ISRCTN13232859 https://doi.org/10.1186/ISRCTN13232859

Take home naloxone intervention in multicentre emergency settings

Submission date
09/02/2018

Recruitment status
No longer recruiting

Registration date
16/02/2018

Overall study status
Completed

Last Edited
04/11/2024

Condition category
Injury, Occupational Diseases, Poisoning

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

Plain English summary of protocol

Background and study aims
People who take opioid drugs such as heroin can overdose. The number of people who die this way is increasing, with tragic consequences for families, friends and communities. Naloxone is a drug that can reverse the effects of opioid overdose. Emergency ambulance staff and doctors in the Emergency Department regularly give drug users naloxone, but some people die before they reach emergency medical services. There are schemes in the UK and internationally where naloxone is given to drug users to give to others in an emergency. This is called 'Take Home Naloxone' (THN). It is not known whether THN saves lives. There are some concerns that it could encourage risk-taking behaviour, with the drug user feeling that they have a 'safety net' and can take a higher dose. The aim of this study is to see whether it is possible for ambulance paramedics and Emergency Department staff to give out THN kits to drug users they see, and to see if it is possible to collect data to find out whether it reduces deaths from overdose.

Who can participate?
Adult (aged 18 or over) opioid users at risk of overdose who are attended by emergency ambulance paramedic or who attend ED, and their accompanying friends, relatives or carers

What does the study involve?
This study is carried out in two areas where THN is given to patients who have overdosed or who are at risk of overdose, and two other areas where THN kits are not given out (treatment as usual). It is very difficult to follow up these patients because they don’t respond to phone calls or may have no fixed address, therefore this study follows what happens to patients using the routine information which health services already collect about everyone they see. Information is collected about deaths, overdoses, emergency ambulance calls and emergency department attendances and admissions up to 1 year after the patients are seen. These figures are compared between the areas which give out THN and the areas which do not. Interviews are also carried out to find out about the experiences and views of patients receiving THN and staff who give out the kits.

What are the possible benefits and risks of participating?
If this study shows it is possible to give out THN kits through emergency services, and that data can be collected about the effects, a larger study will be carried out to find out whether THN

reduces deaths. THN is known to have the potential to save lives on an individual basis, but on an aggregate level the benefits and harms are unknown, which is the reason for this study. There are no participant incentives on offer due to the study design.

Where is the study run from?
1. Bristol Royal Infirmary (UK)
2. Hull Royal Infirmary (UK)
3. Northern General Hospital Sheffield (UK)
4. Wrexham Maelor Hospital (UK)

When is the study starting and how long is it expected to run for?
March 2018 to July 2022 (updated 19/07/2021, previously: November 2020)

Who is funding the study?
NIHR Health Technology Assessment Programme (UK)

Who is the main contact?
Jenna Jones, j.k.jones@swansea.ac.uk
(updated 19/07/2021, previously: Matthew Jones, m.b.jones@swansea.ac.uk)

Contact information

Type(s)
Public

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Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HTA 16/91/04

Study information

Scientific Title
Take home naloxone Intervention Multicentre Emergency setting feasibility trial

Acronym
TIME

Study objectives
That it is feasible to conduct a fully powered randomised controlled trial to measure the clinical and cost effectiveness of take home naloxone distributed from emergency care settings using a cluster design and linked anonymised routine data.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 16/10/2018, NHS HRA Wales REC 4 (Health and Care Research Wales Support Centre, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB; +44(0)7976 982591; tracy.biggs@wales.nhs.uk), ref: 18/WA/0337
2. Approved 07/01/2019, NHS HRA CRA (Skipton House, 80 London Road, London, SE1 6LH; +44 (0)20 7972 2557; hra.cag@nhs.net), ref: 18/CAG/0176

Study design
Feasibility study for a randomized controlled trial

Primary study design
Interventional

Secondary study design
Cluster randomised trial

Study setting(s)
Other

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Opioid overdose

Interventions
This is a feasibility study for an RCT of Take Home Naloxone (THN) in emergency settings clustered by emergency department (ED) catchment area and local ambulance service. Anonymised linked data outcomes will be captured for trial participants and their peers, and aggregate outcomes at general population level. The trialists will also collect qualitative data to examine implementation, patient safety and experience.

The four sites to be randomly allocated to study arms are:
Bristol: Bristol Royal Infirmary & associated ambulance service catchment area
Hull: Hull Royal Infirmary & associated ambulance service catchment area
Sheffield: Northern General Hospital Sheffield & associated ambulance service catchment area
Wrexham: Wrexham Maelor Hospital & associated ambulance service catchment area
It was agreed that the randomisation would be stratified to ensure that the two sites served by the Yorkshire Ambulance Service would be in different study arms; this reduced the randomisation options to four, as listed below:

Option A:
Intervention: Wrexham, Sheffield
Control: Bristol, Hull

Option B:
Intervention: Bristol, Hull
Control: Wrexham, Sheffield

Option C:
Intervention: Bristol, Sheffield
Control: Wrexham, Hull

Option D:
Intervention: Wrexham, Hull
Control: Bristol, Sheffield

Four identical opaque envelopes, each containing one option, were prepared, presented to a person not involved in their preparation, and one selected at random. The chosen envelope contained Option B, so that the proposed allocation is:
Intervention: Bristol, Hull
Control: Wrexham, Sheffield

The THN intervention will consist of training for participating paramedics and ED staff; a protocol for the supply of THN kits to those eligible for the intervention; a single use THN kit (ampoule of Naloxone Hydrochloride 400 micrograms/ml solution for intramuscular injection

and syringe; and instructions on how to correctly administer the naloxone dose and provide basic life support in event of overdose). The training provided to recipients of THN kits by paramedic or ED staff will include preparation and administration of the naloxone, providing appropriate aftercare including calling 999, and resuscitation techniques. The trialists will consult with patient and public interest (PPI) representatives and a wider group of service users, addiction specialists, paramedics, and ED staff to assess acceptability, and identify advantages and disadvantages of our proposed THN kit. THN will be distributed in the intervention sites for a period of 12 months.

