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# Sugammadex for prevention of postoperative pulmonary complications

**Submission date**
22/09/2022

**Recruitment status**
No longer recruiting

**Registration date**
21/12/2022

**Overall study status**
Ongoing

**Last Edited**
23/11/2026

**Condition category**
Surgery

[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
The aim is to conduct a large clinical trial comparing two drugs used to prevent lung complications and improve recovery from general anaesthesia in patients undergoing major surgery. General anaesthesia for major surgery requires specialised drugs which temporarily paralyse patients' muscles, called neuromuscular blocking agents (NMBAs). At the end of surgery, the NMBA-induced muscle paralysis is reversed with another drug. Despite careful monitoring, incomplete reversal is common, impacting breathing patterns and predisposing to lung complications such as pneumonia. These complications are common, delay patient recovery and increase the risk of death and long-term health problems. Anaesthetists choose between two drugs to reverse muscle paralysis, neostigmine or a newer drug, sugammadex, which reverses paralysis faster and may help to prevent lung complications after surgery. However, this benefit has not yet been proven and must be weighed against two problems with sugammadex. Firstly, it is more expensive than neostigmine, doubling the drug costs of a general anaesthetic. Secondly, there is concern that allergic reactions may become more common over time with widespread use, although these are extremely rare at present.

Who can participate?
Patients aged 50 years and over undergoing major chest or abdominal surgery

What does the study involve?
Each patient who agrees to participate will be randomly allocated to receive either sugammadex or neostigmine for NMBA reversal after surgery. The researchers will follow patients up to find out if using one drug results in faster recovery or lower risk of death than the other. In a subgroup of patients, the researchers will test to find out whether there are any signs that an allergy to sugammadex has developed and could be a problem in a second operation. This will help them to understand the risks and benefits of each drug.

What are the possible benefits and risks of participating?
Participants will be exposed to one of two drugs to reverse neuromuscular paralysing drugs at the end of surgery. Both drugs are in widespread use in the NHS for this indication, with the decision typically determined by individual anaesthetist preference, and participants would be receiving one or other drug anyway. There is therefore no additional risk to the patient from the

intervention.
The researchers have worked with patient representatives to minimise the burden on participants. Apart from the trial intervention, they aim to keep all other aspects of treatment unchanged from usual care. The researchers will collect only the minimum data required for the study and have outlined elsewhere how this will be kept confidential. They will offer participants a range of contact options for follow-up (e.g. email/telephone/post) in order to minimise the inconvenience involved.
The burden to participants in the allergic sensitisation substudy is greater, as they have a blood sample performed at baseline, and are asked to attend a clinic at 6 weeks to 6 months following surgery for a repeat blood sample, and a skin test if deemed appropriate by an allergy expert. Researchers will be requested, where possible, to take the baseline blood sample from an existing indwelling line (e.g. arterial or central venous line) while the patient is under anaesthesia to minimise any pain or discomfort. The amount of blood being taken (10 ml) is not clinically significant and no adverse effects are anticipated. The blood sample at the follow-up clinic will require venepuncture, but since it will be done by experienced staff and only 10 ml is required, this will be kept to a minimum. The skin test lasts for about 2 hours and involves injections of different concentrations of sugammadex into the skin using very fine needles. Redness, itch and pain are possible, but these are typically minimal and transient and can be treated with antihistamines and paracetamol if required. Patients participating in the allergic sensitisation substudy will be compensated for their time and any transport costs in keeping with NIHR guidance.
In patients undertaking the allergic sensitisation substudy, there is a very small risk of an allergic reaction to the skin test. While this risk is miniscule, it will be mitigated by the test being carried out under the supervision of an allergy expert who is trained in the management of allergic reactions, in a closely monitored environment with all necessary equipment and drugs available to treat an allergic reaction if it were to occur.

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

When is the study starting and how long is it expected to run for?
September 2022 to May 2027.

