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A long-term observational study evaluating the presentation and management of acute respiratory tract infections in primary care across Europe

Submission date
05/06/2023

Recruitment status
Recruiting

Registration date
20/07/2023

Overall study status
Ongoing

Last Edited
24/10/2024

Condition category
Respiratory

[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
Acute respiratory infection (ARI) is the commonest reason for consulting in community care. Furthermore, new and re-emerging pathogens are often first noticed in primary care (PC). The POS-ARI-PC study is a long-term study, with the aim of describing the nature of ARI in adults and children presenting to PC across Europe. The POS-ARI-PC study will provide critically important data on the presentation and management of ARI, and build a research-ready infrastructure for studies related to the treatment, diagnosis, and prevention of ARI in primary care settings.
POS-ARI-PC-001
This embedded study is appended to the POS-ARI-PC-Core Protocol with an SSA. This study is to estimate the overall incidences of medically-attended respiratory syncytial virus, human metapneumovirus, human parainfluenza virus and rhinovirus amongst older adults in Europe.

Who can participate?
Patients of any age group with an ARI.
POS-ARI-PC-001: Patients aged 60 years and over with an ARI

What does the study involve?
Participation in the study will last for 28 days. Once consented to the study, a member of the study team will complete a short questionnaire collecting the participants' names and contact information, some details about them, and the symptoms they have been experiencing. A combined throat/nose swab will be collected from the patient for study purposes.

Participants will also be asked to tell us about how they are feeling today and for the next 14 days via an online or paper daily diary. They might be telephoned to ask some questions if they are unable to complete the daily diary. Their GP will be contacted after day 28 to collect information about their consultations and hospital referrals in the 28-day period.

A small number of enrolled participants who consented (optional) to be contacted by the research team about the nested qualitative study will be invited for a process evaluation interview.

What are the possible benefits and risks of participating?
Participants may not personally benefit from taking part but will help researchers and doctors learn more about the presentation and treatment of people with respiratory infections. It is not anticipated that there are any risks involved in taking part in the study.

POS-ARI-PC-001
Same as POS-ARI-PC-Core study procedures. In addition, participants who indicated in their diary not feeling recovered from the RTI will be phoned on Day 28 (+/-7 days) using the Day 28 phone questionnaire, with the same questions as the Day 14 phone questionnaire.
A small number of enrolled participants who consented (optional) to be contacted by the research team about the nested qualitative study will be invited for a process evaluation interview.

Where is the study run from?
POS-ARI-PC AUDIT- The study is sponsored by the University Medical Center Utrecht (UMCU, Netherlands) and is managed and run by the University of Oxford (UK). The study is a European-wide study. In each country, there will be a coordinating centre which will run the study on behalf of UMCU.
POS-ARI-PC-Core - The study is sponsored by European Clinical Research Alliance on Infectious Diseases (Ecraid). The project is delivered in collaboration between the UMCU, the University of Oxford (UK), and the University of Antwerp (Belgium).

When is the study starting and how long is it expected to run for?
POS-ARI-PC AUDIT- November 2023 to February 2026.
POS-ARI-PC-Core: February 2024 to February 2026.

Who is funding the study?
POS-ARI-PC AUDIT and POS-ARI-PC CORE-The European Union’s Horizon 2020 Research and Innovation Programme (ECRAID-Base) grant agreement No. 965313
POS-ARI-PC-001
Subsidising Party: Sanofi Pasteur S.A

Who is the main contact?
Dr Nguyen Tran (Senior Project Manager), ecraid-base@phc.ox.ac.uk (UK)

Study website
https://www.ecraid.eu/

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
324504

ClinicalTrials.gov number
NCT06282718

Secondary identifying numbers
CPMS 55487, IRAS 324504

Study information

Scientific Title
Perpetual Observational Study of Acute Respiratory Infections in primary care settings (PC) across Europe (POS-ARI-PC)

Acronym
POS-ARI-PC

Study objectives
Continuous observation of early presentation of acute respiratory illness in the community will allow the early identification of potential infectious disease threats, descriptions of existing care on which to base interventions to eliminate unwarranted clinical variation, building prediction models, and will be a fundamental enabler of rapid response efforts to (potential) infectious disease threats.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 21/04/2023, East of England - Cambridgeshire and Hertfordshire Research Ethics Committee (Equinox House, City link , Nottingham, NG2 4LA, United Kingdom; +44 (0)20 7104 8096 ; cambsandherts.rec@hra.nhs.uk), ref: 23/EE/0050

