data are extracted. The only key identifier to be extracted from the MIQUEST software will be NHS numbers. The practice will use an Open-Pseudonymiser and CHART software to encrypt the NHS number into a unique hash (#) code creating an Excel spreadsheet containing only pseudonymised data. This will be appropriately and securely transferred to the research team at University of Leicester. PRIMIS will not be able to identify patients at any point during the study [28, 29]. The practice ID code will not be encrypted as it will be required by the study team to identify which randomisation arm the data belong in.

National changes to data recording in general practice are expected from April 2018. Due to this the use of MIQUEST as the chosen data extraction method might be subject to change throughout

the duration of the study. If this occurs an alternative method equivalent to the information governance safeguards offered by MIQUEST would be adopted.

Data are de-identified. Re-identification could only occur in very rare circumstances when a person with access to the research database also had access to the individual practice database together with other information.

The transferred Excel spreadsheet will contain one line per patient pseudonymised data from all patients with T2DM registered at the participating practices during the study period. Data recorded over the measurement periods (Months 0-3, 3-12, 12-21, and 21-33) will be extracted.

One line per patient anonymised data extraction will include the following data (note that for medication variables, the brand name, dose and mode of delivery will be extracted):

Variable	**Value of Interest**	**To be extracted**
Type 2 diabetes diagnosis	First recorded	Value and date
NHS number	Last recorded	Pseudonymised value
Age	Last recorded	Value
Sex	Last recorded	Value
Ethnicity	Last recorded	Value
Smoking status	Last recorded	Value and date
SME: Referred	Last recorded	Value and date
SME: Not suitable	Last recorded	Value and date
SME: Declined	Last recorded	Value and date
SME: Did not attend	Last recorded	Value and date
SME: Not completed	Last recorded	Value and date
SME: Attended	Last recorded	Value and date
SME: Completed	Last recorded	Value and date
HbA1c	Last recorded within measurement period	Value and date
Body mass index	Last recorded within measurement period	Value and date
Weight	Last recorded within measurement period	Value and date
Height	Last recorded	Value and date
Total cholesterol	Last recorded within measurement period	Value and date
LDL cholesterol	Last recorded within measurement period	Value and date
HDL cholesterol	Last recorded within measurement period	Value and date
Systolic blood pressure	Last recorded within measurement period	Value and date
Diastolic blood pressure	Last recorded within measurement period	Value and date
QRisk2 score	Last recorded within measurement period	Value and date

Medication: Glucose lowering	All recorded within measurement period	Value and date
Medication: Lipid lowering	All recorded within measurement period	Value and date
Medication: Blood pressure lowering	All recorded within measurement period	Value and date
Hospital admission	All recorded within measurement period	Value and date

If dial-in occurs then practices will be asked to create a unique PRIMIS account on the clinical system which will only grant access to the MIQUEST interpreter on the clinical system. Practices will ensure the integrity of the practice audit trail through identification of the user as a member of PRIMIS staff. “Away from my Desk” software will be used to facilitate extraction of patient data and will ensure that all actions performed on the practice computers are fully audited [30]. The “Away from my Desk” software must be authorised by a member of the practice staff before a connection can be established with PRIMIS. PRIMIS cannot access the practice system without explicit authorisation. All actions undertaken by PRIMIS on the practice system can be monitored on screen by the user at the practice; the practice staff have the capability to terminate the connection at any point during remote access. The practice is responsible for ensuring that only the MIQUEST interpreter is visible to PRIMIS staff. All patient records must be closed to ensure that no access to patient identifiable data is viewed by PRIMIS staff.

