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Metoclopramide for avoiding pneumonia after stroke

Submission date 25/05/2021	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [X] Record updated in last year
Registration date 17/06/2021	**Overall study status** Ongoing	
Last Edited 18/10/2024	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims

Stroke is the fourth most common cause of death in the UK. Despite great progress over the last 20 years, the only treatments shown to reduce the death rate are admission to a specialist stroke unit, prevention of blood clots by intermittent pneumatic leg compression, and surgery for brain swelling. Pneumonia is the most common cause of death after stroke and, even if not fatal, weakens the patient and delays recovery. Patients with a stroke often lose the ability to swallow safely. This can lead to food and drink spilling into the lungs. Stroke patients with swallowing problems are therefore at high risk of pneumonia.

When stroke patients are turned in bed, moved, or even when just resting in bed, they often vomit and inhale the contents of the mouth and/or stomach into the lungs. This is the most common cause of pneumonia after stroke. In a small pilot study conducted in a single hospital the researchers were able to show that metoclopramide, an anti-sickness drug, prevents pneumonia in patients with severe stroke when given regularly in the first 2 weeks. The aim of this study is to confirm this finding in a wider range of hospitals and to establish whether this can also reduce the number of patients who die from stroke.

This study will test whether metoclopramide, given early after stroke onset and continued for 2 weeks, is better than sham control (dummy treatment) for preventing pneumonia and death after stroke.

Who can participate?

Adult patients admitted to hospital with moderate to severe acute stroke and dysphagia within 9 hours of symptom onset

What does the study involve?

The duration of each participant's involvement in the study will be 6 months. Participants are allocated randomly to be treated with metoclopramide hydrochloride or a normal saline solution through a vein or tube into the nose (nasogastric tube) three times a day for 14 days or until discharge into the community, if this is before 14 days. For each patient, a daily log of whether they have signs or symptoms of pneumonia and if they have any side effects will be recorded for 2 weeks. A neurological assessment, to see how the patient is recovering from their stroke, will be made on day 14. After 6 months, the patient or their carer will be telephoned by a member of the study team to assess their level of disability (if any), their quality of life, whether they still

have problems swallowing, if they are still in hospital or, if not, where they are living. A health economic analysis will be done to look at potential cost savings as a result of shorter hospital stays and fewer re-admissions.

What are the possible benefits and risks of participating?
There are no expected benefits. If the treatment is effective, it might prevent pneumonia and reduce the risk of death, but this is not guaranteed.

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

When is the study starting and how long is it expected to run for?
February 2021 to May 2027

Who is funding the study?
National Institute for Health and Care Research (NIHR) Health Technology Assessment (HTA) (UK).

Who is the main contact?
Christine Roffe
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Study website
https://stroke.nottingham.ac.uk/maps-2/

Contact information

Type(s)
Scientific

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Type(s)
Public

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Prof Christine Roffe

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Additional identifiers

EudraCT/CTIS number
2021-003853-40

IRAS number
290474

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
HTA - NIHR130689, IRAS 290474

Study information

Scientific Title
The Metoclopramide for Avoiding Pneumonia after Stroke (MAPS-2) trial: a single-blind, randomized controlled trial of metoclopramide for the prevention of pneumonia in patients with dysphagia after an acute stroke

Acronym
MAPS-2

Study objectives
Pneumonia is a major cause of death after stroke. It is most commonly caused by aspiration of vomited or regurgitated gastric contents. Prevention of regurgitation and vomiting by regular administration of an antiemetic (metoclopramide) could improve outcomes by prevention of pneumonia. the hypothesis to be tested in this study is that metoclopramide, started early after symptom onset and continued for 14 days will reduce mortality and prevent pneumonia after stroke.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 17/11/2021, East Midlands – Nottingham 2 Research Ethics Committee (Equinox House, City Link, Nottingham, NG2 4LA, United Kingdom; +44 207 10148051; nottingham2.rec@hra.nhs.uk), ref: 21/EM/0246

Study design
Multicentre phase III participant-blinded parallel two-arm randomized sham-controlled trial with an internal pilot

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

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
Prevention of pneumonia caused by dysphagia after an acute stroke

Interventions
Participants will be individually randomized 1:1 via a web-based interface to metoclopramide or sham control by minimization using NIH Stroke Scale/Score (NIHSS), age, modified Rankin score (mRS), time from stroke onset, and type of trial centre as factors. The trial will be single-blind with blinded assessment of primary outcome.

