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PROTECT-CH
Prophylactic Therapy in Care Homes Trial

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Research Nurse (RN) Training Module

Final Version 1.0 24-Aug-2021

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RN Training Module Overview

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This training module includes the following sections:

1. Brief Overview of the Trial
2. Roles & Responsibilities
3. Eligibility: Care Home Criteria
4. Eligibility: Resident Criteria
5. Therapies: Background & Safety
6. Prescribing
7. Safety
8. Trial Assessments & Follow-up
9. Data Protection
10. Trial Database
11. Outbreak
12. Randomisation
13. Onsite Visits
14. Record Keeping
15. Final Reminders

1. Brief overview of the trial

Background

Since its emergence in December 2019, there have been well over 200 million confirmed cases of COVID-19, causing millions of deaths worldwide.

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In the UK, care home residents have particularly suffered from the virus.

Most care homes have had at least one resident or staff member test positive for COVID-19.

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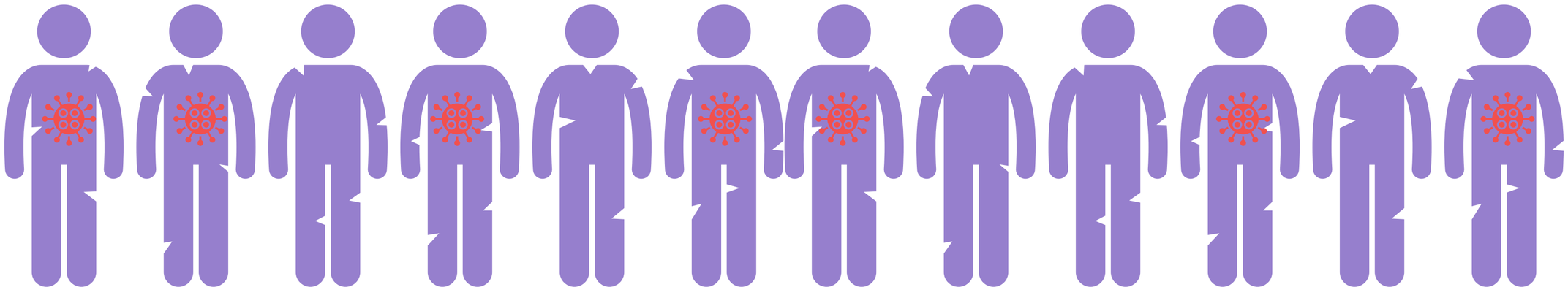
At least

42,000

care home residents have died with COVID-19.



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- Vaccination has been shown to be hugely beneficial, however no vaccine prevents all disease.
- Research has shown that vaccines are effective, however little research has been conducted in the over 80s.
- The risk that vaccines may be less effective against new virus mutations means that there is an urgent need to discover treatments that can prevent transmission or reduce severity of COVID-19, especially in high-risk environments like care homes.

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Prophylactic Therapy in Care Homes Trial

PROTECT-CH has been developed as a result of a commissioned call from the National Institute of Health Research to design a platform trial for prophylactic treatments for COVID-19 in care homes.

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Prophylactic Therapy in Care Homes Trial

- Urgent Public Health trial
- Funded by the National Institute for Health Research
- Managed by the University of Nottingham

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FUNDED BY
NIHR | National Institute for Health Research

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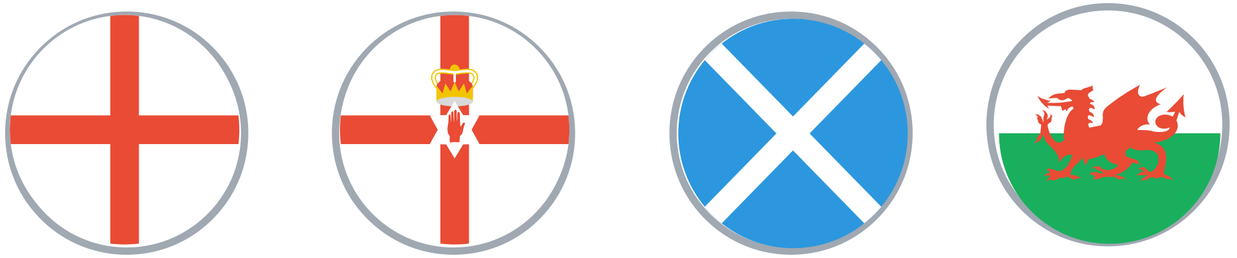
SETTING

- 750 care homes (nursing, residential and mixed) in the UK
- Recruiting approximately 24,000 care home residents



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Research Question

To determine which drug or antibody interventions
when compared to standard care
are effective, safe and cost-effective
as prophylaxis for COVID-19.

