Participant Information Sheet

Hypertonic saline nasal irrigation and gargling for suspected or confirmed COVID-19: pragmatic web-based Bayesian adaptive randomised controlled trial (ELVIS COVID-19)

You are being invited to take part in a research study. Before you decide whether to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish. Contact us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of the study?

COVID-19, a recently identified disease has spread worldwide rapidly and is now a pandemic. There is no cure for it yet. Though it causes mild to moderate illness in most people, it can cause serious illness and death, particularly in the elderly, those with chronic illness or a weakened immune system.

This study is to find out if nasal washout (i.e. irrigation) and gargling with salt water (hypertonic saline) helps individuals with COVID-19 get better faster. Preliminary data from those with the common cold has found that nasal washouts and gargling with salty water may be helpful in reducing the length of the illness. We do not however know if this same benefit is also seen in those with suspected or confirmed COVID-19. This trial will help us find out if nasal washouts and gargling with salty water are helpful in COVID-19.

Why have I been invited to take part?

You have been asked to take part as you are self-isolating with a suspected or confirmed diagnosis of COVID-19 and have responded to an advertisement about this study.

Do I have to take part?

No, it is up to you to decide whether or not to take part. If you do decide to take part, you will be asked to sign an online consent form. If you decide to take part, you are still free to withdraw at any time, without giving a reason. Deciding not to take part or withdrawing from the study will not affect the healthcare that you receive.

What will happen if I take part?

1. Inclusion and exclusion criteria
You will be asked to answer some online questions to check if you meet the criteria to take part:

- You live in the UK
- You are 18 and over
- Your illness started within 48 hours and you are self-isolating

- You are not pregnant
- You do not have a weakened immune system
- You have a supply of salt or can arrange a supply of sea-salt/table salt (maximum 250g)
- You are willing and able to perform nasal washout and gargling with self-made salty water if you are in the intervention group
- You are not taking part in another medical trial
- You are not needing hospital care right now
- You have access to email or the internet
- You are not living in a household with another person currently participating in this study

If you are allocated to the control group, you should continue to follow the existing UK Government's advice regarding personal and household hygiene, and you should not use nasal washout or gargling with salty water. It is important that you follow the advice individually provided to you so the groups can be compared at the end of the study.

2. Consent
If you take part, you will be asked to complete an online consent form by answering a number of questions. By submitting the form, you will be signing the form electronically, which is the equivalent of signing a physical document. Your participation is voluntary, and you are free to withdraw from the study at any time.

3. Contact details
Your contact details will be collected in case a member of the trial team has to be in touch with you (see Sections 6 and 7).

4. Randomisation
You will be allocated either to an intervention or control group. The allocation will be random and hence there is a chance that you could be in either the intervention or control group.

5. What is expected of me?
All participants:

- **Online Daily Diary:** Participants in both intervention group and control group will complete an online daily diary first thing in the morning. The diaries will have to be maintained until you report that are well or a maximum of 14 days or until you stop the trial. If the diaries are not maintained regularly, a member of the trial team may contact you to remind you to document the diary. If you haven't completed your daily diary in the morning, you will receive a reminder to your email address approx. every 5 hours. This is so we can ensure we have as complete data as possible for the study. If you miss a daily diary, you will continue to be sent your daily diary links until you report you are well, withdraw from or complete the study.
- **Personal and household hygiene:** Continue with UK Government advised personal and household hygiene as recommended: https://www.nhs.uk/conditions/coronavirus-covid-19/self-isolation-advice/

In each questionnaire, we will ask if you have been tested for COVID-19 and what the result of this test is.
If you have either a positive or negative COVID-19 test result or have not taken a test after you have consented to take part in the study, we ask that you still follow the advice of your allocated group until you feel well, or Day 14 (the end of the study).

The intervention group only:
You will be shown an online video on how to prepare the salty water (hypertonic saline) solution and perform nasal washout and gargling, which is a procedure to washout the nasal passages and throat. You will be asked to make use of bowls/cups/containers and equipment available in your own house. You can either make the solution fresh every time or you could make it in bulk and use it for up to 24 hours. You will be asked to perform the nasal washout and gargling at home. The number of times you will need to perform the nasal washout and gargling will depend on the severity of your symptoms. You will be can expect to perform the procedure up to 12 times a day until you become well or until day 14.

6. Follow-up
During the study, you will be sent daily reminders and links by email to complete your daily diaries.

7. Further visits
There are no visits planned although you can consent to allowing us to contact you in the future to collect samples for further analysis of your illness.

8. Linkage to NHS records
We will link your study data with your NHS records to help assess, where possible, whether you actually had COVID-19. The data you provide to us is important and may be useful to other research studies. So that your data can be used anonymously for further research in the public interest, an NHS organisation will replace your identifying details with a unique anonymous code. This will enable your data to be linked to routinely-collected data, including your health records. The data can then be used for research in anonymous form in a secure environment.

9. Information to GP
A letter explaining the trial will be sent to your GP.

10. Do I need to collect any specimen?
No specimens need to be collected in this part of the study, but with your consent, we may contact you in the future to collect samples.

What are the possible benefits of taking part?

There are no direct benefits to you taking part in this study, but the results from this study might help to improve the healthcare of patients in the future. If you are in the intervention group, your symptoms may or may not get better quicker. If you are in the control group, you will be maintaining a diary, but not doing anything extra, over and above continuing to observe the UK Governments personal and household hygiene advice (https://www.nhs.uk/conditions/coronavirus-covid-19/self-isolation-advice/).

What are the possible disadvantages of taking part?

It is possible that you may be inconvenienced by having to maintain the diaries daily.
If you are in the intervention group, you will have to perform nasal washout and gargling around 6-12 times a day for the first 5 days and around 3-12 times a day until you are well or for a maximum of 14 days. This may or may not be convenient for you. Hypertonic saline solution has been used safely in other studies. In previous studies, a small

proportion of individuals have had side effects such as irritation/stinging in the nose and post-nasal drip (which makes you clear your throat or swallow often). However, most individuals did not think these were severe enough to stop them from performing the procedure. To reduce the chance of irritation/stinging in the nose you will be given instructions on how to choose the concentration of the solution that you find comfortable.

There is a remote possibility that hypertonic saline nasal washout and gargling increases spreading of the virus, which will be investigated by analysing the data for increase in illness amongst household contacts.

What if there are any problems?

If you have a concern about any aspect of this study, please contact the study team via email ELVIS-COVID19@ed.ac.uk who will do their best to answer your questions. Please note that this email inbox is monitored Monday-Friday during normal working hours. If you have an urgent query regarding the study, please contact Dr Sandeep Ramalingam who will do his best to answer your questions. Contact details for Dr Sandeep Ramalingam can be found at the end of this information sheet.

If your symptoms worsen significantly, please report this on your daily diary and a study clinician may contact you if deemed clinically necessary. If you want to seek medical help please use the NHS COVID-19 services - https://www.nhsinform.scot/illnesses-and-conditions/infections-and-poisoning/coronavirus-covid-19 in Scotland, https://www.nhs.uk/conditions/coronavirus-covid-19/ in England, https://111.wales.nhs.uk/coronavirus(2019ncov) in Wales and https://www.nidirect.gov.uk/campaigns/coronavirus-covid-19 in Northern Ireland and phone 111 or contact your GP. Always dial 999 in an emergency.

In the unlikely event that something goes wrong and you are harmed during the research and this is due to someone‘s negligence then you may have grounds for a legal action for compensation against NHS Lothian but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

What will happen if I don’t want to carry on with the study?

If you no longer want to take part, you can stop at any time. There is an option on the online diaries to let us know that you no longer want to take part and this will let us know not to contact you further. You will also be asked if it is ok for us to use any data you have given us up to the point when you stop your participation.

What happens when the study is finished?

At the end of the research we will analyse the data and publish the results. We will also publish a summary of the results online. This will give you the information that you may require if you wish to continue the performing the procedure once the trial is completed. The data generated from the study will be stored on a secure server. Anonymised data will be made available to accredited researchers for additional analyses.

Will my taking part be kept confidential?

All the information we collect during the course of the research will be kept confidential and there are strict laws which safeguard your privacy at every stage. We will inform your GP that you are taking part in this trial.

What will happen to the results of the study?

The study findings will be communicated to policymakers and will be written up and published in a journal. We will also upload a link to this article or provide a summary of the results on the study website.

Who is organising and funding the research?

This study has been organised by Professor Aziz Sheikh, an experienced clinical trialist and Director of the Usher Institute. The study is funded by BREATHE, a Health Data Research Hub for Respiratory Health.

Who has reviewed the study?

The East of Scotland Research Ethics Service REC 1, which has responsibility for scrutinising all proposals for medical research on humans, has examined the proposal and has raised no objections from the point of view of research ethics. It is a requirement that your records in this research, together with any relevant medical records, be made available for scrutiny by monitors from ACCORD, whose role is to check that research is properly conducted and the interests of those taking part are adequately protected.

Researcher Contact Details

If you have any further questions about the study please contact the study team through email: ELVIS-COVID19@ed.ac.uk or for urgent enquiries, please contact Dr Sandeep Ramalingam on Email: sandeep.ramalingam@nhslothian.scot.nhs.uk or Phone: 0131 242 6014.

Independent Contact Details

If you would like to discuss with someone independent of the study, please contact Dr. Ian Laurenson (Consultant Microbiologist, Head of Speciality, Department of Laboratory Medicine, Royal Infirmary of Edinburgh; ian.laurenson@nhslothian.scot.nhs.uk).

Complaints

If you wish to make a complaint about the study please contact:
NHS Lothian Complaints Team
Waverley Gate
2 – 4 Waterloo Place
Edinburgh
EH1 3EG
Telephone: 0131 536 3370;
Email: complaints.team@nhslothian.scot.nhs.uk.