ISRCTN17545443 https://doi.org/10.1186/ISRCTN17545443

Optimal pathway for treatIng neuropathic pain in diabetes mellitus (OPTION-DM)

Submission date
09/09/2016

Recruitment status
No longer recruiting

Registration date
12/09/2016

Overall study status
Completed

Last Edited
20/10/2022

Condition category
Nervous System Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The number of people with diabetes is growing rapidly in the UK and is predicted to increase from 3.2 million in 2013 to 5 million by 2025. People living with diabetes often have to live with long-term complications of the disease. One of these complications is diabetic peripheral neuropathy, where the nerves in the arms and legs become damaged, leading to painful symptoms. One quarter of all people with diabetes experience these symptoms, known as “painful diabetic neuropathy”. Patients may present with burning, aching or “electric-shock” type pains. In some patients normal touch by day time or bed clothes can cause severe pain as the skin becomes extremely sensitive to touch. As the pain is felt every day, patients may have difficulty doing simple daily activities such as walking to the shop or socializing with friends. This results in a poor quality of life and depression. Unfortunately current individual medications provide only partial benefit in around of half of all patients, with many enduring inadequate pain relief and unwanted reactions. Not surprisingly therefore, many patients are frustrated with not being able to work and too many visits to see the doctor. The negative impact on them, their families and the NHS is considerable. The National Institute for Heath and Care Excellence (NICE) recommends a choice of four drugs; amitriptyline, duloxetine, and pregabalin or gabapentin, as initial treatment for painful diabetic neuropathy. If the initial treatment is not fully effective NICE recommends adding one of the other drugs in combination with the first drug. The aim of this study is to find out which of these drugs is the most effective initial treatment and then the best additional treatment for patients with painful diabetic neuropathy.

Who can participate?
Adults with painful diabetic neuropathy

What does the study involve?
Participants are randomly allocated to receive the three treatment pathways in a different order. The first pathway involves taking amitriptyline for six weeks and then amitriptyline in combination with pregabalin for a further 10 weeks (if amitriptyline alone is not giving effective relief). The second pathway involves taking duloxetine for six weeks and then duloxetine in combination with pregabalin for a further 10 weeks (if necessary). The third pathway involves taking pregabalin for six weeks and then pregabalin in combination with amitriptyline for a further 10 weeks (if necessary). The total length of the study for each patient will be one year.

During this period patients will be contacted by telephone and seen in hospital on multiple occasions. Study medications will be started at a low dose and increased gradually to find the right dose for each individual patient. Throughout the study, response to treatment will be measured using pain diaries which patients will be asked to complete. Participants also complete questionnaires at the start of the study and after 6 and 16 weeks of each treatment pathway the measure quality of life, mood, sleep and reactions to the drugs.

What are the possible benefits and risks of participating?
Possible benefits of the study are that participants will be contacted weekly by the study nurse during the study, and will be seen in clinic regularly, so are likely to have more follow-up than normal. Participants may also find a treatment pathway that is effective in treating their painful diabetic neuropathy. When the study is complete, participants will be advised which order they received the treatments, so that they are able to request their preferred treatment from their care team going forward. Possible risks are that participants will be required to stop all current pain medication before starting the study and between each pathway will need to stop taking the study medication. The amount of time without any treatment will be short but if concerns should be discussed with the study team. Also, taking part in this research may mean additional appointments at the hospital, compared to the number of appointments received normally. Although this means extra travel, travel costs in attending these hospital appointments will be reimbursed if required.