Study design
Non-randomized prospective observational qualitative study design

Primary study design
Observational

Secondary study design
Non-randomised

Study setting(s)
GP practice, Home, Internet/virtual, Laboratory, Telephone

Study type(s)

Prevention

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Observation of early presentation and management of acute respiratory illness in the community

Interventions
Study design: We have developed two overarching protocols for the POS-ARI-PC. The POS-ARI-PC AUDIT protocol allows for a flexible annual anonymous prospective audit-type registration to describe the presentation and management of patients presenting in primary care with ARI. This provides the infrastructure for patient sampling and follow-up, and in which randomisation can be activated for platform trials to evaluate a range of interventions that can be added and replaced over time. This has resulted in the POS-ARI-PC CORE protocol.
POS-ARI-PC AUDIT will be delivered through a prospective, multi-country, audit-type anonymous registration of presentation and management of approximately 2,000 patients presenting to PC annually across Europe. This audit will benchmark the case mix and care of patients consulting in PC. These can include general practice, urgent care centres, accident and emergency and other acute services in hospitals, for adult and paediatric patients, both in and out of office hours.
POS-ARI-PC CORE has the following three objectives:
Objective 1. A prospective, observational study of ARI patients in primary care to undergo study-specific sampling upon inclusion and be followed up for 28 days to capture the aetiology of their ARI and describe clinical outcomes.
Objective 2. A qualitative study with research professionals, clinicians, and patients to a) gain a deep understanding of the research process, and the meaning of results and to identify barriers and opportunities for implementation of changes considering findings, and b) explore the views and experiences of patients who consult European primary care services for ARI symptoms since the COVID-19 pandemic.
Objectives 3. To ensure research readiness for including embedded observational and randomised evaluations to answer questions about the effectiveness of diagnostic, behavioural or therapeutic management strategies for ARI in PC. When a new embedded observational study or RCT is added to the POS-ARI-PC a study-specific appendix (SSA) or an intervention-specific appendix (ISA) will be developed which details the (changes in) the study population, the research question, objectives, outcomes, study-specific processes and analysis. This will be appended to the POS-ARI-PC CORE Protocol and all appropriate approvals will be gained for each SSA or ISA.
Study participants: Patients presenting in PC, with symptoms suggestive of a lower respiratory tract infection (predominant symptom: cough, with a duration of fewer than 28 days); and/or symptoms suggestive of an upper respiratory tract infection (predominant symptom: sore throat and/or coryza, with a duration of fewer than 14 days); and/or patients with suspected of COVID-19, Influenza, RSV.
For POS-ARI-PC AUDIT: Potential patients will be identified when they present to their participating PC healthcare facility with symptoms suggestive of an ARI (see eligibility criteria). Any patients consulting with participating clinicians that meet the inclusion/exclusion criteria can be registered. This is an audit, that will generate aggregated, personally non-identifiable data about routine care, without intervention, no follow-up, and no linked data collection. Therefore, individual consent will not be required. We will record only age and sex. Names, dates of birth, address, or any other personally identifiable data will not be recorded.
For POS-ARI-PC CORE: Potential participants will be referred for eligibility assessment and