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Aims

1. Reduce the incidence and severity of SARS-CoV-2 infection at care homes

2. Reduce transimission of SARS-CoV-2 at care homes

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Intervention:

A treatment chosen by the Department of Health which aims to reduce transmission and seriousness of COVID-19 (plus standard care).

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Comparator:

Standard care

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Intervention:

A treatment chosen by the Department of Health which aims to reduce transmission and seriousness of COVID-19 (plus standard care).

Comparator:

Standard care*

**This is how care homes routinely treat residents with COVID-19.*

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PRE-EXPOSURE prophylaxis (PrEP):

Given before an outbreak of COVID-19 occurs at a care home

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PRE-EXPOSURE prophylaxis (PrEP):

Given before an outbreak of COVID-19 occurs at a care home

OR

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PRE-EXPOSURE prophylaxis (PrEP):

Given before an outbreak of COVID-19 occurs at a care home

OR

POST- EXPOSURE prophylaxis (PEP):

Given after an outbreak of COVID-19 occurs at a care home

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PRE-EXPOSURE prophylaxis (PrEP):

Given before an outbreak of COVID-19 occurs at a care home

OR

POST- EXPOSURE prophylaxis (PEP):

Given after an outbreak of COVID-19 occurs at a care home

At the moment we are testing PEP treatments.

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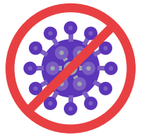
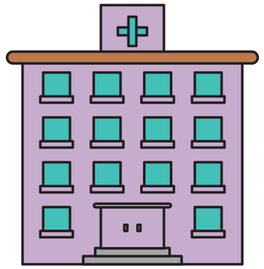
Primary Outcome Measures

Participants will be classified according to the most serious event they experience during the 60-day period following randomisation:

- No SARS-CoV-2 infection



- SARS-CoV-2 infection but resident remains in care home
- Admission to hospital, all-cause



- Death, all-cause

Outcome Measures Data Collection

- Data to support the primary outcome measures will be collected from residents' medical records and also recorded by care home staff on the trial database.

- SARS-CoV-2 status (positive or negative) will be diagnosed using PCR or lateral flow testing (or equivalent) in accordance with the care home’s routine testing schedule.
  Please note, there will not be any additional trial-specific testing.

2. What is the role of the Research (RN) in PROTECT-CH?

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The PROTECT-CH Research Nurse role:

In PROTECT-CH, the role of the research nurse (RN) can be undertaken by other suitably qualified Allied Healthcare Professionals (AHP) or research coordinator/practitioner.

Therefore, where the RN is mentioned in any trial material it should be understood that this also refers to AHPs and research practitioners/coordinators unless stated otherwise.

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The PROTECT-CH RN: Role & responsibilities

The PROTECT-CH Research Nurses will be aligned with the Principal Investigators (PIs), where appropriate, and may be responsible for:

1 – Maintenance of the Investigator Site File (ISF) and other documentation for the care homes assigned to them.

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The PROTECT-CH RN: Role & responsibilities

2 – Managing and conducting conversations with the resident or their personal legal representative to inform them of the study and seek consent.

3 – Assisting care homes at the point of outbreak to administer trial medication and facilitate trial processes.

4 – Assisting care homes with completion of data collection on day 60.

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The role of the RN in the Consent process:

For residents with capacity:

1. Arrange consent appointment with care home staff for resident (virtual or face-to-face if preferable).
2. Discuss trial with resident, answer any questions and consent resident.
3. Electronically countersign the consent form once it has been submitted by the resident or care home staff witnessing consent.

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The role of the RN in the Consent process:

For residents without capacity:

1. Arrange virtual consent appointment with personal legal representative (PLR) - the resident's family member or close friend.
2. Discuss trial with PLR, answer any questions and consent PLR.
3. Trigger email from the database to the PLR, containing a link to the consent form (if PLR is completing e-consent).
4. Electronically countersign the consent form once it has been submitted by the PLR.