Where is the study run from?
12 hospital clinics and 80 GP practices across England (UK)

When is the study starting and how long is it expected to run for?
June 2016 to March 2021 (updated 13/04/2021, previously: January 2021)

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
1. Miss Jennifer Petrie (public)
j.petrie@sheffield.ac.uk
2. Professor Solomon Tesfaye (scientific)
solomon.tesfaye@nhs.net

Contact information

Type(s)
Public

Contact name
Miss Jennifer Petrie

Contact details
Clinical Trials Research Unit, ScHARR
Regent Court
30 Regent Street
Sheffield
United Kingdom
S1 4DA

+44 114 222 0676
j.petrie@sheffield.ac.uk

Type(s)
Scientific

Contact name
Prof Solomon Tesfaye

ORCID ID
https://orcid.org/0000-0003-1190-1472

Contact details
Sheffield Teaching Hospitals and University of Sheffield,
Royal Hallamshire Hospital
Glossop Road
Sheffield
United Kingdom
S10 2JF
+44 114 271 2204
solomon.tesfaye@nhs.net

Additional identifiers

Clinical Trials Information System (CTIS)
2016-003146-89

Protocol serial number
STH18976

Study information

Scientific Title
A multicentre, double-blind, centre-stratified multi-period crossover trial to evaluate the efficacy of the Optimal Pathway for TreatIng neurOpathic paiN in Diabetes Mellitus

Acronym
OPTION-DM

Study objectives
Null hypothesis:
There is no difference between the study Treatment Pathways (amitriptyline supplemented with pregabalin, duloxetine supplemented with pregabalin and pregabalin supplemented with amitriptyline).

Alternative hypothesis:
There is a true difference between the study Treatment Pathways (amitriptyline supplemented with pregabalin, duloxetine supplemented with pregabalin and pregabalin supplemented with amitriptyline).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Yorkshire and the Humber - Sheffield REC, 09/12/2016, ref: 16/YH/0459

Study design
Multicentre double-blind centre-stratified multiperiod crossover trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Painful diabetic neuropathy

Interventions
All participants will receive all 3 treatment pathways. A web-based randomisation system will determine the order in which they receive the pathways. Participants will be allocated to one of 6 sequences in an equal allocation to sequences (1:1:1:1:1:1).

Treatment pathways:
1. Amitriptyline supplemented with pregabalin (if necessary)
2. Duloxetine supplemented with pregabalin (if necessary)
3. Pregabalin supplemented with amitriptyline (if necessary)

Each treatment pathway has 2 treatment periods: 6 weeks monotherapy followed by 10 weeks combination therapy. Those patients who have adequate pain relief after 6 weeks will remain on monotherapy for the second treatment period. Each treatment pathway is preceded by a one week washout period. Each treatment pathway will last around 4 months and participants will receive treatment within the trial for around one year.

There will be 3 dose levels for each drug. Participants will start on the lowest dose level of each drug and the dose will be titrated up to a maximum tolerated dose over the first 2 weeks of treatment.

Blinding will be maintained with over-encapsulated drugs and matching placebo. The participants and the local research team will be blinded to treatment allocation with the exception of the site pharmacist who will be unblinded.

Participants in all groups will be followed up after 6 and 16 weeks.

Intervention Type
Drug

Drug/device/biological/vaccine name(s)
Amitriptyline Duloextine Pregabalin

Primary outcome(s)

Difference between 7 day average 24-hour pain evaluated at patient level using an 11 point NRS scale measured during the final follow-up week of each treatment pathway (Week 16)

Key secondary outcome(s))

Efficacy
1. Difference between 7-day average 24-hour pain (evaluated at patient level) on an 11 point NRS scale at Week 6 among monotherapies in each treatment pathway.
2. Health status is measured using RAND SF-36 physical mean scores at week 6 and 16 of each treatment pathway
3. Health status is measured using RAND SF-36 mental mean scores at week 6 and 16 of each treatment pathway
4. Proportion of patients having treatment success, defined as a reduction in 30% value at follow up compared to baseline, is measured by 7-day average 24-hour pain evaluated at patient level using an 11 point NRS scale at week 16 of each treatment pathway
5. Proportion of patients having treatment success, defined as a reduction in 50% value at follow up compared to baseline, is measured by 7-day average 24-hour pain evaluated at patient level using an 11 point NRS scale at week 16 of each treatment pathway
6. Pain interference with function total score is measured using the BPI-MSF at week 6 and 16 of each treatment pathway
7. Insomnia is measured using the Insomnia Severity Index at week 6 and 16 of each treatment pathway
8. Patient impression of change is measured using the Patient Global Impression of Improvement at week 16 of each treatment pathway
9. Care pathway preferred by participants is measured by patient interview at week 50