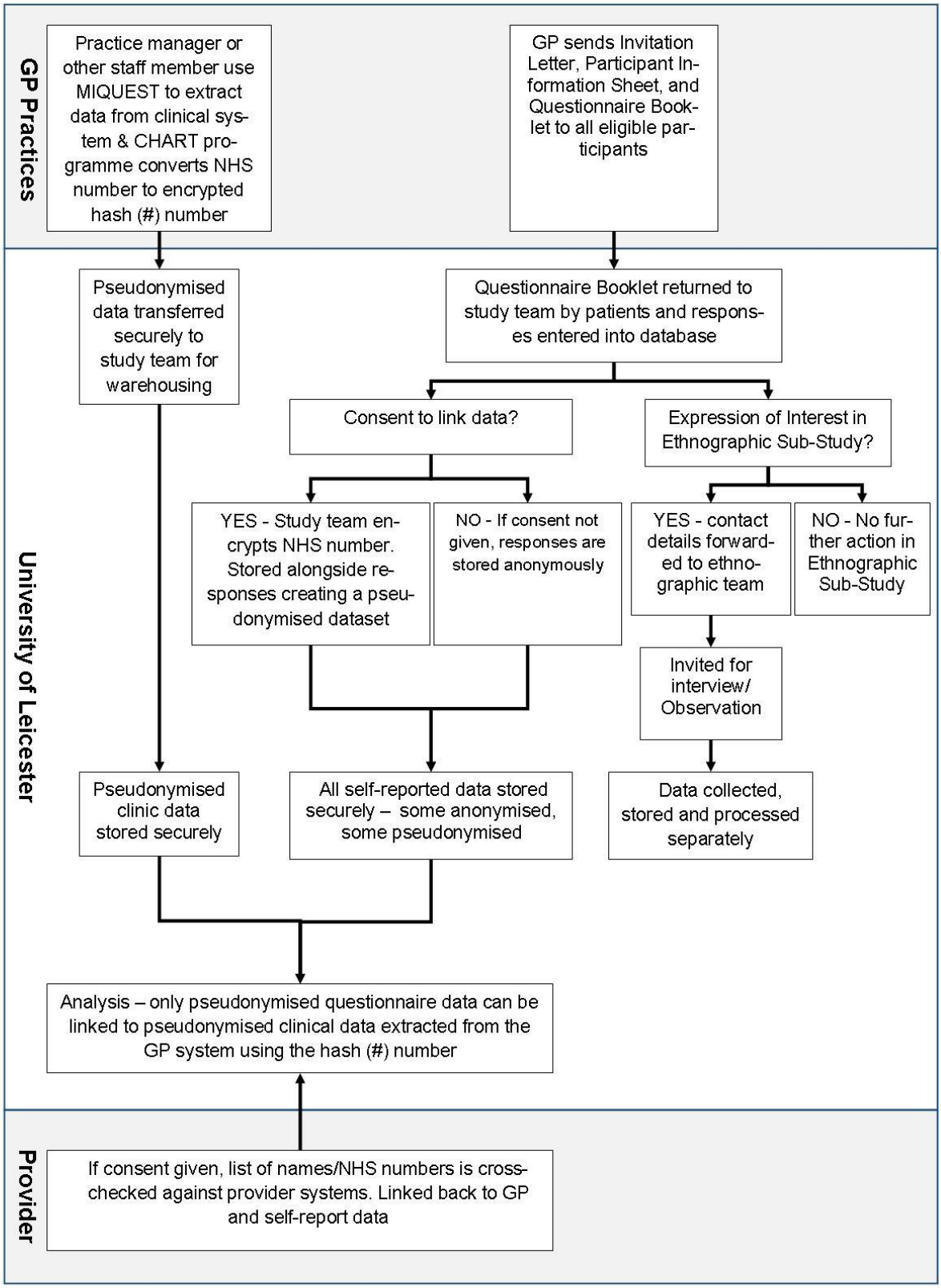
Each questionnaire booklet sent to patients via a practice mail shot will be pre-assigned a unique PID. Consent and patient details (practice name, NHS number, patient name and contact details) will be collected on a separate form and will be stored separately from the questionnaire responses, so that they are anonymous. The following data will be collected on the form:

- Whether or not the patient was referred to and attended SME
- Where the patient has previously received diabetes information from
- Whether or not the patient is willing to complete an additional study questionnaire (postal copy).If the patient agrees to complete the additional questionnaire the following data will be collected:
    - Patient Activation Measure
    - Well-Being (W-BQ12)
    - Problem Areas in Diabetes (PAID) score.

If the questionnaire booklet is completed and returned with consent, the study team will use the NHS number to identify the individual patient data in the data extracted from primary care. PRIMIS will provide the study team with the encryption algorithm so a NHS number can be converted to the unique hash (#) code to allow this linkage. Additionally, if consent is given, the list of names and NHS numbers of patients will be cross-checked against relevant Provider systems, and data on SME invitation and attendance held by the Provider for these individuals will be sent to the study team at the University of Leicester and linked with their GP and self-report data. The study team

will only have access to the name and NHS number of patients returning their questionnaire booklets and will only link data of consenting patients. The flow of patient data is shown in Figure 3.

Figure 3. Flow of patient data.



