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Glucocorticoids in adults with acute respiratory distress syndrome (GuARDS Trial)

Submission date
15/06/2023

Recruitment status
Recruiting

Registration date
26/09/2023

Overall study status
Ongoing

Last Edited
07/04/2025

Condition category
Respiratory

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

Plain English summary of protocol

Background and study aims
Every year about 120,000 adults who are admitted to Intensive Care Units (ICUs) require a machine, called a ventilator, to help them breathe. In patients who need ventilation, about 1 in 4 have a life-threatening condition with severe breathing difficulties called acute respiratory distress syndrome (ARDS) where there is a large amount of inflammation in the lung. Unfortunately, around 40% of patients with ARDS die within 60 days of developing this condition. At present, there are no drugs that cure ARDS. However, in 2020, a small research study (the DEXA-ARDS trial) looked at dexamethasone as a treatment for ARDS. Dexamethasone is a well-known steroid, which is a cheap anti-inflammatory drug, that is already widely used to treat other illnesses. The result of the DEXA-ARDS trial showed that it may help patients survive ARDS but to help us know how effective it is, dexamethasone needs to be tested in a much bigger group of patients who come into the NHS with ARDS. A large clinical trial is planned to be conducted across the UK to answer if dexamethasone treatment in patients with ARDS can save lives, reduce the need for extended ICU care, improve longer-term patient quality of life and find the best value for the public and health services. The study design is called a randomised controlled trial (RCT).

Who can participate?
Patients aged 16 years old and over with ARDS

What does the study involve?
The study plans to recruit up to patients with ARDS, in approximately 60 ICUs throughout the UK. Patients, or their Legal Representatives (relatives) if patients cannot make decisions about their care will be asked to agree (consent) to participating in the study. They will also be asked if they can be followed up for 6 months after their treatment, as this will give us important information about the clinical effectiveness and cost-effectiveness of the treatment.

What are the possible benefits and risks of participating?
Participants may or may not see an improvement in their long-term health from taking part in GuARDS but their taking part will give us information to help us treat others in the future.

There may be some discomfort and bruising from blood sampling. The sampling is done by an experienced person to minimise discomfort. The amount of blood taken is minimal and poses no risk.

Dexamethasone has routinely been used in clinical practice for over 60 years for a number of conditions where it is well tolerated. However, for the patients in Group A getting the dexamethasone treatment, some side effects are possible such as a higher risk of infection and high blood sugar - but the DEXA-ARDS study mentioned above did not see an increased risk of these. More likely side effects are indigestion or heartburn, difficulty sleeping, and changes in mood and behaviour - such as feeling irritable or anxious. These should pass when this short course of treatment of up to 10 days stops.
Although all patients need to take part in the study follow-ups, they will be given a reasonable time to complete the follow-up questionnaire by a phone call with a member of the research team and/or by email.

Where is the study run from?
The Queen's Medical Research Institute (UK)

When is the study starting and how long is it expected to run for?
June 2023 to June 2028

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

Who is the main contact?
Study team, guards@ed.ac.uk

Study website
https://guards-trial.ed.ac.uk/

Contact information

Type(s)
Scientific

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Type(s)
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1007694

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
AC23038, IRAS 1007694, CPMS 58497

Study information

Scientific Title
Glucocorticoids in adults with acute respiratory distress syndrome: A randomised, parallel-group, allocation-concealed, open-label, pragmatic, group-sequential design, clinical and cost-effectiveness trial with internal pilot

Acronym
GuARDS

Study objectives
To determine the clinical effectiveness of dexamethasone in patients with ARDS with moderate to severe hypoxaemia (referred to as patients with moderate to severe ARDS) on the primary outcome of 60-day mortality.

To determine the clinical effectiveness of dexamethasone in moderate to severe ARDS on a range of clinically relevant secondary outcomes included within the CoVENT core outcome set (COS) for ventilation trials.