Cost Effectiveness
1. Cost Effectiveness is measured using the EuroQoL-5D-5L and a modified version of the Client Service Receipt Inventory (CSRI) at week 6 and week 16 of each treatment pathway

Safety
1. Proportion of patients reporting at least one Adverse Event for each of the pathway is measured by patient interview at each study visit or telephone call.
2. Frequencies of Adverse Events for each of the pathway is measured bypatient interview at each study visit or telephone call.
3. Listing of Adverse Events for each of the pathway is measured by patient interview at each study visit or telephone call.
4. Proportion of patients reporting at least one Serious Adverse Event for each of the pathway is measured by patient interview at each study visit or telephone call.
5. Frequencies of Serious Adverse Events for each of the pathway is measured by patient interview at each study visit or telephone call.
6. Listing of Serious Adverse Events for each of the pathway is measured by patient interview at each study visit or telephone call.

Subgroup analysis:
All participants will complete the Neuropathic Pain Symptom Inventory (NPSI) questionnaire, which is used to categorise patients for subgroup analysis relating pain phenotype to treatment response. In particular these outcomes will be evaluated:
1. Difference between “Burning (superficial) spontaneous pain” NPSI mean subscores - (evaluated at patient level) at week 6 and week 16 among pathways
2. Difference between “Pressing (deep) spontaneous pain” NPSI mean subscores - (evaluated at patient level) at week 6 and week 16 among pathways
3. Difference between “Paroxysmal pain” NPSI mean subscores - (evaluated at patient level) at

week 6 and week 16 among pathways
4. Difference between “Evoked pain” NPSI mean subscores - (evaluated at patient level) at week 6 and week 16 among pathways
5. Difference between “Paresthesia/dysesthesia” NPSI mean subscores - (evaluated at patient level) at week 6 and week 16 among pathways
6. Difference between NPSI mean total scores - (evaluated at patient level) at week 6 and week 16 among pathways

Added 01/08/2017:

1. Difference between Hospital Anxiety and Depression Scale (HADS) mean anxiety scores (evaluated at patient level) at week 6 among pathways
2. Difference between Hospital Anxiety and Depression Scale (HADS) mean anxiety scores (evaluated at patient level) at week 16 among pathways
3. Difference between Hospital Anxiety and Depression Scale (HADS) mean depression scores (evaluated at patient level) at week 6 among pathways
4. Difference between Hospital Anxiety and Depression Scale (HADS) mean depression scores (evaluated at patient level) at week 16 among pathways

Patient-perceived tolerability
1. Difference between tolerability (evaluated at patient level) on an 11-point NRS scale at week 16 among pathways
2. Difference between tolerability (evaluated at patient level) on an 11-point NRS scale at week 6 among monotherapies

Completion date
24/03/2021

Eligibility

Key inclusion criteria
Current inclusion criteria as of 29/01/2019:
1. Participant aged ≥18 years
2. Neuropathic pain affecting both feet and / or hands for at least 3 months or taking pain medication for neuropathic pain for at least 3 months
3. Bilateral distal symmetrical neuropathic pain confirmed by the Douleur Neuropathique 4 (DN4) questionnaire at screening visit (52). The participant is eligible if 4 or more questions are answered as “yes”.
4. Bilateral distal symmetrical polyneuropathy confirmed by modified Toronto Clinical Neuropathy Score (mTCNS) > 5 at screening visit (53)
5. Stable glycaemic control (HbA1c < 108mmol/mol)
6. Participants will have a mean total pain intensity of at least 4 on an 11-point numeric rating scale (NRS; with 0 being ‘no pain’ and 10 ‘worst pain imaginable’) during 1 week off pain medications (Baseline Period). Patients could be invited to attend Randomisation Visit sooner if it’s clear that their mean pain score for the week is above 4 i.e. as soon as the total sum of the pain scores is ≥ 28 (e.g. randomisation could take place after 3 days if a patient scores 10 on each of the first 3 days of monitoring). This is to minimise the length of time patients remain off neuropathic pain treatments.
7. Willing and able to comply with all the study requirements and be available for the duration of the study. This will be a 1 year study in which all participants will undergo all Treatment Pathways regardless of treatment response and this point will be made clear