RN Responsibilities Flowchart

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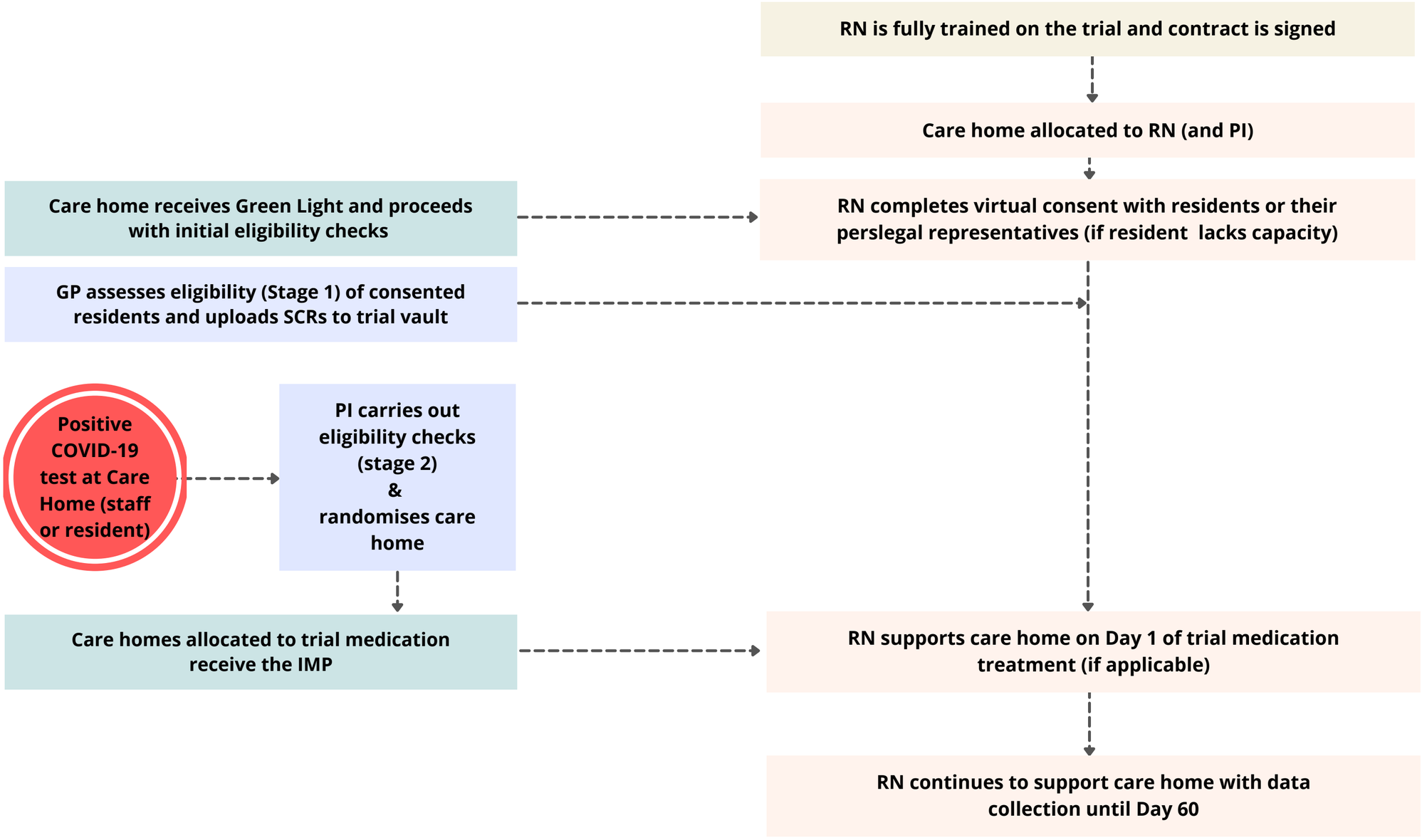