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

Who is the main contact?
SINFONIA@warwick.ac.uk

# Contact information

### Type(s)
Public

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Principal investigator

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## Additional identifiers

### Integrated Research Application System (IRAS)
1006043

### Central Portfolio Management System (CPMS)
54659

### Protocol serial number
21021JS-AS

## Study information

### Scientific Title
Sugammadex for prevention of postoperative pulmonary complications

### Acronym
SINFONIA

## Study objectives
Primary objective:
To determine whether sugammadex is superior to neostigmine after elective or emergency major abdominal or non-cardiac thoracic surgery in terms of days alive and out of hospital at 30 days (DAH30).

Secondary objectives:
1. To determine whether sugammadex is superior to neostigmine after elective or emergency major abdominal or non-cardiac thoracic surgery in terms of patient-centred clinical outcomes.
2. To determine the cost-effectiveness of sugammadex compared with neostigmine.
3. To estimate the rate of allergic sensitisation after a single exposure to sugammadex in a sub-group of participants.

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
Approved 20/12/2022, East Midlands - Nottingham 2 Research Ethics Committee (Equinox House, City Link, Nottingham, NG2 4LA, UK; +44 (0)207 104 8169, (0)2071048035, (0)20 71048016; nottingham2.rec@hra.nhs.uk), ref: 22/EM/0231

## Primary study design
Interventional

## Study design
Single-blind randomized controlled parallel group trial

## Study type(s)
Treatment

## Health condition(s) or problem(s) studied
Elective or emergency major abdominal or non-cardiac thoracic surgery

## Interventions
Current interventions as of 04/04/2025:
This randomised trial will compare the effectiveness of two drugs for the reversal of neuromuscular blocking agents at the end of anaesthesia to prevent postoperative pulmonary complications and thus recovery after major surgery.

Participants will be randomised on a 1:1 basis to receive either sugammadex or neostigmine. Randomisation will be undertaken through a simple and secure web-based randomisation system that has been established by the programming team at Warwick Clinical Trials Unit.

Sugammadex:
Participants randomised to the sugammadex arm should receive an intravenous bolus of sugammadex (2-4 mg/kg) for reversal of neuromuscular blockade around the end of the surgery. Within these parameters, the precise dose and timing are left to the discretion of the treating anaesthetist. If deemed necessary by the treating anaesthetist, patients allocated to the sugammadex treatment group may be administered a second dose of sugammadex. The maximum total dose of sugammadex (whether one or two doses are used) should not exceed

8mg/kg. A third or subsequent dose of sugammadex, or any dose of neostigmine administered, will be outside the trial intervention and will constitute a protocol deviation for monitoring purposes. If the dose of sugammadex administered is outside the specified range, reasons for this will be collected.

Neostigmine:
Participants randomised to the neostigmine arm should receive an intravenous bolus of neostigmine (30-70 mcg/kg) for reversal of neuromuscular blockade around the end of surgery, with co-administration of glycopyrrolate at an appropriate dose to prevent muscarinic side effects (for example 200 mcg per 1mg of neostigmine). The precise dose and timing are left to the discretion of the treating anaesthetist. If deemed necessary by the treating anaesthetist, patients allocated to the neostigmine treatment group may be administered a second dose. The maximum total dose of neostigmine (whether one or two doses are used) should not exceed 5mg neostigmine or 70 mcg/kg, whichever is less. A third or subsequent dose of neostigmine, or any dose of sugammadex administered, will be outside the trial intervention and will constitute a protocol deviation for monitoring purposes. If the dose of neostigmine administered is outside the specified range, reasons for this will be collected.

Following the surgery patients in both arms will follow this schedule. On Day 1 they will undertake a standard questionnaire to evaluate their recovery. On Day 7 they will be checked for any postoperative pulmonary complications that have occurred within the 7 days since surgery, Day 30 they will be checked for hospital readmission and mortality by review of medical records, and if necessary by telephone contact by site research staff with the participant or their General Practitioner. Participants will be contacted by telephone and/or by email at 30 days post-surgery (or as close as possible) and 180 days (or as close as possible) by site research staff to collect data on health resource use based on participant diary and quality of life using EQ-5D-5L.