8. Willing to discontinue current neuropathic pain relieving medications
9. Informed consent form for study participation signed by participant

Previous inclusion criteria, as of 19/03/2018:
1. Aged 18 years and over
2. Neuropathic pain affecting both feet and / or hands for at least 3 months or taking pain medication for neuropathic pain for at least 3 months
3. Bilateral distal symmetrical polyneuropathy confirmed by modified Toronto Clinical Neuropathy Score (mTCNS) > 5 at screening visit
4. Bilateral distal symmetrical polyneuropathy confirmed by the Douleur Neuropathique 4 (DN4) questionnaire at screening visit
5. Stable glycaemic control (HbA1c < 108mmol/mol)
6. Participants will have a mean total pain intensity of at least 4 on an 11-point numeric rating scale (NRS; with 0 being 'no pain' and 10 'worst pain imaginable') during 1 week off pain medications (Baseline Period)
7. Willing and able to comply with all the study requirements and be available for the duration of the study. This will be a 1 year study in which all participants will undergo all Treatment Pathways regardless of treatment response and this point will be made clear
8. Willing to discontinue current neuropathic pain relieving medications
9. Informed consent form for trial participation signed by participant

Previous Inclusion Criteria:
1. Aged 18 years and over
2. Daily pain for at least 3 months or taking pain medication for neuropathic pain for at least 3 months
3. Bilateral distal symmetrical polyneuropathy confirmed by Michigan Neuropathy Screening Instrument (MNSI) score > 3 at screening visit
4. Bilateral distal symmetrical polyneuropathy confirmed by the Douleur Neuropathique 4 (DN4) questionnaire at screening visit
5. Stable glycaemic control (HbA1c < 108mmol/mol)
6. Participants will have a mean total pain intensity of at least 4 on an 11-point numeric rating scale (NRS; with 0 being 'no pain' and 10 'worst pain imaginable') during 1 week off pain medications (Baseline Period)
7. Willing and able to comply with all the study requirements and be available for the duration of the study. This will be a 1 year study in which all participants will undergo all Treatment Pathways regardless of treatment response and this point will be made clear
8. Willing to discontinue current neuropathic pain relieving medications
9. Informed consent form for trial participation signed by participant

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
140

Key exclusion criteria
Current exclusion criteria as of 25/02/2020:
1. Non-diabetic symmetrical polyneuropathies
2. History of alcohol/substance abuse which would, in the opinion of the investigator, impair their ability to take part in the study
3. History of severe psychiatric illnesses which would, in the opinion of the investigator, impair their ability to take part in the study
4. History of epilepsy
5. Contraindications to study medications
6. Pregnancy/breast feeding or planning pregnancy during the course of the study
7. Use of prohibited concomitant treatment (as detailed in section 8.10) that could not be discontinued with the exception of prior concomitant and safe use of selective serotonin reuptake inhibitors (SSRIs) with study medication (duloxetine and/or amitriptyline). Note that concomitant use of citalopram is not permitted
8. Use of high dose morphine equivalent (>100mg/day)
9. Liver disease (AST/ALT >2 times upper limit of normal)
10. Significant renal impairment (eGFR <30mL/minute/1.73m2)
11. Heart failure New York Heart Association (NYHA) ≥ class III
12. Clinically significant cardiac arrhythmias on 12 lead ECG or current history of arrhythmia, second or third degree heart block or left bundle branch block (patients with right bundle branch block or first degree heart block may be included following discussion with cardiology team)
13. Patients with a recent myocardial infarction (<6 months prior to randomisation)
14. Symptomatic postural hypotension which in the opinion of the investigator is clinically significant and would be a contraindication to the study medication
15. Prostatic hypertrophy or urinary retention to an extent which would, in the opinion of the investigator, be a contraindication to the study medication
16. Patients with other painful medical conditions where the intensity of the pain is significantly more severe than their diabetic peripheral neuropathic pain (patients will not be excluded if the pain is transient in nature)
17. Any suicide risk as judged by the investigator or as defined by a score of ≥2 on the suicide risk questionnaire
18. Significant language barriers which are likely to affect the participants understanding of the medication schedule or ability to complete outcome questionnaires
19. Concurrent participation in another clinical trial of an investigational medicinal product
20. Major amputations of the lower limbs
21. Foot ulcers, only if in the opinion of the local PI will have a confounding/detrimental effect on study primary outcome or participation e.g. localised foot pain from the ulcer site

