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A trial to evaluate a complex intervention for deprescribing potentially inappropriate medications in frail older people with type 2 diabetes

Submission date
10/08/2021

Recruitment status
No longer recruiting

Registration date
16/08/2021

Overall study status
Completed

Last Edited
26/11/2024

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Many older people suffer from frailty, characterised by a decline in both their physical and mental health and a number of health conditions requiring treatment. In type 2 diabetes, managing frailty means striking a balance to prevent overtreatment with some diabetes medications which increase the risk of low blood sugar and lead to more falls, fractures and deaths. The aim of this study is to help clinical practice staff with prescribing responsibilities to reduce the proportion of potentially inappropriate diabetes medications prescribed in older people (aged 65 years and over) with type 2 diabetes and frailty. Managing medication for this group of patients is complex and they often require multiple medications. Reducing unnecessary diabetes medication prescriptions may prevent the adverse treatment effects associated with overtreatment. This may also reduce unnecessary prescription costs. This study is investigating an intervention involving an electronic decision-support system, accompanied by clinical training, follow-up support and performance review, designed to support practice staff to reduce potentially inappropriate diabetes medications in a primary care setting.

Who can participate?
GP practices (4000 to 12,000) within three or four different English regions that use either EMIS Web or SystmOne clinical database systems and have categorised their older patients with type 2 diabetes with the electronic frailty index (eFI) in line with the Quality Outcomes Framework (QOF)

What does the study involve?
All practices will be asked to participate in the export of study data at the beginning of the study and again at 6 and 12 months. GP practices are randomly allocated to an intervention or control group. Practices in the control group will continue with ‘usual’ care for their patients and will not have to participate in any other activities. Practices in the intervention group will be asked to undertake the following activities. An electronic decision-support system will be remotely installed on the practice IT system for 12 months to facilitate the identification and

management of older frail people with type 2 diabetes. This software will allow practice staff to run a search to generate a list of potential patients for a medication review and it will also generate automatic screen alerts when patients, who are potentially eligible for medication review, attend an appointment. Criteria used to identify these patients will include their age, diagnoses, most recent HbA1c result, their prescribed medications and their electronic Frailty Index (eFI) score. Training on how to use this system will be delivered as part of a webinar training session for intervention practices. At least two members of the practice clinical team with responsibility for managing prescriptions for older patients with type 2 diabetes (for example a practice nurse with prescribing rights, a general practitioner or a practice clinical pharmacist where there is one) will be asked to complete a webinar training session with a clinical advisor. This will take about 1 hour and will upskill the clinicians in the management of this high-risk patient group - learning when and how to safely reduce, stop or switch diabetes medications. Additionally, each intervention practice will have access to email support, short online booster-training sessions and will receive a 3-month performance review with a clinical advisor. A clinical advisor will also contact the practice on a monthly basis to monitor patient safety and discuss any issues or concerns.

What are the possible benefits and risks of participating?
Clinical practitioners in intervention practices will benefit from the opportunity to upskill and receive follow-up support with a trained clinical advisor to manage their older, frail type 2 diabetes patients more confidently and effectively in line with current guidance. Additionally, practices will also benefit from having the electronic decision-support system to easily identify potential patients for deintensification, and to guide them through the deintensification process. Practices may also benefit from a possible cost saving due to the potential reduction in the prescribing of expensive medications.
The main risk for participating practices is the potential of serious adverse events (hypo- and hyperglycaemic events, diabetic ketoacidosis events, falls and fractures hospital admissions and death) occurring, caused by the deintensification of treatment. This risk is an unavoidable part of the clinical decision-making process for the deintensification of diabetes medications. To help minimise this risk, practices will have access to email support; they will also receive monthly telephone calls from a clinical advisor to discuss any issues and concerns and to ensure that patients are being closely monitored during the study.
All patient data will be pseudonymised at the point of extraction. However, there is a small, potential risk that this data could be re-identified. To minimise any risk of re-identification, robust procedures will be in place so nobody out with the practice setting will have access to any patient identifiable data. Re-identification could only occur in very rare circumstances where a person with access to the data also had access to the individual practice database together with other information.
Capacity and time to attend training and to become familiar with how the electronic-based decision support system works may be a burden for some practices. To minimise this potential burden the researchers will aim to keep training time to a minimum and the decision-support system simple so that it is easy to use with little instruction. Also, there will be short, online booster-training sessions to help consolidate the key learning outcomes from the main training webinar, which participants will be able to access at their own convenience.

Where is the study run from?
The University of Leicester (UK)

When is the study starting and how long is it expected to run for?
July 2019 to November 2024

Who is funding the study?
The National Institute for Health Research Applied Research Collaboration East Midlands (NIHR ARC-EM) (UK)

Who is the main contact?
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Study website
https://arc-em.nihr.ac.uk/research/de-intensification-medications-d-med-study

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Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
280971

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 49818, IRAS 280971

Study information

Scientific Title
Evaluation of an electronic decision-support system, plus training with follow-up support and performance review, for the deintensification of potentially inappropriate medications (D-Med) to prevent overtreatment in the management of older frail people with type 2 diabetes: a 12-month follow-up cluster randomised trial

Acronym
D-Med

Study objectives
The null hypothesis for the study is that the D-Med intervention will have no effect in reducing the number of prescriptions for potentially inappropriate diabetes medications, in older frail type 2 diabetes patients, when compared to a ‘usual’ care control.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 03/08/2021, East Midlands - Leicester Central Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)2071048138; leicestercentral.rec@hra.nhs.uk), REC ref: 21/EM/0163

Study design
Randomized; Interventional; Design type: Process of Care, Complex Intervention, Management of Care

Primary study design
Interventional

Secondary study design
Cluster randomised trial

Study setting(s)
GP practice

Study type(s)

Treatment

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Type 2 diabetes

Interventions
The null hypothesis for the study is that the D-Med intervention will have no effect in reducing the number of prescriptions for potentially inappropriate diabetes medications, in older frail type 2 diabetes patients, when compared to a 'usual' care control. To reject this hypothesis and show that the intervention has an effect, a difference of 10% will be required between the intervention and control groups. This difference was decided after discussion with clinicians to find an appropriate minimum clinically important difference to assess. The number of prescriptions for potentially inappropriate diabetes medications was chosen as the primary outcome because prescribing data is routinely recorded and can be easily extracted, for audit and research purposes, at general practice level. Moreover, this data can be easily pseudonymised at the point of extraction. Coupled with a randomised cluster design, chosen as the study is targeting the upskilling of a group of health providers at practice level rather than individual patients, removes the need for individual informed patient consent and the recruitment of individual patients. Furthermore, it reduces the risk of contamination between patients which could bias the results of the study. The trial is also designed to be pragmatic so that we can evaluate what will happen to patient care in a real practice setting, when compared to 'usual' care, if a practice-wide upskilling intervention is delivered.

Based on preliminary searches, assuming an average of 40 patients per practice being eligible for deintensification of their medication, and a conservative intra-class correlation of 0.05, we will need to recruit 40 practices (20 in each arm, total number of patients = 1520), to detect a difference of 10% in the primary outcome of medication deintensification and to allow for the dropout of two practices. This assumes a small change in deintensification of 5% in the control arm (due to current practices and changes in care) and 15% in the intervention arm, during the trial. The plan is to run the study in the East Midlands and 2-3 other English regions, in which case 10 to 14 practices per region will be needed. The sample size was calculated with 90% power and for a 5% significance level. Variation in cluster size between practices was allowed for, and the inflation for unequal cluster size was based on a reported average coefficient of variation of 0.65. The sample size was calculated in Stata using the clustersampsi command.

Practices will be approached to take part and pre-screened for practice eligibility. In line with the Remote Access Agreement, remote searches will then be carried out by PRIMIS to identify older frail people with type 2 diabetes who fulfil the study inclusion criteria. This will be followed by the baseline data extraction. All outcomes data will be extracted from primary care records and will consist of pseudonymised demographic, clinical and prescription data collected routinely as part of diabetes care. All outcomes will be measured at baseline (0-month), 6-months (0-6 months), and 12-months (6-12 months). Each new time point period will start following the previous extraction and will include all dates up to the date of the next extraction. The data extractions will be carried out remotely and have been planned to require minimal practice time and input.

Following consent, the randomisation process will be carried out by an independent statistician from the University of Leicester to ensure allocation concealment from practices and from the study team staff. Otherwise, this will be an open, unblinded trial as study staff and practices will need to be made aware of their group allocation. However, in line with what happens in real practice settings, we consider there will be minimal contamination between practices. Cluster (GP practice) numbers will be assigned sequentially as each practice enters the study. The practices will be assigned to either the control or intervention arm on a 1:1 basis, stratified for region and ethnicity (White European or other ethnic minority including Black and Asian). The decision to stratify by ethnicity was based on previous experience with a similar study in which an unequal randomisation allocation of ethnic minority participants occurred. As we will be running this study in the same location, which has a high ethnic minority population, stratification by ethnicity is considered to be necessary.

Practices randomised to the intervention group will have an electronic decision-support system installed remotely followed by a remote practice training session, with a trained clinical advisor, on how to use the system and the guidelines for deintensification. Follow-up support will be available via a email support, online booster-training sessions and a 3-month performance review with the clinical advisor. This will involve an additional 3-month data extraction of prescribing and adverse event data, for diabetes medications, to produce a performance report for the review. The clinical advisor will also provide monthly calls to monitor any safety concerns or issues. Throughout the study, patients in the control group will continue to visit their GP practice, as per usual, for the management of their diabetes. Their health providers will be free to make changes to medication including deintensification changes; however, they will not have access to the electronic decision-support system to identify patients and prompt a review of medication, nor will they have access to the study algorithm to guide them through the deintensification process. Moreover, they will not receive any training or support from a clinical advisor, nor will they be sent any performance data.

Analysis will take place following the final data extraction, and no interim analyses will be carried out.

The broad study timetable (unless delayed due to the Covid-19 pandemic) is as follows for completion of key milestones:
Jul 2021 – Feb 2022 Practice recruitment and study set-up
Sep 2021– Feb 2023 Delivery of study
Mar 2023 – Aug 2023 Analysis and report writing

Intervention Type
Other

Primary outcome measure
The proportion of patients at 12-months post-baseline assessment who have had potentially inappropriate diabetes medications deintensified (stopped, reduced or switched), measured using prescription data extracted from primary care records at baseline and 12 months

Secondary outcome measures
1. The proportion of patients at 6-months post-baseline assessment who have had potentially inappropriate diabetes medications deintensified (stopped, reduced or switched), measured using prescription data extracted from primary care records at baseline and 6 months
2. Continued tight Hb1Ac control <53 mol/mols (7.0%) measured using the latest Hb1Ac value extracted from primary care records at baseline, 6 and 12 months

3. Hb1Ac level >86 mmol/mol (10.0%) measured using the latest Hb1Ac value extracted from primary care records at baseline, 6 and 12 months
4. Blood pressure (BP) <110/75 mmHg measured using the latest BP value extracted from primary care records at baseline, 6 and 12 months
5. Falls and fractures measured using new coded entries (within a measurement period) extracted from primary care records at baseline, 6 and 12 months
6. Hypoglycaemic-related adverse events measured using new coded entries (within a measurement period) extracted from primary care records at baseline, 6 and 12 months
7. Hyperglycaemic-related adverse events measured using new coded entries (within a measurement period) extracted from primary care records at baseline, 6 and 12 months
8. Emergency hospital admissions for hypoglycaemic related events measured using new coded entries (within a measurement period) extracted from primary care records at baseline, 6 and 12 months
9. Emergency hospital admissions for hyperglycaemic-related events measured using new coded entries (within a measurement period) extracted from primary care records at baseline, 6 and 12 months
10. Death measured using the latest cause of death or died entry extracted from primary care records at baseline, 6 and 12 months
11. The proportion of patients who have had potentially inappropriate blood pressure medication stopped, reduced or switched, measured using prescription data extracted from primary care records at baseline, 6 and 12 months
12. The ongoing proportion of patients in the whole practice prescribed potentially inappropriate diabetes medications, measured using prescription data extracted from primary care records at baseline, 6 and 12 months

Overall study start date
31/07/2019

Completion date
22/11/2024

Eligibility

Key inclusion criteria
Practice inclusion criteria:
As this is a cluster randomised trial, individual patient consent will not be sought. Instead, consent will be obtained at the practice level from a GP, designated as the principal investigator (PI), for the practice to take part as the study participant. In addition, an Organisational Information Document (OID), which will include a data agreement, will be signed by the PI to confirm capability and capacity as an investigator site. Additionally, the PI will need to confirm acceptance of the Remote Access Agreement which will allow PRIMIS (University of Nottingham) to process the data on behalf of the University of Leicester. A Service-Level Agreement is in place for this activity. Therefore, practices will need to comply with the following conditions:
1. A list size between approximately 4000 and 12000 patients
2. A principal investigator (PI), on behalf of the practice, is willing and able to give informed consent to take part (as the research participant) in the cluster randomised trial
3. The PI, on behalf of the practice is willing and able to sign an OID, including a data agreement, with the University of Leicester to confirm capability and capacity to deliver the study
4. The PI is willing for PRIMIS to carry out a remote database search and data extractions (at 0, 6- and 12-months), on behalf of the lead study team at the University of Leicester and in line with the Remote Access Agreement

5. The PI is willing, if allocated to the intervention group, to have an electronic decision-support system remotely installed by PRIMIS and have clinical staff participate in the training and follow-up
6. The PI is able and willing (in the Chief Investigator's opinion) to comply with all other study requirements
7. The GP practice is using either the EMIS Web or SystmOne clinical database systems
8. The GP practice has categorised moderate to severe frail patients with type 2 diabetes in line with the Quality Outcomes Framework (QOF)

Patient inclusion criteria:
At baseline, PRIMIS will run a remote database search to identify potential patients eligible for deintensification who fulfil the following inclusion criteria:
1. Confirmed diagnosis of type 2 diabetes
2. Issued diabetes medication in the last 3 months prior to the baseline search
3. Aged 65 years or older
4. Last HbA1c reading <53 mmol/mol (7.0%) in the previous 12 months prior to the baseline search
5. Categorised as moderate to severe frailty (i.e. an electronic frailty index (eFI) >0.24)

The patients identified at the baseline search will create the main study cohort and will have pseudonymised demographic, clinical and prescription data extracted at the 6- and 12-month timepoints.

Additionally, the initial search criteria will be rerun at the 6- and 12-month time points to track any practice-level changes in prescribing rates of inappropriate diabetes medications during the study.

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 1520; UK Sample Size: 1520

Key exclusion criteria
Practice exclusion criteria:
The researchers will exclude practices that meet any of the following criteria:
1. The PI is not willing and able to give informed consent
2. The PI is not willing and able to sign the OID and data agreement
3. The PI is not willing to let PRIMIS remotely install electronic software on their system to carry out the database search and data extractions
4. The PI is not willing to let PRIMIS remotely install the electronic decision-support system nor have clinical staff participate in the training and follow-up
5. The PI is not able and willing (in the chief investigator's opinion) to comply with all other study requirements
6. The GP practice is not using either EMIS Web or SystmOne clinical database systems

7. The GP practice has not categorised moderate to severe frail patients with type 2 diabetes in line with QOF

Patient exclusion criteria:
At the baseline and subsequent 6- and 12-month searches, the researchers will exclude patients who fulfil any of the following criteria:
1. No confirmed diagnosis of type 2 diabetes
2. No diabetes medication issued in the last 3 months
3. Aged 64 years old and younger
4. Last Hb1AC reading ≥53 mmol/mol (7.0%) in the previous 12-months prior to the baseline search
5. Receiving palliative/end of life care
6. No frailty categorisation available or eFI ≤0.24
7. Patient has opted out of sharing their personal data as part of the national data opt-out policy

Date of first enrolment
05/01/2022

Date of final enrolment
31/12/2022

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
NIHR CRN: East Midlands
Knighton Street Outpatients
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United Kingdom
LE1 5WW

Study participating centre
NIHR CRN: West Midlands
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WV7 3FA

Study participating centre
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Study participating centre
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Sponsor type
University/education

Website
http://www.le.ac.uk/

ROR
https://ror.org/04h699437

Funder(s)

Funder type
Government

Funder Name
NIHR Applied Research Collaboration East Midlands

Results and Publications

Publication and dissemination plan
Additional documents to be made available at a later date. Planned publication in a high-impact peer reviewed journal.

Intention to publish date
30/11/2025

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Protocol article		13/01/2024	15/01/2024	Yes	No