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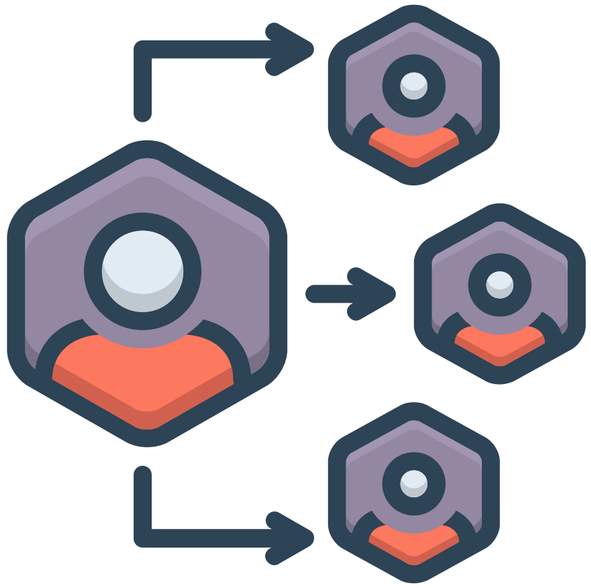
Delegation of Responsibilities



Research Nurse (RN) tasks will be delegated to all the RNs by the Principal Investigators (PI)s.

The RNs will be aware of this delegation and cannot undertake any tasks until they have signed the delegation log.

3. Eligibility - Care Home Criteria

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Care Home eligibility is assessed at the point of entry to the trial by the University of Nottingham Research Team.

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Care Home - Inclusion Criteria

Location:

- UK care homes for older people, with or without nursing

Size:

- At least 20 beds

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Care Home - Exclusion Criteria

Rated inadequate by the CQC (or the equivalent in the devolved administrations)

<u>Exclusions In the treatment phase</u>:

Positive PCR or lateral flow test (or equivalent) for SARS-CoV2 in any staff member or resident in the previous four weeks

4. Eligibility - Resident Criteria

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Residents' eligibility is assessed after the care home has received the green light and is a two-stage process:

GPs will assess residents' eligibility (stage 1 eligibility check) immediately after consent.

PIs will be assessing residents' eligibility at the point of the outbreak (stage 2 eligibility check).

An initial eligibility screen will also be done by the care home prior to consent.

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Resident Inclusion Criteria

- Resident in a care home.
- Age 65 or over.
- Able to give informed consent for participation or a personal legal representative has been identified who can give consent if resident lacks capacity.

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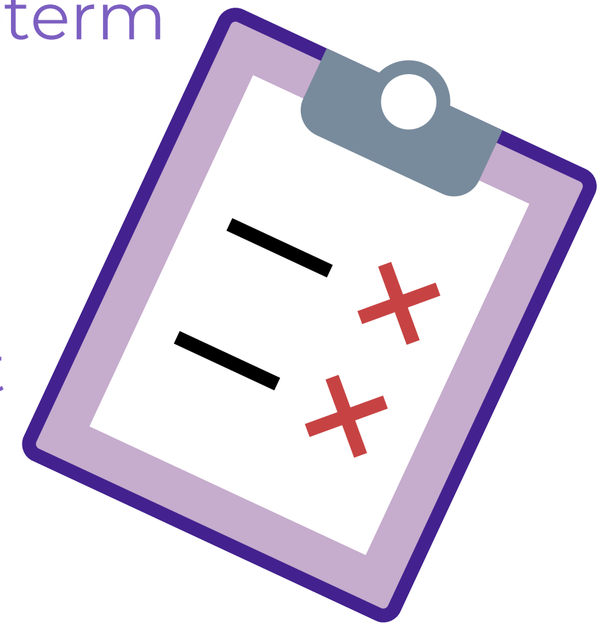
Resident Exclusion Criteria

- Identified by care home staff to have entered end-stage palliative care.
- Resident in the care home for short-term respite care.
- Resident's general practitioner is unable to support their involvement in the trial.



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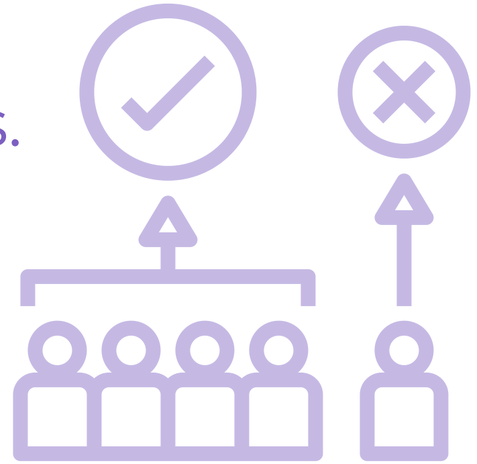
Resident Exclusions in the Treatment Phase - PI Assessment of Eligibility

- Currently taking all of the trial interventions.
- Contraindication to all trial interventions.
- In treatment phase of another COVID-19 prevention or treatment trial.