_____
Previous exclusion criteria as of 29/01/2019:
1. Non-diabetic symmetrical polyneuropathies
2. History of alcohol/substance abuse which would, in the opinion of the investigator, impair their ability to take part in the study
3. History of severe psychiatric illnesses which would, in the opinion of the investigator, impair their ability to take part in the study

4. History of epilepsy
5. Contraindications to study medications
6. Pregnancy/breast feeding or planning pregnancy during the course of the study
7. Use of prohibited concomitant treatment (as detailed in section 8.10) that could not be discontinued with the exception of prior concomitant and safe use of selective serotonin reuptake inhibitors (SSRIs) with study medication (duloxetine and/or amitriptyline)
8. Use of high dose morphine equivalent (>100mg/day)
9. Liver disease (AST/ALT >2 times upper limit of normal)
10. Significant renal impairment (eGFR <30mL/minute/1.73m2)
11. Heart failure New York Heart Association (NYHA) ≥ class III
12. Clinically significant cardiac arrhythmias on 12 lead ECG or current history of arrhythmia
13. Patients with a recent myocardial infarction (<6 months prior to randomisation)
14. Symptomatic postural hypotension which in the opinion of the investigator is clinically significant and would be a contraindication to the study medication
15. Prostatic hypertrophy or urinary retention to an extent which would, in the opinion of the investigator, be a contraindication to the study medication
16. Patients with other painful medical conditions where the intensity of the pain is significantly more severe than their diabetic peripheral neuropathic pain (patients will not be excluded if the pain is transient in nature)
17. Any suicide risk as judged by the investigator or as defined by a score of ≥2 on the suicide risk questionnaire
18. Significant language barriers which are likely to affect the participants understanding of the medication schedule or ability to complete outcome questionnaires
19. Concurrent participation in another clinical trial of an investigational medicinal product
20. Major amputations of the lower limbs
21. Foot ulcers, only if in the opinion of the local PI will have a confounding/detrimental effect on study primary outcome or participation e.g. localised foot pain from the ulcer site

Previous exclusion criteria as of 06/09/2018:
1. Non-diabetic symmetrical polyneuropathies
2. History of alcohol/substance abuse which would, in the opinion of the investigator, impair their ability to take part in the study
3. History of severe psychiatric illnesses which would, in the opinion of the investigator, impair their ability to take part in the study
4. History of epilepsy
5. Contraindications to study medications
6. Pregnancy/breastfeeding or planning pregnancy during the course of the study
7. Use of prohibited concomitant treatment (as detailed in section 8.10) that could not be discontinued, with the exception of prior concomitant and safe use of selective serotonin reuptake inhibitors (SSRIs) with study medication (duloxetine and/or amitriptyline)
8. Use of high dose morphine equivalent (>100mg/day)
9. Liver disease (AST/ALT >2 times upper limit of normal)
10. Significant renal impairment (eGFR <30mL/minute/1.73m2)
11. Heart failure New York Heart Association (NYHA) ≥ class II
12. Clinically significant cardiac arrhythmias on 12 lead ECG or current history of arrhythmia
13. Patients with a recent myocardial infarction (<6 months prior to randomisation)
14. Postural hypotension (reduction of > 20mmHg)
15. Prostatic hypertrophy or urinary retention to an extent which would, in the opinion of the investigator, be a contraindication to the study medication
16. Patients with other painful medical conditions where the intensity of the pain is significantly more severe than their diabetic peripheral neuropathic pain (patients will not be excluded if the pain is transient in nature)