Intervention: Metoclopramide hydrochloride (5mg per 1ml solution for injection) 2 ml (10 mg) to be given iv or via nasogastric tube three times a day for 14 days or until discharge into the community, if this is before 14 days. Reduce dose to 1 ml (5 mg) if bodyweight <60 kg.

Control: Sodium chloride (0.9% solution for injection) 2 ml to be given iv or via nasogastric tube three times a day for 14 days or until discharge into the community, if this is before 14 days. Reduce dose to 1 ml if bodyweight <60 kg.

For each patient, a daily log of whether they have signs or symptoms of pneumonia and if they have any side effects will be recorded for 2 weeks. A neurological assessment, to see how the patient is recovering from their stroke, will be made on day 14. After 6 months, the patient or their carer will be telephoned by a member of the study team to assess: their level of disability (if any); their quality of life; whether they still have problems swallowing; if they are still in hospital or, if not, where they are living. A health economic analysis will be done to look at potential cost savings as a result of shorter hospital stays and fewer re-admissions. Health economic outcomes are:
1. Cost per death avoided over 6 months
2. Cost per quality-adjusted life-year (QALY) gained over 6 months
3. Cost per QALY gained over patient lifetime

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Metoclopramide

Primary outcome measure
All-cause mortality by 6 months (time-to-event), ascertained by contacting the general practitioner in the first instance. Missing data will be completed with the team who recruited the patient and via linkage with Hospital Episode Statistics and The Office of National Statistics.

Secondary outcome measures
1. Development of pneumonia, diagnosed by the clinical care team and retrieved from medical notes at 14 days
2. Development of pneumonia specifically attributed to the stroke event (diagnosis based on standard criteria determined by the Stroke Consensus group published in 2015) retrieved from daily clinical log at 14 days
3. Antibiotic treatment, measured as the number of days on treatment, retrieved from medical notes and drug charts at 14 days
4. Difficulty in swallowing measured using the standard Dysphagia Severity Rating Scale Score (DSRS) at 14 days and 6 months
5. Severity of stroke assessed by the NIH Stroke Score at baseline and 14 days
6. Quality of life assessed by the EuroQol EQ-5D questionnaire at 14 days and 6 months
7. Degree of disability evaluated by an ordinal shift in the modified Rankin score (mRS) at 6 months
8. Vulnerability to poor health outcomes assessed by Clinical Frailty Scale index at 6 months
9. Home time, defined as the number of days spent at home rather than hospitalised, at 6 months

Overall study start date
01/02/2021

Completion date
31/05/2027

Eligibility

Key inclusion criteria
Current inclusion criteria as of 04/04/2024:

1. Adults (18 years and over) with a clinical diagnosis of acute stroke (WHO definition excluding duration)
2. Within 24 hours of symptom onset (in wake-up stroke the onset is defined as the time the patient awoke or was found unless this is more than 12 h from last known well)
3. One of the two below criteria:
3a. Moderate to severe neurological impairment (NIH Stroke Scale/Score (NIHSS) ≥10) OR
3b. Dysphagia and NIHSS ≥6, unable to take normal unmodified oral diet or fluids because:
i) Too drowsy to be assessed formally or
ii) Failed bedside assessment of swallowing

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Previous inclusion criteria as of 14/03/2023:

1. Adults (18 years and over) with a clinical diagnosis of acute stroke (WHO definition excluding duration)
2. Within 24 hours of symptom onset (in wake-up stroke the onset is defined as the time the patient awoke or was found unless this is more than 12 h from last known well)
3. Moderate to severe neurological impairment (NIH Stroke Scale/Score (NIHSS) ≥10)
4. Unable to take normal unmodified oral diet or fluids because:
4.1. Too drowsy to be assessed formally or
4.2. Failed bedside assessment of swallowing

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Previous inclusion criteria:

1. Adults (18 years and over) with a clinical diagnosis of acute stroke (WHO definition excluding duration)
2. Within 9 hours of symptom onset (in wake-up stroke the onset is defined as the time the patient awoke or was found unless this is more than 12 h from last known well)
3. Moderate to severe neurological impairment (NIH Stroke Scale/Score (NIHSS) ≥10)
4. Unable to take normal unmodified oral diet or fluids because:
4.1. Too drowsy to be assessed formally or
4.2. Failed bedside assessment of swallowing