5. Therapies: Background & Safety

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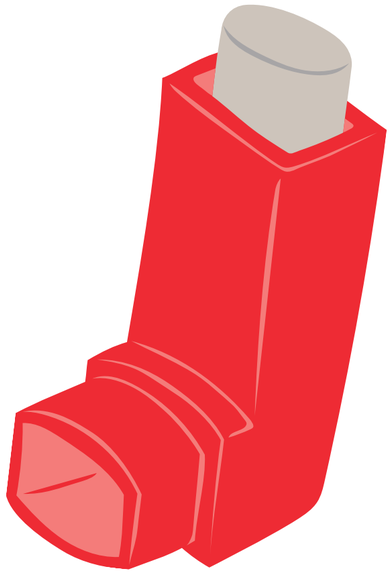
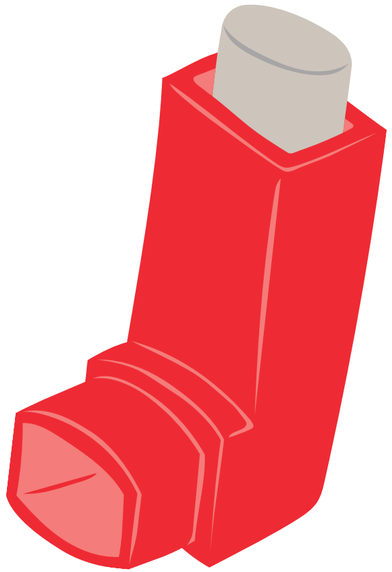
Ciclesonide



- **Ciclesonide** (by inhalation of aerosol) is currently licensed in the UK as a treatment to control persistent asthma in adults and adolescents (12 years and older). Ciclesonide is not licensed for COVID-19 prophylaxis.
- Ciclesonide has been shown to block SARS-CoV-2 RNA replication by targeting the viral replication-transcription complex and inhibiting SARS-CoV-2 cytopathic activity.
- The product being supplied for use in the trial is an unlicensed formulation identical to that of the UK licensed formulation (Alvesco).
- One puff via spacer and mask through nose (where possible) followed by two puffs via spacer and mask through mouth should be administered once daily.
- Further information on Ciclesonide is available in Appendix A of the protocol and the Alvesco SmPC.

Ciclesonide



Appox 5% of patients experienced adverse reactions in clinical trials with Alvesco.
In the majority of cases these were mild and did not require discontinuation of treatment (refer to section 4.8 of Alvesco SmPC for more details).

Side effects sometimes reported with nebulization procedures include bronchospasm and coughing.

Ciclesonide: Exclusions & Contraindications

1. Already taking, or definite need for, an inhaled or intranasal corticosteroid: beclometasone dipropionate (aerosol inhaler and dry powder inhaler), budesonide (dry powder inhaler and single-dose units for nebulization), ciclesonide (aerosol inhaler), fluticasone propionate (dry powder inhaler, aerosol inhaler, and single-dose units for nebulization), mometasone furoate (dry powder inhaler).

2. Known allergy/hypersensitivity to ciclesonide or any excipient.

Ciclesonide: Exclusions & Contraindications

3. Received a live vaccine within last 14 days - ciclesonide increases risk of generalised infection: influenza*, MMR, rotavirus, typhoid, varicella-zoster (shingles), yellow fever.

*Influenza live vaccine is not indicated for older people.

4. Severe liver impairment.

Participants will be made aware that the Ciclesonide formulation contains a small amount of ethanol.

Niclosamide

- Recent studies have shown **Niclosamide** may be a potential treatment for viral infections such as SARS-CoV-2 (COVID-19).