17. Any suicide risk as judged by the investigator or as defined by a score of ≥2 on the suicide risk questionnaire
18. Significant language barriers which are likely to affect the participants understanding of the medication schedule or ability to complete outcome questionnaires
19. Concurrent participation in another clinical trial of an investigational medicinal product
20. Major amputations of the lower limbs
21. Foot ulcers, only if in the opinion of the local PI will have a confounding/detrimental effect on study primary outcome or participation e.g. localised foot pain from the ulcer site

Previous exclusion criteria, as of 19/03/2018:
Exclusion Criteria:
1. Non-diabetic symmetrical polyneuropathies
2. History of alcohol/substance abuse which would, in the opinion of the investigator, impair their ability to take part in the study
3. History of severe psychiatric illnesses which would, in the opinion of the investigator, impair their ability to take part in the study
4. History of epilepsy
5. Contraindications to study medications
6. Pregnancy/breastfeeding or planning pregnancy during the course of the study
7. Use of prohibited concomitant treatment (as detailed in section 8.10) that could not be discontinued
8. Use of high dose morphine equivalent (>100mg/day)
9. Liver disease (AST/ALT >2 times upper limit of normal)
10. Significant renal impairment (eGFR <30mL/minute/1.73m2)
11. Heart failure New York Heart Association (NYHA) ≥ class II
12. Clinically significant cardiac arrhythmias on 12 lead ECG or current history of arrhythmia
13. Patients with a recent myocardial infarction (<6 months prior to randomisation)
14. Postural hypotension (reduction of > 20mmHg)
15. Prostatic hypertrophy or urinary retention to an extent which would, in the opinion of the investigator, be a contraindication to the study medication
16. Patients with other painful medical conditions where the intensity of the pain is significantly more severe than their diabetic peripheral neuropathic pain (patients will not be excluded if the pain is transient in nature)
17. Any suicide risk as judged by the investigator or as defined by a score of ≥2 on the suicide risk questionnaire
18. Significant language barriers which are likely to affect the participants understanding of the medication schedule or ability to complete outcome questionnaires
19. Concurrent participation in another clinical trial of an investigational medicinal product
20. Major amputations of the lower limbs
21. Active diabetic foot ulcers

Previous exclusion criteria as of 19/03/2018 (added 01/08/2017):
1. Non-diabetic neuropathies
2. History of alcohol/substance abuse which would, in the opinion of the investigator, impair their ability to take part in the study
3. History of severe psychiatric illnesses which would, in the opinion of the investigator, impair their ability to take part in the study
4. History of epilepsy
5. Contraindications to study medications
6. Pregnancy/breastfeeding or planning pregnancy during the course of the study
7. Use of prohibited concomitant treatment (as detailed in section 8.10) that could not be discontinued

8. Use of high dose morphine equivalent (>100mg/day)
9. Liver disease (LFTs >2 times upper limit of normal)
10. Significant renal impairment (eGFR <30mL/minute/1.73m2)
11. Heart failure New York Heart Association (NYHA) ≥ class II
12. Clinically significant cardiac arrhythmias on 12 lead ECG
13. Patients with a recent myocardial infarction (<6 months prior to randomisation)
14. Postural hypotension (reduction of > 20mmHg)
15. Prostatic hypertrophy or urinary retention to an extent which would, in the opinion of the investigator, be a contraindication to the study medication
16. Patients with other painful medical conditions where the intensity of the pain is significantly more severe than their diabetic peripheral neuropathic pain (patients will not be excluded if the pain is transient in nature)
17. Any suicide risk as judged by the investigator or as defined by a score of ≥2 on the suicide risk questionnaire
18. Significant language barriers which are likely to affect the participants understanding of the medication schedule or ability to complete outcome questionnaires
19. Concurrent participation in another clinical trial of an investigational medicinal product
20. Major amputations of the lower limbs
21. Active diabetic foot ulcers