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
2100

Key exclusion criteria
1. Definite or probable pneumonia (abnormal chest X-ray suggestive of pneumonia or focal chest signs with fever ≥38°C, or receiving antibiotic treatment at time of presentation)
2. Contraindications to metoclopramide (hypersensitivity to metoclopramide, epilepsy, gastrointestinal obstruction, perforation, or haemorrhage, gastrointestinal surgery within the last week, Parkinson’s disease, treatment with levodopa or dopaminergic agonists, phaeochromocytoma or neuroleptic malignant syndrome or tardive dyskinesia or methaemoglobinaemia or NADH cytochrome –b5 deficiency)
3. Clinical indication for regular antiemetic treatment
4. Known cirrhosis of the liver

5. Known severe renal dysfunction (eGFR <30 ml/hour)
6. Pregnant or breastfeeding
7. Moribund (expected to die within the next 48 hours)
8. Co-morbid conditions with life expectancy <3 months
9. Inability to gain consent (patient or legal representative) or consent declined

Date of first enrolment
28/02/2022

Date of final enrolment
31/10/2026

Locations

Countries of recruitment
England

Northern Ireland

United Kingdom

Wales

Study participating centre
Royal London Hospital
Whitechapel Road
Whitechapel
London
United Kingdom
E1 1FR

Study participating centre
Addenbrooke's Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Queens Medical Centre
Nottingham University Hospitals NHS Trust
Derby Road
Lenton

Nottingham
United Kingdom
NG7 2UH

Study participating centre
West Suffolk Hospital
West Suffolk NHS Foundation Trust
Hardwick Lane
Bury St Edmunds
United Kingdom
IP33 2OZ

Study participating centre
Royal Victoria Infirmary
Queen Victoria Road
New Victoria Wing
Newcastle Upon Tyne
United Kingdom
NE1 4LP

Study participating centre
Leighton Hospital
Mid Cheshire Hospital Trust
Middlewich Road
Crewe
United Kingdom
CW1 4QJ

Study participating centre
James Cook University Hospital
Marton Road
Middlesbrough
United Kingdom
T34 3BW

Study participating centre
Milton Keynes University Hospital
Standing Way
Eaglestone

Milton Keynes
United Kingdom
MK6 5LD

Study participating centre
St George's Hospital
St George's University Hospitals NHS Foundation Trust
Blackshaw Road
Tooting
London
United Kingdom
SW17 0QT

Study participating centre
South West Acute Hospital
124 Irvinestown Road
Enniskillen
United Kingdom
BT74 6DN

Study participating centre
King's College Hospital
King's College Hospital NHS Foundation Trust
Denmark Hill
London
United Kingdom
SE5 9RS

Study participating centre
Northampton General Hospital
Northampton General Hospital NHS Trust
Cliftonville
Northampton
United Kingdom
NN1 5BD

Study participating centre
University Hospital Dorset - The Royal Bournemouth Hospital
Castle Lane East

Bournemouth
United Kingdom
BH7 7DW

Study participating centre
Royal Stoke University Hospital
Newcastle Road
Stoke-on-trent
United Kingdom
ST4 6QG

Study participating centre
Whiston Hospital
Warrington Road
Prescot
United Kingdom
L35 5DR

Study participating centre
Prince Philip Hospital
Bryngwynmawr
Dafen
Llanelli
United Kingdom
SA14 8QF

Study participating centre
Aberdeen Royal Infirmary
Foresterhill Road
Aberdeen
United Kingdom
AB25 2ZN

Study participating centre
Sunderland Royal Hospital
Kayll Road
Sunderland
United Kingdom
SR4 7TP

Study participating centre
Bronglais General Hospital
Bronglais Hospital
Caradoc Road
Aberystwyth
United Kingdom
SY23 1ER

Study participating centre
University Hospital of North Durham
University Hospital of Durham
Dryburn Hospital
North Road
Durham
United Kingdom
DH1 5TW

Study participating centre
West Wales General Hospital
Dolgwili Road
Carmarthen
United Kingdom
SA31 2AF

Study participating centre
Royal Devon and Exeter Hospital
Royal Devon & Exeter Hospital
Barrack Road
Exeter
United Kingdom
EX2 5DW

Study participating centre
Norfolk and Norwich Hospital
Colney Lane
Colney
Norwich
United Kingdom
NR4 7UY