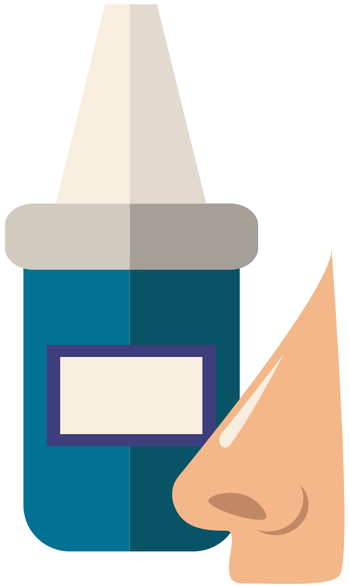
- SARS-CoV-2 initially replicates predominantly in the nasal cavity so the administration of Niclosamide as a nasal spray may be an effective post-exposure prophylactic for early-stage infection when the viral load is the main issue.

- Niclosamide is not licensed for COVID-19 prophylaxis but is approved and marketed overseas for the oral treatment (at 500x dose of that used in PROTECT-CH) of tapeworm infections.

- In PROTECT-CH, one intranasal spray should be administered into each nostril twice daily.

- Further information on Niclosamide is available in Appendix B of the protocol and the investigators brochure.

Niclosamide



Niclosamide has previously been administered as oral tablets. Side effects of the nasal spray are not yet known.

The occasional side effects reported for the oral tablet are detailed below.
These are not expected when using the nasal spray.

Allergic reaction (e.g. patches of skin redness (erythema), itching (and skin rash), nausea, gastrointestinal pain, abdominal pain, gagging, diarrhoea, dizziness, blue colour to skin or lips (cyanosis), excessive sweating (hyperhidrosis) and fatigue.

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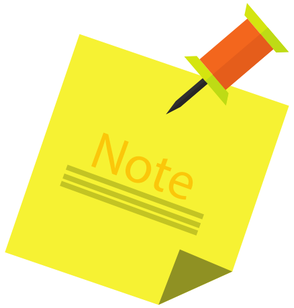
Niclosamide: Contraindications & Anticipated Side Effects

Contraindications

Known allergy
to niclosamide or excipients

Anticipated side effects

Although these are not known, we anticipate nasal itching, nasal irritation, nasal crusting, nasal drip and nasal bleed.



Please note that only nurses can give out drugs - in this case the relevant slides do not apply to AHPs or research coordinators.

Additional treatments may be added during the trial.
In this case, participants and their representatives (for those participants lacking capacity) will be reconsented for the additional medications.

6. Prescribing

Prescribing of trial IMP will be the responsibility of the on-duty PI.

Once a care home has been randomised, each eligible participant will need to be prescribed the correct IMP:

- Each participant in a care home randomised to **Ciclesonide**:

  Treatment: 2 x Ciclesonide 160 micrograms per actuation inhaler

  Dosage: Using the spacer device and technique described in the leaflet, inhale ONE puff through the NOSE followed by TWO puffs through the mouth. If you cannot inhale the first dose through your nose, only inhale the two puffs through your mouth.

- Each participant in a care home randomised to **Niclosamide**:

  Treatment: 3 x 8.5 mL Niclosamide ethanolamine (UNI911) 1% (10 mg in 1 mL) nasal spray

  Dosage: ONE spray to be used in EACH nostril TWICE a day

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7. Safety

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Safety and Reporting Process

- Care home staff and resident GPs are trained to report any Serious Adverse Event (SAE) in the REDCap database **within 24 hours** of becoming aware of the event.

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Safety and Reporting Process

- Care home staff and resident GPs are trained to report any Serious Adverse Event (SAE) in the REDCap database **within 24 hours** of becoming aware of the event.

- If **you become aware of an unreported SAE**, you should **alert the care home** and **assist them with the completion of the SAE report** where necessary.

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Safety and Reporting Process

- Care home staff and resident GPs are trained to report any Serious Adverse Event (SAE) in the REDCap database **within 24 hours** of becoming aware of the event.

- If **you become aware of an unreported SAE**, you should **alert the care home** and **assist them with the completion of the SAE report** where necessary.

- Upon completion of a SAE form, the care home PI will receive immediate notification via email.

SAE Assessment (i)

The PI will assess the causality of the event and its relatedness to trial interventions, using the corresponding Investigational Medical Product's (IMP's) Reference Safety Information (RSI).

SAE Assessment (i)

Based on the relatedness, the event will be classified as below:

- Not SAE (incorrectly reported)
- SAE (serious, not related to IMP)
- Serious Adverse Reaction (SAR) (related to IMP, not unexpected)
- Suspected Unexpected Serious Adverse Reaction (SUSAR) (related to IMP, unexpected)

Protocol Violations (i)

If you notice non-compliance to the trial protocol, you should ask the care home to record it on the relevant violation form on the REDCap trial database.

All instances of non-compliance reported on the violation form will be reviewed by NCTU and where believed to constitute a protocol violation or a potential serious breach will be further investigated.

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Protocol Violations (ii)

The following will be considered protocol violations and will need to be reported immediately:

- Treatment without consent
- Treatment administered to ineligible residents
- Non-reporting of primary outcome measures
- Non-reporting of serious adverse events

8. Trial Assessments & Follow-up

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Follow-up (i)

The PROTECT-CH follow-up period lasts 120 days
(Day 0 = Randomisation).
From Day 0 to Day 60, care home staff will be asked to share data with us that may include the following:

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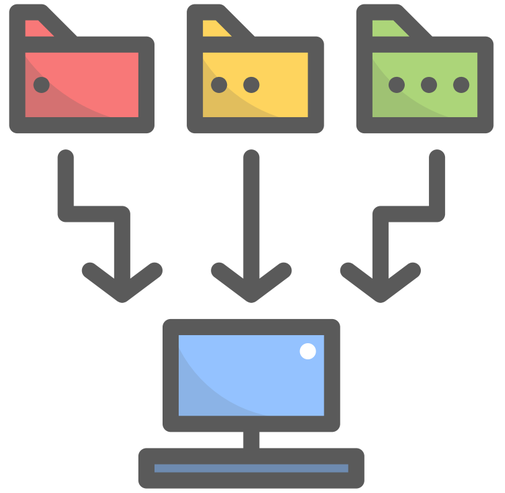
Follow-up (i)

The PROTECT-CH follow-up period lasts 120 days
(Day 0 = Randomisation).
From Day 0 to Day 60, care home staff will be asked to share data with us that may include the following:

- Number of care home residents (in trial or not) who became COVID-19 positive
- **All cause** hospitalisation including number of infections that led to hospitalisation



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Follow-up: Day 0-60 Data Collection (ii)

- **All cause** death including number of infections that led to death
- Other Clinical Data (See Protocol)
- Safety data (See Safety section)
- Economic evaluation
  (incl. Healthcare Resource Use data)

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Trial Questionnaires

In PROTECT-CH, the trial assessments include two Quality-of-Life (QoL) questionnaires: EQ-5D-5L and EQ-VAS.

These will be carried out by residents with capacity and care home staff at two timepoints: 1) following consent and 2) on day 60; where randomisation is day 0.

9. Data Protection

It is essential that to collect and use a resident's:

- **personal data** (name, date of birth, NHS number and address)

AND

- **research data** (any data collected as part of the trial)

the research staff must have received consent from either the resident or their personal legal representative.

All data collected as part of the trial must be stored securely, either on the trial password-protected database or a locked cabinet in a restricted-access office.

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All data collected as part of the trial must be stored securely, either on the trial password-protected database or a locked cabinet in a restricted-access office.

Please ensure that all resident personal and research data is stored securely.

10. Trial Database

Trial Database

Data for this trial will be entered electronically into a database called REDCap.

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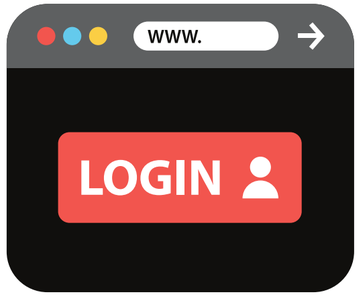

RNs will need to complete a database access form in order to be granted permissions to access the PROTECT-CH trial database, known as REDCap.

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Logging onto the REDCap Trial Database

REDCap can be accessed via the following link:
https://redcap01.nottingham.ac.uk/
or
by scanning this QR code from a mobile device:

PROTECT-CH REDCap Database

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PROTECT-CH REDCap Database

Please refer to the ***Research Nurse (RN) Data Entry User Guide*** for information on completion of specific forms on the trial database.

11. Outbreak

- Care home staff are trained to report via the trial database as soon as they are aware of an outbreak of COVID-19 in their home.

- Care home staff are trained to report via the trial database as soon as they are aware of an outbreak of COVID-19 in their home.

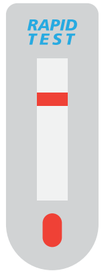
- An outbreak is defined as a positive COVID-19 test result in either a resident or a member of staff, known as the ‘index case’.