Ethnographic Sub-Study

Ethnographic data collection (interviews and observations) will take place in the 12 practices taking part, as well as in associated management and commissioning organisations relating to these practices (e.g. the CCG, NHS England regional offices and areas teams, commissioning support units, education Providers, and other bodies that become involved in the delivery of the Embedding Package) and will involve:

- Observational work in a range of contexts (including practices, CCGs and Providers). This is likely to include observation of: 'usual care'; implementation of the Embedding Package; continued observation of the Package context. This will include informal discussions with relevant staff, structured field notes and collation of key documents, including publically available information [31].
- Semi-structured interviews (involving stakeholders involved in commissioning, training and implementing SME and/or the Embedding Package, plus people with T2DM). Interviews will explore perceptions and experiences related to the various elements of the Package, and preferred modalities of SME (such as group-based, one-to-one or online). Interviews will last approximately 30-45 minutes and may be conducted at their place of work, home, another convenient location, or by telephone, depending on participant preference. All interviews will be audio-recorded (after seeking consent) and transcribed.

Cost-Effectiveness Sub-Study

The 'Embedder(s)' (i.e. the person(s) responsible for driving the implementation of the Embedding Package) will complete a simple tick-box tracker of the pre-identified implementation activities for months 3-12, 12-21 and 21-33. This tracker will cover the type of activity, the duration over which it was applied, and whether it is still ongoing. An analogous process will be applied to the CCG/Providers, with a tracker being completed by a designated member of staff. As well as providing a census of what activities have been attempted, the tracker data will provide a measure of resource use against which unit costs can be applied to estimate the costs associated with the Embedding Package. The unit costs will be generated by structured interviews undertaken with practice managers (or other appropriate staff member) within a sub-sample of 12 practices and designated staff in all CCG/Providers. These interviews will relate to the individual activities that have been identified within their particular survey response. The interview will ask for details of staff time, consumables, and other costs that have been devoted to each individual activity over the duration that the activity was undertaken. A pro-forma for the activity data requirements will be sent in advance of the meeting. A follow-up e-mail to confirm the data discussed at the meeting will be sent to the interviewees. A maximum of two further e-mails will be sent to resolve any outstanding data queries.

8.4 Randomisation

This is an open-label trial as it will not be possible to blind practices to their treatment arm, i.e. they will be aware whether they are receiving the Embedding Package. Practices will be randomised prior to baseline (Month 0) in a 1:1 fashion to either:

1. Immediate group: Provide usual care for months 0-3 then receive the Embedding Package for months 3-21,

Or

2. Wait-list group: Provide usual care for months 0-12 then receive the Embedding Package for months 12-21.

Randomisation will be stratified by CCG, and performed by an independent statistician from the Leicester Diabetes Centre. The statistician will provide the study team with the randomisation list so that they can inform practices of their allocation.

8.5 Definition of End of Trial

The end of the trial is defined as when the last data extraction (Month 33) has occurred for all practices.

8.6 Discontinuation/Withdrawal of Participants from Study Treatment

Each participating patient, stakeholder, or practice has the right to withdraw from the study at any time. However, if a participant returns their questionnaire anonymously (i.e. if they do not complete their name on the consent form) then they will be unidentifiable and therefore unable to be withdrawn.

The Investigators may withdraw a participating patient, stakeholder, or practice if they consider it necessary for any reason including:

- Ineligibility (either arising during the study or retrospective having been overlooked at recruitment)
- Significant protocol deviation
- Significant non-compliance with the study requirements
- Consent withdrawn
- Lost to follow up
- Loss of capacity.

The reason for withdrawal will be recorded in the TMF and study database.

8.7 Source Data

Excel spreadsheets containing one line per patient data extracted via a MIQUEST query at months 3, 12, 21, and 33 will be considered source data. Excel spreadsheets will be stored on secure drives at the University of Leicester, according to standard organisational practice.

The original copy of the consent form and questionnaire booklet filled out and returned by patients will be treated as source data. Forms and questionnaires will be stored separately in locked filing

cabinets in offices at the University of Leicester or University Hospitals of Leicester, as appropriate. Questionnaire data will be entered on to a study-specific database.

Data provided by SME Providers

Information provided by SME Providers will be in the form of electronic spreadsheets or paper records. Emails from SME Providers may also contain source data. Electronic records and emails will be stored on secure drives at the University of Leicester, University Hospitals of Leicester, De Montfort University, or the University of Sheffield. Paper records will be stored in locked filing cabinets in offices at the University of Leicester, University Hospitals of Leicester, De Montfort University, or the University of Sheffield.