Study participating centre
Monklands District General Hospital
Monkscourt Avenue
Airdrie
United Kingdom
ML6 0JS

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

Study participating centre
Northwick Park Hospital
Watford Road
Harrow
United Kingdom
HA1 3UJ

Study participating centre
New Cross Hospital
Wolverhampton Road
Heath Town
Wolverhampton
United Kingdom
WV10 0QP

Study participating centre
Southampton
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
Royal Cornwall Hospital (treliske)
Treliske

Truro
United Kingdom
TR1 3LJ

Study participating centre
Glasgow Royal Infirmary
84 Castle Street
Glasgow
United Kingdom
G4 0SF

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
Musgrove Park Hospital (taunton)
Musgrove Park Hospital
Taunton
United Kingdom
TA1 5DA

Study participating centre
Royal Victoria Hospital
Radnor Park Avenue
Folkestone
United Kingdom
CT19 5BN

Study participating centre
Leeds General Infirmary
Great George Street
Leeds
United Kingdom
LS1 3EX

Study participating centre
Queen Elizabeth Hospital
Mindelsohn Way
Edgbaston
Birmingham
United Kingdom
B15 2GW

Study participating centre
Arrowe Park Hospital (site)
Arrowe Park Hospital
Arrowe Park Road
Wirral
United Kingdom
CH49 5PE

Study participating centre
Tayside
Ninewells Hospital
Dundee
United Kingdom
DD1 9SY

Study participating centre
Luton and Dunstable University Hospital
Lewsey Road
Luton
United Kingdom
LU4 0DZ

Study participating centre
Royal Derby Hospital Utc
Blue Area
Uttoxeter Road
Derby
United Kingdom
DE22 3NE

Study participating centre
North Tees and Hartlepool Ft
Hardwick Road

Stockton-on-tees
United Kingdom
TS19 8PE

Study participating centre
Neurology (calderdale Royal Hospital)
The Calderdale Royal Hospital
Huddersfield Road
Halifax
United Kingdom
HX3 0PW

Study participating centre
Watford General Hospital
60 Vicarage Road
Watford
United Kingdom
WD18 0HB

Study participating centre
Cumberland Infirmary
Newtown Road
Carlisle
United Kingdom
CA2 7HY

Study participating centre
Gateshead - Queen Elizabeth Hospital
Queen Elizabeth Hospital
Sherriff Hill
Gateshead
United Kingdom
NE9 6SX

Study participating centre
Dorset County Hospital
Dorset County Hospital
Williams Avenue
Dorchester
United Kingdom
DT1 2JY

Study participating centre
Charing Cross Hospital
Fulham Palace Road
London
United Kingdom
W6 8RF

Study participating centre
Hairmyres Hospital
Eaglesham Road
East Kilbride
United Kingdom
G75 8RG

Study participating centre
Northumbria Specialist Emergency Care Hospital
Northumbria Way
Cramlington
United Kingdom
NE23 6NZ

Study participating centre
Antrim Area Hospital
45 Bush Rd
Antrim
United Kingdom
BT41 2RL

Study participating centre
Doncaster Royal Infirmary
Armthorpe Road
Doncaster
United Kingdom
DN2 5LT

Study participating centre
York District Hospital
Wigginton Road

York
United Kingdom
YO31 8HE

Study participating centre
Salford Royal
Stott Lane
Salford
United Kingdom
M6 8HD

Study participating centre
St Helier NHS Trust
St Helier Hospital
Wrythe Lane
Carshalton
United Kingdom
SM5 1AA

Study participating centre
Bth NHS Foundation Trust
Bradford Royal Infirmary
Duckworth Lane
Bradford
United Kingdom
BD9 6RJ

Sponsor information

Organisation
University of Nottingham

Sponsor details
Research and Innovation
East Atrium
Jubilee Conference Centre
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angela.shone@nottingham.ac.uk

Sponsor type
University/education

Website
https://www.nottingham.ac.uk/fabs/research-innovation/meettheteam/angela.shone

ROR
https://ror.org/01ee9ar58

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

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal. The research findings will be disseminated via oral presentation at national and international meetings. The documents are not available yet but the researchers' policy is always to publish the protocol and statistical analysis plan.

Intention to publish date
01/05/2026

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. Christine Roffe (christine.roffe@uhnm.nhs.uk)

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 1.4	06/03/2023	15/03/2023	No	No
HRA research summary			28/06/2023	No	No