Previous interventions:
This randomised trial will compare the effectiveness of two drugs for the reversal of neuromuscular blocking agents at the end of anaesthesia to prevent postoperative pulmonary complications and thus recovery after major surgery.

Participants will be randomised on a 1:1 basis to receive either sugammadex or neostigmine. Randomisation will be undertaken through a simple and secure web-based randomisation system that has been established by the programming team at Warwick Clinical Trials Unit.

Sugammadex:
Participants randomised to the sugammadex arm will receive an intravenous bolus of sugammadex (2-4 mg/kg) for reversal of neuromuscular blockade around the end of the surgery. Within these parameters, the precise dose and timing are left to the discretion of the treating anaesthetist. If deemed necessary by the treating anaesthetist, patients allocated to the sugammadex treatment group may be administered a second dose of sugammadex, up to a maximum total dose of 8 mg/kg. A third or subsequent dose of sugammadex, or any dose of neostigmine administered, will be outside the trial intervention and will constitute a protocol deviation for monitoring purposes.

Neostigmine:
Participants randomised to the neostigmine arm will receive an intravenous bolus of neostigmine (30-70 mcg/kg) for reversal of neuromuscular blockade around the end of surgery, with co-administration of glycopyrrolate at an appropriate dose to prevent muscarinic side effects (for example 200 mcg per 1 mg of neostigmine). The precise dose and timing are left to the discretion of the treating anaesthetist. If deemed necessary by the treating anaesthetist,

patients allocated to the neostigmine treatment group may be administered a second dose, up to a maximum total dose of 5 mg neostigmine (or 70 mcg/kg, whichever is less). A third or subsequent dose of neostigmine, or any dose of sugammadex administered, will be outside the trial intervention and will constitute a protocol deviation for monitoring purposes.

Following the surgery patients in both arms will follow this schedule. On Day 1 they will undertake a standard questionnaire to evaluate their recovery. On Day 7 they will be checked for any postoperative pulmonary complications that have occurred within the 7 days since surgery, Day 30 they will be checked for hospital readmission and mortality by review of medical records, and if necessary by telephone contact by site research staff with the participant or their General Practitioner. Participants will be contacted by telephone and/or by email at 30 days post-surgery (or as close as possible) and 180 days (or as close as possible) by site research staff to collect data on health resource use based on participant diary and quality of life using EQ-5D-5L.

## Intervention Type
Drug

## Phase
Phase III

## Drug/device/biological/vaccine name(s)
Sugammadex sodium, neostigmine methylsulfate, glycopyrronium bromide, glycopyrronium bromide and neostigmine metilsulfate

## Primary outcome(s)
Days alive and out of hospital at 30 days following surgery (DAH30), captured via questions on case report form (CRF): 'Patient still alive at 30 days' – 'Since their initial discharge after surgery, has the patient been readmitted to hospital', if yes space provided to add dates, captured on the day 30 post Op form.

## Key secondary outcome(s)
1. Postoperative Pulmonary Complications (PPCs) within 7 days after surgery, captured via questions on CRF: 'Post-operative pulmonary complications' – list of these with Yes/No captured on the day 7 post Op form
2. Mortality at 30 and 180 days after surgery, captured via questions on CRFs:
2.1. Patient still alive at 30 days – captured on day 30 post op form
2.2. Patient still alive at 180 days – captured on day 180 post op form
2.3. If no date of death – captured on day 30/180 post op form
3. Quality of recovery on the first post-operative day, measured using QoR-15 on day 1 post op form
4. Health-related quality of life at 7, 30 and 180 days measured using EQ-5D-5L at baseline, day 7 post op, day 30 post op and day 180 post op
5. Allergic reaction within 24 hours after administration of IMP (clinician defined), captured via question on CRF - In the 24 hours following administration of the IMP, has the patient had an allergic reaction? – collected on day 1 post-op form
6. Health resource use during the 180 days after surgery, captured via questions on CRFs, Details of hospital stay (including critical care admissions and re-admissions) Details of community and outpatient visits, captured on both day 30 and day 180 post-op forms
7. Rate of allergic sensitisation to sugammadex (for the allergic sensitisation sub-study only), captured via a CRF – there will be a Final adjudication panel with overall outcome of allergy testing – captured on the Sub-Study Form with the following options:

7.1. Evidence of clinically relevant sensitisation
7.2. No evidence of clinically relevant sensitisation (all test modalities negative OR a single positive test followed by a negative drug provocation test)
7.3. Low certainty of clinically relevant sensitisation (equivocal results)
7.4. Unable to confirm whether clinically relevant sensitisation present (testing not completed)

### Completion date
01/05/2027

## Eligibility

### Key inclusion criteria
1. Patients presenting for elective or emergency major abdominal or non-cardiac thoracic surgery
2. Age ≥50 years
3. Planned use of rocuronium or vecuronium for neuromuscular blockade
4. Planned reversal of neuromuscular blockade at the end of surgery

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Mixed

### Lower age limit
50 Years

### Upper age limit
120 Years

### Sex
All

### Total final enrolment
2501

### Key exclusion criteria
1. Known allergy to sugammadex, neostigmine or glycopyrrolate
2. Lack of written informed consent for trial participation
3. Planned invasive mechanical ventilation before or after surgery
4. Previous participation in SINFONIA trial
5. Clinician refusal (with reason)

### Date of first enrolment
15/02/2023

### Date of final enrolment
01/11/2025

# Locations

## Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Wales

## Study participating centre
**Aberdeen Royal Infirmary**
Foresterhill Road
Aberdeen
Scotland
AB25 2ZN

## Study participating centre
**Aneurin Bevan University Health Board**
Lodge Road
Caerleon
Newport
Wales
NP18 3XQ

## Study participating centre
**Belfast City Hospital**
51 Lisburn Rd
Belfast
Northern Ireland
BT9 7AB

## Study participating centre
**Freeman Hospital**
Freeman Road
High Heaton
Newcastle upon Tyne
England
NE7 7DN

**Study participating centre**
**Golden Jubilee National Hospital**
Agamemnon Street
Clydebank
Scotland
G81 4DY

**Study participating centre**
**James Cook University Hospital**
Marton Road
Middlesbrough
England
TS4 3BW

**Study participating centre**
**Leeds Teaching Hospitals**
Great George Street
Leeds
England
LS1 3EX

**Study participating centre**
**North Bristol NHS Trust**
Southmead Hospital
Southmead Road
Westbury-on-trym
Bristol
England
BS10 5NB

**Study participating centre**
**University Hospital Birmingham**
Queen Elizabeth Hospital
Edgbaston
Birmingham
England
B15 2TH

**Study participating centre**

**Royal London Hospital**
Whitechapel Road
London
England
E1 1FR

**Study participating centre**
**Royal Victoria Hospital**
274 Grosvenor Road
Belfast
Northern Ireland
BT12 6BA

**Study participating centre**
**The Royal Victoria Infirmary**
Queen Victoria Road
Newcastle upon Tyne
England
TS1 4LP

**Study participating centre**
**St. Bartholomews Hospital**
West Smithfield
London
England
EC1A 7BE

**Study participating centre**
**Vale University Health Board**
Heath Park
Cardiff
Wales
CF14 4XW

**Study participating centre**
**Whipps Cross Hospital**
Whipps Cross Road
London
England
E11 1NR

**Study participating centre**
**Bronglais General Hospital**
Bronglais Hospital
Caradoc Road
Aberystwyth
Wales
SY23 1ER

**Study participating centre**
**Conquest Hospital**
The Ridge
St. Leonards-on-sea
England
TN37 7RD

**Study participating centre**
**Craigavon Area Hospital**
Lurgan Rd
Craigavon
Northern Ireland
BT63 5QQ

**Study participating centre**
**University Hospitals Plymouth NHS Trust**
Derriford Hospital
Derriford Road
Derriford
Plymouth
England
PL6 8DH