Observations and interviews

Source data will be interview recordings/transcripts and observational notes from meetings attended by a member of the research team. Electronic records will be stored on secure drives at the University of Leicester, University Hospitals of Leicester, De Montfort University, or the University of Sheffield, as required. Paper records will be stored in locked filing cabinets in offices at the University of Leicester, University Hospitals of Leicester, De Montfort University, or the University of Sheffield, as appropriate.

Practice activity survey

Trackers completed by the practice managers and/or other staff will be source data. Email correspondence and the final pro-forma generated as a result of the interviews will also be source data. Electronic records will be stored on secure drives at the University of Sheffield, University of Leicester, or University Hospitals of Leicester, as appropriate. Paper records will be stored in locked filing cabinets in offices at the University of Sheffield, University of Leicester, or University Hospitals of Leicester.

9. TREATMENT OF TRIAL PARTICIPANTS

9.1 Description of the Intervention (Embedding Package)

The Embedding Package underwent development based on a range of qualitative and experiential work, as well as piloting in an earlier feasibility study and comprises of four key components:

1. Clear Marketing Strategy
2. User friendly and effective referral pathways
3. New/amended roles including a local clinical champion and an 'Embedder'
4. Toolkit of resources (for patients, HCPs and other key stakeholders)

Points 1, 2 and 4 have been combined into one user-friendly website ('The Toolkit'). The toolkit contains a wide selection of patient-facing resources (e.g. promotional posters, invitation letters and self-referral forms), HCP-oriented resources and guidance (e.g. document templates, guidance for recruiting staff, referring patients and increasing staff engagement) and coordination/Provider/commissioner-oriented resources (e.g. audit collection and reporting, electronic administration and referral systems, and sample referral pathways). It will also include guidance on constructing and carrying-out marketing and communication strategies, how to carry out local needs assessments, as well as detail about how to ensure patient accessibility and course tailoring.

The new/amended roles will include the appointment of an 'Embedder' working across CCG's (or potentially up skilling of an individual already holding an analogous post) who will liaise between all relevant stakeholders to promote SME, use of the Toolkit, communication and referrals etc. A local clinical champion in each CCG (for example the Diabetes Lead at one of the participating practices) will be identified to promote SME across the whole locality. Together the two roles and the online Toolkit make up the 'Embedding Package' (the intervention).

Patients will also be able to access online versions of DESMOND as a complement to attendance at the group-based version as some patients may prefer education delivered via a different modality. In order to track the use of this, practice-specific log-ins will be generated that participating practices can give to patients with T2DM. There will be posters in participating practices to make patients aware of this option.

Due to the long-term nature of this project, the study design will need to account for the changing landscape of the NHS, including taking into account changes in technology, workforce, capacity and infrastructure, to ensure that its outputs remain relevant. To allow for these alterations whilst maintaining the integrity of the study, any changes to the Embedding Package will only be made at Month 12, i.e. when the wait-list group begin receiving the intervention, so that the Embedding Package received during any one time period is consistent. The details of the Embedding Package that is actually delivered in each time period will be recorded and considered in secondary analyses, as appropriate.

On commencing of the study in a CCG, the Embedder will hold a Toolkit Action Plan meeting to look at which elements of the Toolkit can be implemented. This will then be written up and circulated for finalisation including assigning of tasks to relevant personnel. Review meetings will be scheduled to look at progress.

Actions relating to practices will then be disseminated by the 'Embedder' to the relevant staff within each practice, and additional discussion meetings arranged, if necessary.

9.2 Description of the Control (Usual Care)

Usual care will be practice-dependent; therefore, each practice will continue to provide their usual activities related to SME whilst in the control period. These activities vary greatly between CCGs and their associated practices, and due to the ever-changing landscape of the NHS (for example, with new and emerging local Sustainability and Transformation Plans; STPs), usual care may evolve overtime. However, usual care will be monitored and recorded within all practices. Furthermore, this variation is acceptable because, due to the study design, each practice will act as their own control, as described in Section 6.1.

9.3 Compliance with the Intervention

Due to the varying demands on GP practices the amount of time they will choose to spend on actioning elements of the Toolkit will vary between practices. This will be tracked as part of the Cost-Effectiveness trackers (Section 8.3) and therefore variance in compliance will be estimated.

10. SAFETY REPORTING

The study does not have patient interventions. Therefore, upon advice from Sponsor, it is not applicable to report Adverse Events or Serious Adverse Events.