To assess the cost-efficiency of dexamethasone plus usual care versus usual care alone in the treatment of ARDS, as per NICE reference case specifications modelled over 1, 3, and 5 year, and lifetime time horizons.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 26/09/2023, Scotland A Research Ethics Committee (Ethics Department, 2nd Floor Waverley Gate, 2-4 Waterloo Place, Edinburgh, EH1 3EG, United Kingdom; +44 (0)7814609032; Manx.Neill@nhslothian.scot.nhs.uk), ref: 23/SS/0077

Study design
Randomized parallel-group allocation-concealed open-label pragmatic group-sequential-design clinical and cost-effectiveness study with internal pilot

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital, Medical and other records, Telephone

Study type(s)
Treatment, Efficacy

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
Acute respiratory distress syndrome (ARDS)

Interventions
In GUARDS, Usual Care + Dexamethasone will be compared to Usual Care. An online tool will be used to randomise patients. On days 1-5, 20mg/day of intravenous (iv) dexamethasone will be administered to patients in the Usual Care + Dexamethasone arm. On days 6-10, the iv dexamethasone will drop to 10mg/day. The intervention is a 10-day treatment regime whilst patients are in ICU. All other care will be usual practice. The intervention will stop early if patients are well enough to be discharged from ICU before the 10-day intervention is completed. Patients in both arms of the trial will be followed up for 6 months after their randomisation. Mortality data will be collected 60, 90 and 180 days post-randomisation. Patients will also be asked to complete a health-related quality of life questionnaire at 60 and 180 days. Patients will be asked about their use of the health service at 90 and 180 days. Information will also be collected via data linkage health economics at these time points.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacoeconomic

Phase

Phase IV

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

Primary outcome measure
All-cause mortality measured using medical records at 60 days from randomisation

Secondary outcome measures
Our proposed secondary outcomes (endpoints) are from the CoVENT core outcome set (COS) for ventilation trials and are measured using medical records as and when they occur:
1. First successful extubation, defined as the time from randomization until the first successful extubation or the patient's death occurs, measured using a record of the date/time of all periods of ventilation up to day 60. Successful extubation is being free from all tubes, endotracheal tube, and tracheostomy with success being defined as remaining free from tubes at 48 hours. If discharged from the hospital before the 48-hour success period, successful extubation is assumed.
2. Duration of mechanical ventilation - Unassisted breathing, defined as no inspiratory support (includes time receiving invasive mechanical ventilation and non-invasive ventilation) or extracorporeal lung support. Success is defined as remaining to breathe unassisted at 48 hours. Defined as the time from randomization until the first successful unassisted breathing or the patient's death occurs. Death prior to the end of mechanical ventilation or within the 48-hour period after the end of mechanical ventilation is considered censored.
3. Reintubation - All reintubation events with date/time to report the total number of reintubations after planned extubation in each group and the average number of reintubation events/participants in each group. The COS recommends reintubation rates at 60 days. To capture the risk of delayed reintubation we will collect this outcome for up to 180 days from randomization, censored at hospital discharge.
4. Duration of ICU and hospital stay at the time from randomisation until participant first leaves the relevant facility or death
5. Health-related quality of life (HRQoL) measured using the EQ-5D (www.euroqol.org) and is participant reported at 60 and 180 days post-randomisation
6. Mortality - will record the event date/time of the event, as well as the date/time of randomization to enable a survival analysis at 90 and 180 days post-randomisation.
7. Health service use since hospital discharge – will be a telephone questionnaire completed with a research nurse at 90 and 180 days. It will include questions on rehospitalisations and Health service usage. Data will also be collected via data linkage.

Overall study start date
13/06/2023

Completion date
01/06/2028

Eligibility

Key inclusion criteria
1. Provision of informed consent
2. Aged 16 years or older
3. Admitted to intensive care unit or high dependency unit (ICU)
4. Receiving respiratory support via invasive mechanical ventilation or non-invasive ventilatory

support (non-invasive ventilatory support includes mask or helmet) or high flow nasal cannula (HFNC) >30L/min
5. Within 72 hours of diagnosis of ARDS with moderate to severe hypoxaemia defined as
6. Known acute clinical insult or new or worsening respiratory dysfunction (Note: this includes new deterioration at any time-point during the ICU stay), and
6.1. Opacities on chest imaging not fully explained by effusions, lobar/lung collapse/atelectasis, or nodules, and
6.2. Respiratory failure not fully explained by cardiac failure or fluid overload, and
6.3. Assessment of hypoxaemia done with either PaO2/FiO2 ratio <26.7 kPa from arterial blood gases, or SpO2/FiO2 <235 with SaO2<97%