An outbreak will be reported by the care home through completion of the ‘outbreak survey’ within the REDCap database.

An outbreak will be reported by the care home through completion of the ‘outbreak survey’ within the REDCap database.

Upon completion of this survey, the central PI team will receive immediate notification via email and will proceed with the eligibility assessment (stage 2).

If an outbreak is reported on the basis of a positive lateral flow test, then the trial team will liaise with the care home to obtain results of the confirmatory PCR.



If an outbreak is reported on the basis of a positive lateral flow test, then the trial team will liaise with the care home to obtain results of the confirmatory PCR.

If the PCR for the index case is negative (i.e. false positive), and there are no other positive cases in the care home, then the care home should:

If an outbreak is reported on the basis of a positive lateral flow test, then the trial team will liaise with the care home to obtain results of the confirmatory PCR.

If the PCR for the index case is negative (i.e. false positive), and there are no other positive cases in the care home, then the care home should:

1) notify the trial team, 2) treatment must not be given to residents, or must be stopped if already started and 3) the medication should be quarantined.

Detailed guidance will be provided to the care homes.

12. Randomisation

- While the PIs will be conducting the resident eligibility assessments, staff at the University of Nottingham trial team will carry out a final green light assessment of the care home in order to ensure its readiness to deliver the trial effectively.

- The trial team will then provide the PIs with confirmation that the care home is ready to be randomised.

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- As soon as the PI has randomised a care home, the care home will receive an email informing them of the group they have been allocated to.
    - The research nurse team will also receive an email notification that the trial is about to begin at the care home.

13. Onsite Visits

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Onsite visits may be required for care homes in your regions.

Onsite visits will require approval from the care home and you will be required follow any COVID-19 precaution measures they have in place.

Where virtual consent is not possible an alternative is to visit the care home to receive consent form the resident /PLR.

Onsite visits may also be requested to support the first dosing occasion of IMP and/or to facilitate data collection at day 60.

14. Record Keeping

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As with medical records, in trials,
if something is not recorded, it did not happen.

In PROTECT-CH, it is even more important to keep good records as multiple medics might be engaged in conversations with the same care home(s).

Therefore, any advice given to care homes e.g. to respond to a resident-related query, that is not logged on the trial database (REDCap), needs to be recorded.

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You can record such conversations by summarising what has been agreed during your phone call in an email to the care home cc:ing the PROTECT-CH mailbox.

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Prophylactic Therapy in Care Homes Trial

You can record such conversations by summarising what has been agreed during your phone call in an email to the care home cc:ing the PROTECT-CH mailbox.

Please remember **not** to include **confidential** information in your **correspondence**.

If you need to refer to a participant in your correspondence, you may include the following identifiers:

1) their initials,
2) their trial ID number and
3) the name of their care home.

Please include all three identifiers to ensure the correct identification of the individual.

If you need to refer to a participant in your correspondence, you may include the following identifiers:

1) their initials,
2) their trial ID number and
3) the name of their care home.

Please include all three identifiers to ensure the correct identification of the individual.

Please direct any care home queries (not related to specific resident care as part of the trial or SAEs etc.) to the NCTU trial team.

15. Final Reminders

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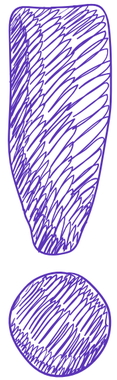
Prophylactic Therapy in Care Homes Trial

Before you engage in any trial-related activities, please ensure:

- You have read the trial protocol.
- You have provided the trial team with your CV and GCP certificate.
- Your contract is in place.
- You have completed this training module.
- You have obtained your training certificate.
- You have signed the care home e-delegation log.



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Thank you for watching!

You have now completed the
Research Nurse (RN)
Training Module.

NEXT

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Please remember to complete your self-certification form to confirm you have undertaken this training.

This can be found at:

https://w3.abdn.ac.uk/hsru/NCTU-Protect/Public/Public/SelfCertification.cshtml?TrainingModule=11&ModuleVersion=1

Or you can access it via mobile here:

University of Nottingham
UK | CHINA | MALAYSIA

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If you have any questions, please do not hesitate to contact us:

protect-trial@nottingham.ac.uk

0115 74 87710