Control sites will operate treatment as usual (TAU).

The study will be carried out in the prehospital environment and at a receiving ED at each site. The prehospital environment will be the geographic catchment area for the receiving ED. Paramedics and clinical ED staff at study sites will be invited to take part.

The target populations eligible for the intervention (THN) will be: opioid users at high risk of fatal overdose who are attended by emergency ambulance paramedic or who attend ED; their accompanying friends, relatives or carers; and people at high risk of fatal overdose who make up a wider peer group of opioid users coming in to contact with emergency ambulance paramedics or ED.

The trialists propose to develop and test two related methods of defining these populations:
1. A discriminant function incorporating routinely recorded risk predictors used in risk indices for opioid-related events. These will be derived from linked opioid-related mortality (from ONS), ED and inpatient data. They have already obtained linked data to study the characteristics of decedents of opioid overdose in Wales during 2015, and they will extend this data set to cover those with ED and inpatient events associated with non-fatal opioid overdoses, and those with no such events. Although discriminant analysis is inherently multivariate in nature, they will also assess whether the discriminant function can be reduced to a single individual-level risk score; consider thresholds used in its definition; and evaluate its performance.
2. The discriminant analysis approach outlined will include recent ED and inpatient data related to opioid overdose and associated events, for which current coding is known to be of variable quality or low specificity. The trialists will therefore test whether the planned Emergency Care DataSet (ECDS) provides reliable data about attendances for opioid overdose and related problems that could be used to improve the ability to identify both the patients eligible for THN provision and the wider peer group.

Intervention Type
Mixed

Primary outcome measure
Mortality (total and opioid overdose related), collected using anonymised data linkage at a single time point 12 months post intervention

Secondary outcome measures
Collected using anonymised data linkage at a single time point 12 months post intervention:
1. Emergency admissions
2. ITU admissions
3. ED attendances (total and opioid overdose related)

4. 999 attendances (total and opioid overdose related)
5. THN kits issued
6. NHS resource usage

Overall study start date
01/03/2018

Completion date
31/07/2022

Eligibility

Key inclusion criteria
Eligible for intervention:
Adult (18 years of age or over, male or female) opioid users at risk of overdose who are attended by emergency ambulance paramedic or who attend ED

Accompanying friends, relatives or carers (18 years of age or over, male or female) of opioid users at risk of overdose who are attended by emergency ambulance paramedic or who attend ED

Eligible for inclusion in outcome follow up and analyses:
High risk peers (18 years of age or over, male or female) - opioid users at high risk of fatal opioid overdose who make up a wider peer group who may or may not make contact with emergency services at study site during the study period

Participant type(s)
Mixed

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
4 clusters. Target of 200 patients actively seen by emergency services (ED or ambulance) during study period. Target of 1000 'high risk' patients to be followed up using routine anonymised linked data from each cluster.

Key exclusion criteria
1. Under 18 years of age
2. Actively dissent from involvement in study
3. Non-opioid overdose

Date of first enrolment
01/02/2019

Date of final enrolment
01/02/2020

Locations

Countries of recruitment
England

United Kingdom

Wales

Study participating centre
Yorkshire Ambulance Service
United Kingdom
WF2 0XQ

Study participating centre
South Western Ambulance Service Foundation Trust
United Kingdom
EX2 7HY

Study participating centre
Welsh Ambulance Service Trust
United Kingdom
LL17 0RS

Study participating centre
Northern General Hospital ED
United Kingdom
S5 7AU

Study participating centre
Hull Royal Infirmary ED
United Kingdom
HU3 2JZ

Study participating centre

Bristol Royal Infirmary ED
United Kingdom
BS2 8HW

Study participating centre
Wrexham Maelor ED
United Kingdom
LL13 7TD

Sponsor information

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Sponsor type
University/education

Website
http://www.swansea.ac.uk/reis/

ROR
https://ror.org/053fq8t95

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The study protocol is currently out for circulation with the wider team but will be submitted for publication in a peer reviewed journal in the near future (BMC Pilot and Feasibility Studies). The trialists will publish their results in journals read by clinicians, policy makers, service managers and researchers. They will give presentations to conferences and meetings where these groups can also discuss the findings with them.

Intention to publish date
31/07/2024

Individual participant data (IPD) sharing plan
Quantitative outcome data will be stored in the SAIL databank and accessed via the secure sail gateway (https://saildatabank.com/). Research team members (myself and Dr Alan Watkins the trial statistician) have access to the gateway via yubikey (https://www.yubico.com/). The trialists are able to access the data but cannot take data outside of the gateway. Requests for exporting linked data in to the gateway are reviewed by internal and then external reviewers prior to being granted. Data will be linked and anonymised prior to export in to the gateway by NHS Digital and NWIS (for Welsh control site).

IPD sharing plan summary
Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	01/01/2019	01/08/2019	Yes	No
HRA research summary			26/07/2023	No	No
Results article		29/08/2024	02/09/2024	Yes	No
Results article		31/10/2024	04/11/2024	Yes	No