Participant type(s)
Patient

Age group
Mixed

Lower age limit
16 Years

Sex
Both

Target number of participants
1708

Key exclusion criteria
1. ARDS due to microbiologically confirmed SARS-Co-V2 infection (COVID-19 ARDS)
2. Major upper gastrointestinal bleeding during current hospital admission, defined as requiring endoscopy and transfusion for two or more units of packed red blood cells. This exclusion criterion will exclude patients with contraindications to glucocorticoids on safety grounds.
3. High-dose glucocorticoids are required for a separate proven clinical indication at the time of randomisation as withholding treatments that have been deemed clinically effective, would be unethical.
Note: Low-dose glucocorticoid treatments for clinical indications (defined as maximum daily dose of 200mg hydrocortisone or equivalent other steroids) is not an exclusion criterion.
4. Known hypersensitivity to dexamethasone
5. Infections that are not being effectively treated as determined by the treating medical team.
Note: Once infections are considered as effectively treated by the treating medical team, they are eligible for the trial.
6. Planned intensive care treatment withdrawal within next 24 hours as determined by the treating medical team
7. Patients who are known to be pregnant
8. Previous enrolment in the GuARDS trial

Date of first enrolment
08/03/2024

Date of final enrolment
10/10/2028

Locations

Countries of recruitment
England

Northern Ireland

United Kingdom

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital
Mindelsohn Way
Edgbaston
Birmingham
United Kingdom
B15 2GW

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

Study participating centre
Northern Care Alliance NHS Foundation Trust
Salford Royal
Stott Lane
Salford
United Kingdom
M6 8HD

Study participating centre
Addenbrookes
Addenbrookes Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Aintree Hospital
Longmoore Lane
Liverpool
United Kingdom
L9 7AL

Study participating centre
Barnsley Hospitals
118 Gawber Road
Barnsley
United Kingdom
S75 2PS

Study participating centre
Basildon University Hospital
Nethermayne
Basildon
United Kingdom
SS16 5NL

Study participating centre
Belfast City Hospital
51 Lisburn Rd
Belfast
United Kingdom
BT9 7AB

Study participating centre
Bristol Royal Infirmary
Marlborough Street
Bristol
United Kingdom
BS2 8HW

Study participating centre
Craigavon Area Hospital
Lurgan Rd
Craigavon
United Kingdom
BT63 5QQ

Study participating centre
East Lancashire Hospitals NHS Trust
Royal Blackburn Hospital
Haslingden Road
Blackburn
United Kingdom
BB2 3HH

Study participating centre
Royal Infirmary of Edinburgh at Little France
51 Little France Crescent
Old Dalkeith Road
Edinburgh
Lothian
United Kingdom
EH16 4SA

Study participating centre
Glan Clwd Hospital
Ysbyty Glan Clwydd
Bodelwyddan
Rhyl
United Kingdom
LL18 5UJ

Study participating centre
Glenfield Hospital NHS Trust
Groby Road
Leicester
United Kingdom
LE3 9QP

Study participating centre
Harefield Hospital
Hill End Road
Harefield
Uxbridge
United Kingdom
UB9 6JH

Study participating centre
Homerton Hospital
Homerton Row
London
United Kingdom
E9 6SR

Study participating centre
Hull Royal Infirmary
Anlaby Road
Hull
United Kingdom
HU3 2JZ

Study participating centre
Kettering General Hospital
Kettering General Hospital
Rothwell Road
Kettering
United Kingdom
NN16 8UZ

Study participating centre
Kings College Hospital
Denmark Hill
London
United Kingdom
SE5 9RS

Study participating centre
Kingston Hospital
Galsworthy Road
Kingston upon Thames
United Kingdom
KT2 7QB

Study participating centre
Macclesfield District General Hospital
Macclesfield District Hospital

Victoria Road
Macclesfield
United Kingdom
SK10 3BL

Study participating centre
Maidstone Hospital
Maidstone Hospital
Hermitage Lane
Maidstone
United Kingdom
ME16 9QQ

Study participating centre
Medway Maritime Hospital
Windmill Road
Gillingham
United Kingdom
ME7 5NY

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

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

Study participating centre
Norfolk and Norwich University Hospital
Rosalind Franklin Road
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Norwich
United Kingdom
NR4 7UY

Study participating centre
Northumbria Healthcare NHS Foundation Trust
North Tyneside General Hospital
Rake Lane
North Shields
United Kingdom
NE29 8NH

Study participating centre
Northampton General Hospital
Cliftonville
Northampton
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NN1 5BD

Study participating centre
Pinderfields Hospitals NHS Trust
Trust Hq, Rowan House
Pinderfields General Hospital
Aberford Road
Wakefield
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WF1 4EE

Study participating centre
Poole Hospital
Longfleet Road
Poole
United Kingdom
BH15 2JB

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

Study participating centre
Rotherham District General Hospital
Moorgate Road
Rotherham
United Kingdom
S60 2UD

Study participating centre
The Royal Bolton Hospital Laboratory
The Royal Bolton Hospital
Minerva Road
Farnworth
Bolton
United Kingdom
BL4 0JR

Study participating centre
Royal Bournemouth General Hospital
Castle Lane East
Bournemouth
United Kingdom
BH7 7DW

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Royal Brompton Hospital
Fulham Road
London
United Kingdom
SW3 6HP

Study participating centre
Royal Cornwall Hospital
Truro
United Kingdom
TR1 3LI

Study participating centre
Royal Devon and Exeter Hospital NHS Trust
Royal Devon & Exeter Hospital
Barrack Road
Exeter

United Kingdom
EX2 5DW

Study participating centre
Royal Liverpool University Hospital
Royal Liverpool University Hospital
Prescot Street
Liverpool
United Kingdom
L7 8XP

Study participating centre
Royal Oldham Hospital
Royal Oldham Hospital
Rochdale Road
Oldham
United Kingdom
OL1 2JH

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

Study participating centre
Royal United Hospitals Bath
Combe Park
Bath
United Kingdom
BA1 3NG

Study participating centre
Royal Victoria Hospital
274 Grosvenor Road
Belfast
United Kingdom
BT12 6BA

Study participating centre
Salford Care Organisation
Eccles
United Kingdom
M6 8HD

Study participating centre
Sherwood Forest Hospitals NHS Foundation Trust
Kings Mill Hospital
Mansfield Road
Sutton-in-ashfield
United Kingdom
NG17 4JL

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

Study participating centre
Southmead Hospital
Southmead Road
Westbury-on-trym
Bristol
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BS10 5NB

Study participating centre
St James University Hospital
Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre
St Georges University Hospital
Blackshaw Road
London

United Kingdom
SW17 0QT

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

Study participating centre
Tunbridge Wells Hospital
The Tunbridge Wells Hospital
Tonbridge Road
Pembury
Tunbridge Wells
United Kingdom
TN2 4QJ

Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
London
United Kingdom
NW1 2PG

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

Study participating centre
University Hospital Lewisham
Lewisham High Street
London
United Kingdom
SE13 6LH

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

Study participating centre
West Middlesex University Hospital
Twickenham Road
Isleworth
United Kingdom
TW7 6AF

Sponsor information

Organisation
University of Edinburgh

Sponsor details
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United Kingdom
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tiago.santos@ed.ac.uk

Sponsor type
University/education

Website
http://www.ed.ac.uk/home

ROR
https://ror.org/01nrxwf90

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care 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
1. Peer reviewed scientific journals
2. Conference presentation
3. Publication on the website
4. Submission to regulatory authorities

Intention to publish date
01/06/2029

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from the study team, guards@ed.ac.uk.

Any decision to share study data will be discussed and agreed between the study team (grant co-applicants). If sharing of data is deemed appropriate, we will share only anonymised data. The participant information leaflet (PIS) explains to patients that we would like to retain trial data after the trial has ended so that it can be used in future research studies. Participants have to explicitly agree to this on the consent form (Yes/No) option. If participants do not agree to us retaining their data this will be recorded within the database thereby ensuring their data is removed from any future exports to external research groups.

IPD sharing plan summary
Available on request