potential trial entry as soon as possible. They will consult with a responsible clinician or appropriately trained delegate, where they will have the trial presented to them and be screened to confirm whether they meet the eligibility criteria. If eligible and willing, they will be recruited into the trial. Where possible, eligibility assessment for any embedded studies will be conducted at the same time as the initial eligibility assessment for the core POS-ARI-PC study.
Informed Consent (POS-ARI-PC CORE only)
Participants will be provided with a participant information leaflet and a member of the clinical team will discuss what the trial involves with them. Participants will be given time to think about whether they would like to take part in the study, and they will be able to ring friends or family members if they wish to discuss taking part. If the participant agrees to take part, they will then be asked to complete a consent form. Instructions on how to fill out the form will be provided. An optional consent question will be included on whether they would like to be contacted by the research team to be invited to a qualitative study interview.
For the nested qualitative study, a participant information leaflet will be provided, and verbal consent will then be sought from the study participants who are invited for an interview. Healthcare workers and network coordinators will also be given a participant information leaflet and will provide verbal consent prior to participating in the nested qualitative study interviews.
Initial Questionnaire
A member of the clinical team will complete a short web-based questionnaire including some details about the participant and their symptoms. We will also collect some contact details such as name, email address and telephone number so that the trial team can contact the participant and ask them questions about their recovery.
Sample
A combined throat/nose swab will be collected from participants for study purposes. The swab will be sent to a local laboratory where it will be frozen, it will then be transported to the central laboratory in Antwerp for analysis later. The participant will not receive the results of this swab.
Follow-Up
The study team will give the participant a paper diary or link to an online diary, as they prefer. The study team will explain how to complete the diary and answer any questions. Participants will be asked to complete the diary for 14 days starting on the day they consulted with their doctor about ARI. It should take no more than five minutes to complete the diary each day. The diary will include questions about illness, symptoms, and recovery. If the participant has completed a paper diary then they will be provided with a stamped addressed envelope to return it to the study team once completed. This data will then be entered into an online database by the study team. If the participant completes their diary online this will automatically be entered into the online database each day.
If the study team has not received the participant's diary after 14 days, they will contact the participant by phone to ask you a brief set of questions at some point in the next 10 days. The telephone call will last no more than five minutes. On or after day 28 network coordinating team will ask the participant's GP to access the medical records to collect information about additional GP consultations for ARI and whether the participant was hospitalized.

(added 28/02/2024)
POS-ARI-PC-001:
The first embedded study, POS-ARI-PC-001, will be conducted as a prospective observational study to estimat e the incidence of medically-at tended RSV, HMPV, HPIV and RV infections in an elderly population. This embedded study is appended to t he POS-ARI-PC CORE Protocol as a study specific appendix (SSA).
Study Procedures:
As detailed in POS-ARI-PC Core protocol.
In addition, the EQ-5D will be added to the diary: the complete EQ-5D on Day 7 and 14, and the VAS daily.

As outlined in the Core protocol, participants who have not returned their diary will be phoned at Day 14 (+7 days) t o capt ure a minimal outcome set (Day 14 phone questionnaire with complet e EQ-5D added). In addition, participants who indicated in their diary not feeling recovered from the RTI will be phoned at Day 28 (+/-7 days) using the Day 28 phone questionnaire, with the same questions as the Day 14 phone questionnaire.

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
Feedback on details of treatment practices and trends across networks linked to patient outcomes:
1. Age bands, the proportion with a preliminary diagnosis of various sub-categories of ARI (e.g. LRTI, URTI), and overall illness severity rating measured using an online CRF at the baseline visit
2. ARI diagnosis measured using retrospective viral/microbiological infection analysis (multiplex PCR) of swab samples taken at the baseline visit
3. Proportion undergoing POC (with results) and lab-based investigations measured using an online CRF at baseline visit and Day 28
4. Proportion given treatment and class of drug treatment for ARI measured using an online CRF at baseline visit and Day 28
5. Details of prescriptions given on presentation of ARI measured using an online CRF at baseline visit
6. Details of tests ordered on presentation of ARI measured at baseline visit using an online CRF
7. Return to usual daily activities, feeling recovered from RTI, use of prescription medication, complications, use of over-the-counter medications measured using an online CRF at the baseline visit, on Day 1-14 using a diary or on Day 14 using a telephone call, and Day 28 using an online CRF
8. Complications reported associated with ARI presentation measured using an online CRF at the baseline visit, on Day 1-14 using a diary or on Day 14 using a telephone call, and on Day 28 using an online CRF
9. Variation in practice and advice from national guidelines, to be fed back to national teams, measured using an online CRF at baseline visit and Day 28

Secondary outcome measures
1. Recommendations on how to improve study processes, recruitment and study communication based on shared understanding and insights from researchers, clinicians, and patients, measured using an interview conducted by the social science team after taking part in the main study and using a descriptive analysis at the end of the study
2. An understanding of the meaning of study results for European primary care, from the perspectives of clinicians and patients, and recommendations regarding the implementation of findings, measured using an interview conducted by the social science team after taking part in the main study and using a descriptive analysis at the end of the study
3. An understanding of changing health-seeking behaviour, management and expectations to inform clinical studies and trials, measured using an interview conducted by the social science team after taking part in the main study and using a descriptive analysis at the end of the study
4. Approval for a study-specific appendix (SSA) or an intervention-specific appendix (ISA) of an

embedded (non) randomised study for ARI in primary care associated with this POS, measured using the number of embedded studies to this POS-ARI-PC platform over the whole duration of the study