Previous exclusion criteria, as of 01/08/2017:
1. Non-diabetic neuropathies
2. History of alcohol/substance abuse
3. History of severe psychiatric illnesses
4. History of epilepsy
5. Contraindications to study medications
6. Pregnancy/breastfeeding or planning pregnancy during the course of the study
7. Use of prohibited concomitant treatment (as detailed in section 8.10) that could not be discontinued
8. Use of high dose morphine equivalent (>120mg/day)
9. Liver disease (LFTs >2 times upper limit of normal)
10. Significant renal impairment (eGFR <30mL/minute/1.73m2)
11. Heart failure New York Heart Association (NYHA) ≥ class II
12. Clinically significant cardiac arrhythmias on 12 lead ECG
13. Prior history of ischaemic heart disease
14. Postural hypotension (reduction of > 20mmHg)
15. Prostatic hypertrophy or urinary retention
16. Any suicide risk as judged by the investigator or as defined by a score of ≥2 on the suicide risk questionnaire
17. Significant language barriers which are likely to affect the participant's understanding of the medication schedule or ability to complete outcome questionnaires

Date of first enrolment
02/11/2017

Date of final enrolment
31/07/2019

Locations

Countries of recruitment

United Kingdom

England

Scotland

Wales

Study participating centre
Sheffield Teaching Hospitals NHS Foundation Trust
Royal Hallamshire Hospital
Glossop Road
Sheffield
United Kingdom
S10 2JF

Study participating centre
Nottingham University Hospitals NHS Trust
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Tameside Hospital NHS Foundation Trust
Fountain Street
Ashton-under-Lyne
United Kingdom
OL6 9RW

Study participating centre
Ipswich Hospital NHS Trust
Heath Road
Ipswich
United Kingdom
IP4 5PD

Study participating centre
King's College Hospital NHS Foundation Trust
Denmark Hill
London

United Kingdom
SE5 9RS

Study participating centre
Lancashire Teaching Hospitals NHS Foundation Trust
Sharoe Green Lane North
Fulwood
Preston
United Kingdom
PR2 9HT

Study participating centre
Birmingham Heartlands NHS Trust
Bordesley Green East
Birmingham
United Kingdom
B9 5SS

Study participating centre
Countess of Chester Hospital
Liverpool Road
Chester
United Kingdom
CH2 1UL

Study participating centre
Harrogate and District NHS Foundation Trust
Lancaster Park Road,
Harrogate,
United Kingdom
HG2 7SX

Study participating centre
Aintree University Hospitals NHS Foundation Trust
Longmoor Lane
Liverpool
United Kingdom
L9 7AL

Study participating centre
Lancashire Care NHS Foundation Trust
Sceptre Point
Sceptre Way
Walton Summit
Preston
United Kingdom
PR5 6AQ

Study participating centre
Royal Liverpool and Broadgreen University Hospitals NHS Trust
Prescot Street
Liverpool
United Kingdom
L7 8XP

Study participating centre
Tayside Health Board, Ninewells Hospital and Medical School
Dundee
United Kingdom
DD1 9SY

Study participating centre
University Hospital Hairmyres
Eaglesham Rd
East Kilbride
Glasgow
United Kingdom
G75 8RG

Study participating centre
University Hospital Monklands
Monkscourt Ave
Airdrie
United Kingdom
ML6 0JS

Study participating centre
New Cross Hospital, The Royal Wolverhampton NHS Trust
Wolverhampton Road,
Heath Town

Wolverhampton
United Kingdom
WV10 0QP

Study participating centre
Queen Elizabeth Hospital, Gateshead Health NHS Foundation Trust
Queen Elizabeth Ave
Gateshead
United Kingdom
NE9 6SX

Study participating centre
Morriston Hospital
Heol Maes Eglwys,
Morriston
Swansea
United Kingdom
SA6 6NL

Sponsor information

Organisation
Sheffield Teaching Hospitals NHS Foundation Trust

ROR
https://ror.org/018hjpz25

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type

Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

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?
Results article		22/08/2022	26/08/2022	Yes	No
Results article		01/10/2022	20/10/2022	Yes	No
Protocol article	protocol	22/10/2018	11/01/2021	Yes	No
Basic results		23/03/2022	23/03/2022	No	No
HRA research summary			28/06/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes