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Participant Information Sheet and Consent Form

Nasal irrigation and gargling for suspected COVID-19: a pragmatic, web-based trial in Pakistan

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, but please bear in mind that you can only join this study within the first 5 days of your first symptom starting.

An NIHR Global Health Research Unit on Respiratory Health (RESPIRE) at the University of Edinburgh project.
www.ed.ac.uk/usher/respire

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Participant Information Sheet

Nasal irrigation and gargling for suspected COVID-19: A pragmatic, web-based trial in Pakistan

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.

This study is to find out if nasal washing and gargling with water helps individuals with COVID-19 get better faster. Some research from patients with the common cold has found that nasal washing and gargling with water may be helpful in reducing the length of the illness (the ELVIS Study http://www.elvisstudy.com/). However, we do not know if this same benefit is also seen in those with suspected or confirmed COVID-19. This study will help us find out if nasal washing and gargling with water are helpful in COVID-19.

The study will involve up to 405 randomly selected individuals who fulfil the criteria of having any of these symptoms:

Cough and shortness of breath; Fever; Muscle pain; Headache; Sore throat; New loss of taste or smell; Severe fatigue; Nausea or vomiting; Diarrhoea and Congestion or runny nose

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.

The study will involve up to 405 randomly selected individuals who fulfil the criteria of having any of these symptoms:

Cough and shortness of breath; Fever; Muscle pain; Headache; Sore throat; New loss of taste or smell; Severe fatigue; Nausea or vomiting; Diarrhoea and Congestion or runny nose

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 Pakistan
- You are 18 years old or over
- Your illness started within the last 5 days and you are self-isolating
- You are not pregnant
- You do not have a weakened immune system
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- 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 any other 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 Government of Pakistan's advice regarding personal and household hygiene, and you should not use nasal washing 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. However, performing of ablution (wuzoo) with clean water is recommended.

2. Consent

If you take part, you will be asked to complete an online consent form by answering a number of questions, including your name and email address. By submitting this online form, you will also certify that you understand that this is equivalent to signing a physical document. Your participation is voluntary, and you are free to withdraw from the study at any time. An investigator associated with this study will then verify the information you entered and certify electronically by clicking a checkbox that it is in order with respect to the approved research protocol. This will also be equivalent to the investigator signing on a physical document.

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. This allocation will be determined by the website in a totally random manner.

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 for 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 followed by a text message or a telephone call. 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. If you do not complete your

daily diary for 3 days, you will be sent a final warning on the 4th day, and then withdrawn from the study.

- **Personal and household hygiene:** Continue with Government of Pakistan's advised personal and household hygiene as recommended:
- http://covid.gov.pk/prevention.

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 using salt which will be provided to you, 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 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 medical records
In case you desire and give permission to share the details of this study or of the nasal washing with your physician or any other healthcare provider, please consent to this in the Consent Form at the end of this document. This will help your physician(s) to assess, where possible, whether you actually had COVID-19. The data you provide is important and may be useful to other research studies. To ensure that your data can be used anonymously (there will be no way to identify you) for further research in the public interest, the Principal Investigator, or his assigned representative, 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
In case you desire and give permission a letter explaining the trial will be sent to your treating physician.

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.

However, some of the patients who join this study, may be randomly selected for testing for SARS-CoV2 infection, which will be a swab sample from your nose and throat, at a local government approved laboratory near your home. If you consent to this, and are randomly selected for these procedures, then you will be provided with the names of the laboratories nearest to your home and an appointment will be scheduled for you to attend the laboratory to have the required test carried out. These tests will include a swab sample from your nose and throat. The cost for this testing will need to be paid up front by yourself. These costs will be reimbursed to you when you provide the results of the tests along with the original receipt of payment for these tests. You can send the test results and receipt of payment by post to the AAIP, Islamabad.

Is there anything I need to do or avoid?

There is no need to avoid anything or to take any special precautions for this study. You can continue any and all treatments being advised to you for the treatment of your illness.

If you are taking part in any other study involving any form of treatment or intervention for COVID-19 or any other illness, then you will not be eligible to take part in this study. You will have to state that you are not enrolled in any other study in the Consent Form.

What are the possible benefits of taking part?

Your taking part in this study will help us understand the benefits of nasal washing and gargling as a part of treatment for those with suspected or confirmed COVID-19 which may benefit patients suffering from similar illnesses in the future.

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 Government of Pakistan's personal and household hygiene advice: http://covid.gov.pk/prevention

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 info@nasalwash.pk or COVID19@allergypakistan.com 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 (name of Study Manager to

be inserted here) who will do his best to answer your questions. Contact details for Dr (name of Study Manager to be inserted here) 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 Government of Pakistan's COVID-19 services - https://doctors247.online/ or call the COVID-19 helpline on 1166.
In case of an emergency, dial 1122.

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 the AAIP but you may have to pay your legal costs. The normal provincial Health Service department's 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.

Will I be paid for this study?

Joining this study is purely voluntary, and you can leave it whenever you wish. You will be paid up to Rs 4,000 (four thousand rupees) for completing the entire study. In case you are selected for testing for SARS CoV-2, then the cost of the test and transport charges will be reimbursed to you, after providing original receipts to the AAIP. In case you do not fill the questionnaire for one day, you will be sent a reminder. You will receive more reminders on days 2 and 3 of missing the questionnaire. However, if there is no response from you after 4 days, your name will automatiocally be removed from the study, and you will no longer be eligible to receive any compensation, nor reimbursement of any costs which you incurred for tests (if applicable).

If you have been referred to join this study by a physician or other healthcare provider, he or she may received a compensation between Rs 500 to Rs 1,000, to ensure that you qualify to join the study and to follow-up to ensure proper completion of all the questionnaires.

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 this study will be stored in a secure server at the Allergy and Asthma Institute, Pakistan's head office in Islamabad. The data will be encrypted and have maximum security features.

After completion of this research, the data generated from the study, and sensitive identifier information such as name, age, gender, phone numbers, email and postal addresses etc. will be removed and the research data will be stored at the DataShare repository of the University of Edinburgh, Edinburgh, UK, for long term storage and retrieval. This de-identified data will be made available to only accredited researchers for additional analyses.

Will my taking part be kept confidential?

All the information we collect during the research will be kept confidential and there are strict laws which safeguard your privacy at every stage. If you desire, we will inform your physician (if you are under treatment) 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. This trial will be registered with Clinical Trials database of the US National Library of Medicine, at "www.clinicaltrials.gov".

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, University of Edinburgh, and is being carried out in Pakistan by Dr M Osman Yusuf, Chief Consultant at the Allergy and Asthma Institute, Pakistan. The study is funded by the National Institute of Health Research (NIHR), UK Government, through RESPIRE, University of Edinburgh, Edinburgh, UK.

Who has reviewed the study?

The study proposal has been reviewed by EMREC, the research ethics committee at the University of Edinburgh, Scotland. In Pakistan, Ethics approval for this study has been granted by the International Research Force, which is valid for the whole of Pakistan.

The Research Ethics Committees (REC), which have responsibility for scrutinising all proposals for medical research on humans, have 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 the RECs, 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: info@nasalwash.pk or COVID19@allergypakistan.com or for urgent enquiries, please contact Dr Osman Yusuf on Email: allergypk@yahoo.com or Phone: 0300 8561115.

Complaints

If you wish to make a complaint about the study, please contact:

The Chief Executive, Developing Health, 275, Gomal Road, Sector E-7, Islamabad, Pakistan. Tel 051-2654445. Email: complaints@dev-health.org.

Independent Contact Details

If you would like to discuss this study with someone independent of the study, please contact

Dr Shahida Ashraf, by email (shahida@asthmapakistan.com), or phone 0334-5505422.

Privacy Notice

The University of Edinburgh is the sponsor for this study based in the United Kingdom, but this study is being conducted in Pakistan. The Sponsor has overall responsibility for the running of the study. To follow the United Kingdom's data protection regulations, we must inform you of how we will use and store your personal data.

As a university, we use personally identifiable information to conduct research to improve health, care and services. As a publicly funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your data in the ways needed to conduct and analyse the research study.

We will use information from you and/or your medical records in order to undertake this study. The sponsor will keep identifiable information about you for 5 years after the study has finished.

The University of Edinburgh will act as the data controller for this study. This means that they are responsible for looking after your information and using it properly.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally identifiable information possible.

Non-identifiable data from this project may be stored in a research data repository at the University of Edinburgh to allow knowledge sharing and learnings about this study. The University of Edinburgh provides its researchers (and their collaborators) two services for sharing and archiving of data which will be used for your information. There is an open access repository for anonymised data, which means that all non-identifiable data is freely available. For sensitive information, a secure repository is used which can only be accessed by approved researchers who have undergone a rigorous application and review process.

Participant ID:		Centre ID (if applicable)	

ONLINE CONSENT FORM

Nasal irrigation and gargling for suspected COVID-19: A pragmatic, web-based trial in Pakistan

Please specify YES or NO

I confirm that I have read and understand the participant information sheet (HSNIG Patient Information Sheet (PIS) Version 2.0 dated 24 August 2021) for the above study and have understood its contents	YES	NO.
I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	YES	NO
I understand that relevant sections of my medical notes and data collected during the trial may be looked at by the trial researchers and individuals from the Sponsor, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	YES	NO
I agree to my treating physician being informed of my participation in this study (if required).	YES	NO
I give permission for the study researchers to contact me by email, phone or text message during the trial.	YES	NO
I agree to the study data being linked with my physician and hospital health records (if required / applicable).	YES	NO
I agree to my data being securely stored on The Allergy and Asthma, Pakistan, secure database, and de-identified coded data being shared with The University of Edinburgh, Edinburgh, UK, via a secure platform.	YES	NO
I understand that my personal data can be used in anonymous form for further research in the public interest.	YES	NO
I understand that I may be randomly selected for additional testing for SARS-CoV2 infection, which, if selected, will give me the opportunity to attend a local laboratory to complete these additional tests.	YES	NO
I consent to giving blood, nasal or nasopharyngeal swab, sputum, saliva or other samples for virus or antibody testing during the study, or at a later date, if required.	YES	NO
I affirm that I am not taking part or enrolled in any other clinical study or trial.	YES	NO
I agree to take part in the above study.	YES	NO

☐ I certify that all the information in the document above is correct. I understand that clicking 'Submit' electronically sign the form and that signing this form electronically is the equivalent of signing a physical document.

☐ **Investigator Counter Signature:** I as the investigator certify that I carefully checked all information submitted by the participant and it is in order with respect to the approved research protocol. I understand that clicking 'Submit' electronically sign the form and that signing this form electronically is the equivalent of signing a physical document.