**Study participating centre**
**East Surrey Hospital**
Canada Avenue
Redhill
England
RH1 5RH

**Study participating centre**

**Eastbourne District General Hospital**
Kings Drive
Eastbourne
England
BN21 2UD

**Study participating centre**
**Forth Valley Royal Hospital**
Stirling Road
Larbert
Scotland
FK5 4WR

**Study participating centre**
**Good Hope Hospital**
Rectory Road
Sutton Coldfield
England
B75 7RR

**Study participating centre**
**Heartlands Hospital**
Bordesley Green East
Bordesley Green
Birmingham
England
B9 5ST

**Study participating centre**
**Hinchingbrooke Hospital**
Hinchingbrooke Park
Huntingdon
England
PE29 6NT

**Study participating centre**
**Liverpool Women's Hospital Cdc**
Liverpool Womens Hospital
Crown Street

Liverpool
England
L8 7SS

**Study participating centre**
**Manchester Royal Royal Infirmary**
Cobbett House
Oxford Road
Manchester
England
M13 9WL

**Study participating centre**
**Newham General Hospital**
Glen Road
London
England
E13 8SL

**Study participating centre**
**Norfolk and Norwich University Hospital**
Colney Lane
Colney
Norwich
England
NR4 7UY

**Study participating centre**
**North Manchester General Hospital**
Delaunays Road
Crumpsall
Manchester
England
M8 5RB

**Study participating centre**
**Peterborough City Hospital**
Edith Cavell Campus
Bretton Gate
Bretton
Peterborough

England
PE3 9GZ

**Study participating centre**
**Pinderfields Hospital**
Aberford Road
Wakefield
England
WF1 4DG

**Study participating centre**
**Raigmore Hospital**
Old Perth Rd
Inverness
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IV2 3UJ

**Study participating centre**
**Rotherham General Hospital**
Moorgate Road
Rotherham
England
S60 2UD

**Study participating centre**
**Royal Berkshire Hospital**
Royal Berkshire Hospital
London Road
Reading
England
RG1 5AN

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

**Study participating centre**
**Royal Liverpool University Hospital NHS Trust**
Royal Liverpool University Hospital
Prescot Street
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L7 8XP

**Study participating centre**
**The Royal Oldham Hospital**
Rochdale Road
Oldham
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OL1 2JH

**Study participating centre**
**Scarborough General Hospital**
Woodlands Drive
Scarborough
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YO12 6QL

**Study participating centre**
**Solihull Hospital**
Lode Lane
Solihull
England
B91 2JL

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

**Study participating centre**
**University Hospital Hairmyres**
Eaglesham Road

East Kilbride
Scotland
G75 8RG

**Study participating centre**
**Ysbyty Maelor Wrexham**
Croesnewydd Road
Wrexham Technology Park
Wrexham
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LL13 7TD

**Study participating centre**
**Wythenshawe Hospital**
Southmoor Road
Wythenshawe
Manchester
England
M23 9LT

**Study participating centre**
**York Hospital**
Wigginton Road
York
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YO31 8HE

# Sponsor information

**Organisation**
Belfast Health and Social Care Trust

**ROR**
https://ror.org/02tdmfk69

# Funder(s)

**Funder type**
Government

### Funder Name
Health Technology Assessment Programme

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

### Funding Body Type
Government organisation

### Funding Body Subtype
National government

### Location
United Kingdom

# Results and Publications

## Individual participant data (IPD) sharing plan

### 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? |
|---|---|---|---|---|---|
| Protocol article | | 28/08/2025 | 01/09/2025 | Yes | No |
| Protocol article | Protocol for an embedded mixed-methods process evaluation | 01/09/2026 | 14/09/2026 | Yes | No |
| HRA research summary | | | 28/06/2023 | No | No |
| Protocol file | version 3.0 | 18/10/2023 | 05/03/2024 | No | No |
| Protocol file | version 4.0 | 02/10/2024 | 04/04/2025 | No | No |
| Study website | Study website | 11/11/2025 | 11/11/2025 | No | Yes |