11. STATISTICS

11.1 Description of Analysis Methods

RCT

Data from the RCT will be analysed once data collection is complete. A CONSORT diagram showing the flow of practices through the trial will be produced. Descriptive summary statistics of baseline characteristics and process variables (e.g. number of education sessions available, back end data for the Toolkit and MyDesmond websites, usual care delivery, etc) will be produced, using mean (standard deviation) for normally-distributed variables, median (interquartile range) for non-normally distributed variables, and count (percentage) for categorical variables.

The primary analysis will compare HbA1c between the control and intervention states using a mixed model that allows for repeated longitudinal outcomes and practice-level clustering, and is adjusted for season. The primary analysis will be based on the intention-to-treat (ITT) population, i.e. all eligible patients will be included. Missing outcome data will need to be imputed for the ITT analyses. This will be done using an appropriate multiple imputation method; it is anticipated that predictive mean matching will be used to impute continuous outcomes as this is able to handle non-linearity and non-normality, and logistic regression will be used for binary outcomes. Predictive variables are likely to include practice level demographics, e.g. sex, ethnic group, or baseline HbA1c. Sensitivity analyses will repeat the primary analyses using complete cases and per protocol populations.

As secondary analyses, the ITT model from the primary analysis will be fitted for the following sub-groups of interest:

1) Including only patients who attended education, seeking a 0.3% clinically significant difference in HbA1c, as seen in the trials of education interventions
2) Excluding patients with HbA1c <6.5% at baseline
3) By baseline education attendance status
4) By patient ethnicity and age to examine the effectiveness of the Embedding Package in hard-to-reach groups
5) By type of programme offered/attended.

Secondary patient-level and practice-level outcomes will be compared in a similar manner to the primary analyses, except that practice-level outcomes will not be adjusted for cluster and the psychosocial outcomes will not account for repeated measures as they will only be measured once.

Summaries of self-reported referral and attendance will be produced using appropriate descriptive statistics for the whole dataset and by pertinent subgroups, such as sex and age. Data on SME referrals and attendance will also be compared between data sources (i.e. self-report, practice, and Provider).

Observational Follow-Up

Summaries of the outcomes measured in the observational follow-up will be produced using appropriate descriptive statistics. HbA1c at 33 months will be compared with the HbA1c estimates

under intervention and control conditions in the RCT using mixed regression models accounting for repeated measures on the same patients and for the practice-level clustering. Similar analyses will be conducted for the secondary outcomes, including the process outcomes which will aid understanding about why changes are, or are not, sustained.

Ethnographic Sub-Study

Observational and interview-based data collected in the RCT will be analysed using the coding and analytical framework based on Normalisation Process Theory [23, 24]. Findings from the ethnographic work will be triangulated with quantitative observational data [32] and integrated into the overall findings of the trial to provide an in-depth explanation of the extent of success of implementing the Embedding Package at different levels and in different settings, and inform how to optimise implementation of the Package (and similar initiatives).

Analysis of the ethnographic data collected during the observational follow-up will be informed by the findings of the feasibility study and the RCT. Normalisation Process Theory will provide a theoretical background to analysis and will utilise the framework approach. This will ensure rapid development of, and integration with findings from the earlier stages. Findings will be used to explain and expand quantitative results in relation to sustainability, particularly differences across and within practices and associated organisations.

Cost-Effectiveness Sub-Study

The general framework for the analysis is to describe the costs and effects of current levels of implementation using published estimates of the cost-effectiveness of patient education programmes, then estimate the incremental costs and benefits of increased implementation. These incremental costs and benefits will be a combination of the costs of the implementation activities, the associated increase in uptake and the cost effectiveness of the patient education programmes. This framework has been applied to implementation of QOF indicators [33] and is currently being developed further by the Department of Health Policy Research Unit for the Economic Evaluation of Health and Care Interventions (EEPRU).

The cost-effectiveness analysis will take an NHS perspective and model costs and effects over the lifetime of patients (with appropriate discounting).

The costs of implementation activities will be generated from within the RCT. The uptake of individual embedding activities in each practice will be recorded through an activity tracker, whilst unit costs for each activity will be generated via interviews in all CCGs and a sample of 12 practices. The resources identified in each interview will be costed using either budget information from the practices/CCGs or external unit costs (e.g. Unit Costs of Health and Social Care (2013)). All other costs relating to diabetes care will be generated by the Sheffield Type 2 diabetes policy model, which will have its data sources updated through literature review and identification of the most recent unit costs.

The effects of the implementation activities will be measured in terms of quality adjusted life years (QALYs) estimated using the Sheffield Type 2 diabetes policy model. The model will generate the QALYs via changes in HbA1c associated with SME. Changes in HbA1c will be estimated in two ways. The primary analysis will be based on individual patient data from this RCT (as described

above), whilst a secondary analysis will use published estimates of the effectiveness of SME generated form a meta-analysis of RCT data; the meta-analysis will be undertaken as part of this Sub-Study.

The central estimate of the incremental cost-effectiveness ratio of the Embedding Package will be presented, together with probabilistic estimates of cost-effectiveness represented in a cost-effectiveness acceptability curve. Value of information analysis will be undertaken using the Sheffield Accelerated Value of Information tool. Deterministic sensitivity analysis will also be undertaken to explore the effects of uncertainties that cannot be adequately represented probabilistically; for example, the length of effect of the Package, uptake rate without the Package, and the mix of alternative education programmes to which patients are referred.

Methods and results will be reported in line with Consolidated Health Economic Evaluation Reporting Standards (CHEERS) recommendations.

11.2 The Number of Participants

The sample size calculation is based on a 0.05% reduction in HbA1c (SD = 1.5%), based on United Kingdom Prospective Diabetes Study (UKPDS) data. To detect this change, a total of 58 practices would be required assuming 80% power, 5% alpha and the median number of eligible patients per practice as 348 (based on Leicester City CCG data). An ICC of 0.05 was utilised to calculate the design effect to adjust for clustering, with one baseline HbA1c measurement to be taken for each individual and only one measurement at each of the 2 steps. The total design effect and variation in cluster size was 1.41. We aim to recruit 66 practices to allow for a 10% practice drop-out rate.

Return of a completed questionnaire booklet (self-report questionnaire and/or consent to link data form) will be recorded as consent to participate in the study. Additionally stakeholders and patients consenting to ethnographic interviews and observations will be recorded as participants. It is anticipated a minimum of 1000 participants will be recruited.

11.3 The Level of Statistical Significance

Statistical significance will be defined as p-values less than 0.05.

11.4 Criteria for the Termination of the Trial

There are no pre-defined criteria for early termination of the trial.

11.5 Procedure for Accounting for Missing, Unused, and Spurious Data

Missing outcome data will be imputed using multiple imputation methods in the primary analyses, as described in Section 11.1.

11.6 Procedures for Reporting any Deviation(s) from the Statistical Plan

A statistical analysis plan will be written prior to database lock. Any deviations from this plan will be detailed in the final report.

11.7 Inclusion in Analysis

All eligible patients from randomised practices will be included in the analysis. If a practice withdraws after randomisation but does not withdraw consent to use already obtained data then all eligible patients from this practice will be included in the analysis with missing data imputed. If a practice withdraws consent for its data to be used then the patients from this practice who were only part of the primary care data extraction will be excluded, however individually consented patients will remain in the study. If a patient or stakeholder withdraws the informed consent they provided for one or more of the Sub-Studies prior to data analysis, then their data will not be used in the relevant Sub-Study/Sub-Studies.

12. DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

Direct access will be granted to authorised representatives from the Sponsor, host institution, and the regulatory authorities to permit trial-related monitoring, audits and inspections.

13. QUALITY CONTROL AND QUALITY ASSURANCE PROCEDURES

The study will be conducted in accordance with the current approved protocol, ICH GCP, relevant regulations and standard operating procedures.

The trial manager will undertake quality checks of the study throughout its life to ensure all relevant standard operating procedures are followed and the study complies with ICH GCP.

Conduct of this study will be overseen by a Trial Management Group (TMG) which will meet regularly (planned monthly) to discuss the progress of the study and address any issues arising.

The Sponsor operates a risk based audit programme to which this study will be subject.

14. CODES OF PRACTICE AND REGULATIONS

14.1 Ethics

Any patient returning an anonymous questionnaire will be unable to withdraw from the study because it will not be possible to identify which form needs to be withdrawn. All other participants will be free to withdraw at any time without providing a reason. Any data collected prior to withdrawal may still be used, unless the participant explicitly withdraws consent for these data to be used.

14.2 Sponsor Standard Operating Procedures

All relevant Sponsor standard operating procedures will be followed to ensure that this study complies with all relevant legislation and guidelines

14.3 Declaration of Helsinki

The Investigator will ensure that this study is conducted in full conformity with the current revision of the Declaration of Helsinki (last amended October 2000, with additional footnotes added 2002 and 2004).

14.4 ICH Guidelines for Good Clinical Practice (GCP)

The Investigator will ensure that this study is conducted in full conformity with relevant regulations and with the ICH Guidelines for GCP (CPMP/ICH/135/95) July 1996.

14.5 Approvals

Once Sponsor authorisation has been confirmed, the protocol, informed consent form, PIS, and any proposed advertising material will be submitted to an appropriate Research Ethics Committee, Health Research Authority, and host institution(s) for written approval.

Once Sponsor authorisation has been confirmed, the Investigator will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents.

14.6 Participant Confidentiality

The study staff will ensure that the participants' anonymity is maintained. The participants will be identified by a PID number on paper records and by a PID and encrypted hash # code in any electronic database. All documents will be stored securely and only accessible by study staff and authorised personnel. Once the data have been analysed, all documentation will be archived in line with University of Leicester policy. The study will comply with the Data Protection Act which requires data to be anonymised as soon as it is practical to do so.

15. DATA HANDLING AND RECORD KEEPING

Participants will be identified by a study specific PID number in any database. This will be assigned upon return of a completed questionnaire. Consent forms and any identifiable information required to facilitate observations or interviews will be stored separately from any clinical or self-reported data. Self-reported patient data will be entered on to a study-specific database.

Electronic records will be stored on secure drives at the University of Leicester, University Hospitals of Leicester, De Montfort University or University of Sheffield. Paper records will be stored in locked filing cabinets in offices at the University of Leicester, University Hospitals of Leicester, De Montfort University or University of Sheffield.

16. STUDY GOVERNANCE

16.1 Trial Steering Committee (TSC)

The TSC will meet annually and will include the Chief Investigator (Prof. Davies), an independent Chair, an independent statistician, an independent external member and an independent PPI representative. The study team will attend the TSC when required. The TSC will act as an independent strategic oversight and will ensure transparency and that the work is reaching the relevant milestones. They will receive reports from the TMG.

16.2 Trial Management Group (TMG)

The TMG will meet monthly to discuss all aspects of the trial and report directly to the TSC. All investigators and other members of the study team, where appropriate, are invited and the meeting will be chaired by the Chief Investigator (Professor Davies). Project targets/milestones and progress will be reviewed, and risk assessment and troubleshooting undertaken. At strategic points of the trial, longer and more in-depth TMG meetings will be held in order to ensure attendance of all investigators.

16.3 Data Safety Monitoring Committee (DSMC)

As there is no patient intervention, a DSMC will not be convened.

17. FINANCING AND INSURANCE

The Embedding Diabetes Education study is funded by the NIHR Programme Grant for Applied Research (PGfAR) (reference number RP-PG-1212-20004) and details have been drawn up in a separate agreement.

The study will be Sponsored by University of Leicester and covered by University of Leicester insurance and indemnity arrangements.

18. PUBLICATION POLICY

The trial will be registered prior to study initiation on ISRCTN registry. The findings of the research will be presented at conferences and will be submitted for publication in relevant peer-reviewed journals. All activity and findings will be submitted and available via open-access in the final report to the NIHR at the end of the study.

19. REFERENCES

1. International Diabetes Federation, *IDF Diabetes Atlas: 6th Edition.* 2013.
2. Health and Social Care Information Centre, *Quality and Outcomes Framework 2014-2015*. 2015: Leeds, UK
3. Healthcare Quality Improvement Partnership, *National diabetes audit 2015-2016: report 1: care processes and treatment targets. England and Wales 31 January 2017*. 2017.
4. Hex, N., et al., *Estimating the current and future costs of Type 1 and Type 2 diabetes in the UK, including direct health costs and indirect societal and productivity costs.* Diabetic Medicine, 2012. **29**(7): p. 855-862.
5. Gillett, M., et al., *Delivering the diabetes education and self management for ongoing and newly diagnosed (DESMOND) programme for people with newly diagnosed type 2 diabetes: cost effectiveness analysis.* Bmj, 2010. **341**: p. c4093.
6. Davies, M.J., et al., *Effectiveness of the diabetes education and self management for ongoing and newly diagnosed (DESMOND) programme for people with newly diagnosed type 2 diabetes: cluster randomised controlled trial.* Bmj, 2008. **336**(7642): p. 491-495.
7. National Institute for Health and Care Excellence, *Guidance on the use of patient-education models for diabetes.* Technology appraisal, 2003. **60**.
8. Deakin, T., et al., *Structured patient education: the Diabetes X-PERT Programme makes a difference.* Diabetic Medicine, 2006. **23**(9): p. 944-954.
9. Sturt, J., et al., *The Diabetes Manual trial protocol - a cluster randomized controlled trial of a self-management intervention for type 2 diabetes [ISRCTN06315411].* BMC Fam Pract, 2006. **7**: p. 45.
10. Sturt, J., et al., *A psychological approach to providing self-management education for people with type 2 diabetes: the Diabetes Manual.* BMC Fam Pract, 2006. **7**: p. 70.
11. Sturt, J.A., et al., *Effects of the Diabetes Manual 1:1 structured education in primary care.* Diabet Med, 2008. **25**(6): p. 722-31.
12. Trento, M., et al., *Rethink Organization to iMprove Education and Outcomes (ROMEO) A multicenter randomized trial of lifestyle intervention by group care to manage type 2 diabetes.* Diabetes care, 2010. **33**(4): p. 745-747.
13. National Institute for Health and Care Excellence, *Hypertension: clinical management of primary hypertension in adults.* National Institute for Clinical Excellence, London, 2011.
14. National Institute for Health and Care Excellence, *NICE Quality and Outcomes Framework indicator*. 2016.
15. Health and Social Care Information Centre. *National Diabetes Audit 2013-2014 and 2014-2015 Report 1: Care Processes and Treatment Targets*. 2016 28/01/2016 [cited 2016 28/06/2016]; Available from: http://www.hscic.gov.uk/catalogue/PUB19900/nati-diab-rep1-audi-2013-15.pdf.
16. All-Party Parliamentary Group for Diabetes, *Taking control: supporting people to self-manage their diabetes.* 2015, Diabetes UK.
17. Winkley, K., et al., *Patient explanations for non-attendance at structured diabetes education sessions for newly diagnosed Type 2 diabetes: a qualitative study.* Diabetic Medicine, 2015. **32**(1): p. 120-128.
18. Carey, M., K. Khunti, and M. Davies, *Structured education in diabetes: A review of the evidence.* Diabetes & Primary Care, 2012. **14**(3).

19. Buchanan, D.A., et al., *Nobody in charge: Distributed change agency in healthcare.* Human Relations, 2007. **60**(7): p. 1065-1090.
20. Martin, G.P., et al., *Innovation sustainability in challenging health-care contexts: embedding clinically led change in routine practice.* Health services management research, 2012. **25**(4): p. 190-199.
21. Stirman, S.W., et al., *The sustainability of new programs and innovations: a review of the empirical literature and recommendations for future research.* Implementation Science, 2012. **7**(1): p. 1.
22. Craig, P., et al., *Developing and evaluating complex interventions: the new Medical Research Council guidance.* BMJ, 2008. **337**: p. a1655.
23. May, C., *A rational model for assessing and evaluating complex interventions in health care.* BMC Health Serv Res, 2006. **6**: p. 86.
24. Murray, E., et al., *Normalisation process theory: a framework for developing, evaluating and implementing complex interventions.* BMC Med, 2010. **8**: p. 63.
25. Bryman, A., *Social research methods*. 2012, Oxford, UK: Oxford University Press.
26. Teddlie, C.Y., F., *Mixed methods sampling: A typology with examples.* Journal of Mixed Methods Research, 2007. **1**: p. 77.
27. Holt, T.A., et al., *AUtomated Risk Assessment for Stroke in Atrial Fibrillation (AURAS-AF)-an automated software system to promote anticoagulation and reduce stroke risk: study protocol for a cluster randomised controlled trial.* Trials, 2013. **14**(1): p. 385.
28. NHS Information Centre for health and social care, *Anonymisation Standard for Publishing Health and Social Care Data. Supporting Guidance: Drawing the line between identifying and non-identifying data.* Information Standards Board for Health and Social Care, 2013.
29. Department of Health, *Information: To Share Or Not To Share? The Information Governance Review* 2013.
30. Away from my Desk, *Away from my Desk Security Design Specification (in commercial confidence).* Away from my Desk, 2010.
31. Wolfinger, N.H., *On writing fieldnotes: collection strategies and background expectancies.* Qualitative Research, 2002. **2**(1): p. 85-95.
32. Benning, A., et al., *Large scale organisational intervention to improve patient safety in four UK hospitals: mixed method evaluation.* BMJ, 2011. **342**: p. d195.
33. Walker, S., et al., *Value for money and the Quality and Outcomes Framework in primary care in the UK NHS.* Br J Gen Pract, 2010. **60**(574): p. e213-20.