Overall study start date
01/03/2021

Completion date
01/03/2026

Eligibility

Key inclusion criteria
Eligible patients will be of any age consulting (telephone, video, face to face) with a participating primary health care facility with:
1. Symptoms suggestive of an acute lower respiratory infection with cough as the predominant symptom, with illness duration less than 28 days,
AND/OR
2. Symptoms suggestive of an acute upper respiratory infection with a sore throat and/or coryza as the predominant symptom, with illness duration of less than 14 days
AND/OR
3. Other symptoms suggestive of COVID-19, Influenza, RSV
4. Participant or legal guardian(s) willing and able to provide informed consent and comply with study procedures

Added 28/02/2024:
POS-ARI-PC-001 Study:
1. Eligible patients will be 60 years of age and over consulting (telephone, video, or face-to-face in the practice, or home visit) with a participating primary health care facility with:
1.1. Symptoms suggestive of an acute lower RTI with new or increased cough as the predominant symptom, with illness duration <=7 days; AND/OR
1.2. Symptoms suggestive of an acute upper RTI with sore throat and/or coryza as the predominant symptoms, with illness duration <=7 days; AND
1.3. Willing and able to provide informed consent and have a swab taken

Updated 24/10/2024:
POS-ARI-PC-001 Study:
Symptoms and Duration:
Symptoms suggestive of an acute lower RTI with new or increased cough as the predominant symptom, with illness duration ≤10 days
AND/OR
Symptoms suggestive of an acute upper RTI with sore throat and/or coryza as the predominant symptom, with illness duration ≤10 days

Age:
Aged 60 years and over
OR
Aged 50 to 59 years and have a long-term health condition which makes them eligible for the yearly influenza vaccination under the national influenza vaccination programme

Consent:
Willing and able to provide informed consent and have a swab taken

Participant type(s)
Patient

Age group
All

Sex
Both

Target number of participants
Total UK sample size: 400 Total international sample size (including UK): 8000. Further details: For POS-ARI-PC AUDIT (prospective, multi-country, audit-type anonymous registration): Total of approx. 8000 participants across 5-20 European countries. For POS-ARI-PC CORE (Objective 1): Total of 2000 participants across all participating European countries. Total UK recruitment: 400

Key exclusion criteria
Patients will not be eligible if:
1. According to the judgement of the recruiting clinician, they will not be able to comply with study procedures, for example, because they do not understand the language in which the study is being conducted locally (and have no one to help and translate for them); have a serious psychiatric disorder; or are terminally ill
2. Symptoms of presumed non-infective origin
3. Participant requires admission to the hospital on the day of inclusion. Additional in/exclusion criteria might apply to embedded studies and will be described in the SSA or ISA

(added 28/02/2024)
POS-ARI-PC-001 Study
As per the POS-ARI-PC CORE Protocol, with one exception: patients needing hospitalisation can be recruited into the study if timing allows. Patients can provide a swab and decide not to participate in the follow-up procedures.

Date of first enrolment
19/02/2024

Date of final enrolment
01/03/2026

Locations

Countries of recruitment
England

United Kingdom

Study participating centre

NIHR CRN: Thames Valley and South Midlands
John Radcliffe Hospital
Headley Way
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United Kingdom
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Sponsor information

Organisation
European Clinical Research Alliance for Infectious Diseases (Ecraid)

Sponsor details
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Sponsor type
Hospital/treatment centre

Website
https://www.ecraid.eu/

Funder(s)

Funder type
Government

Funder Name
European Commission

Alternative Name(s)
European Union, Comisión Europea, Europäische Kommission, EU-Kommissionen, Euroopa Komisjoni, Ευρωπαϊκής Επιτροπής, Европейската комисия, Evropské komise, Commission européenne, Choimisiúin Eorpaigh, Europskoj komisiji, Commissione europea, La Commissione

europea, Eiropas Komisiju, Europos Komisijos, Európai Bizottságról, Europese Commissie, Komisja Europejska, Comissão Europeia, Comisia Europeană, Európskej komisii, Evropski komisiji, Euroopan komission, Europeiska kommissionen, EC, EU

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Publication and dissemination plan
Study results will be disseminated in compliance with ECRAID-Base publication policy, via manuscripts in peer-reviewed open-access scientific journals, conference abstracts, posters and /or oral presentations.

Intention to publish date
31/12/2027

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publicly available ECRAID-Base Central Data Repository.

ECRAID-Base Central Data Repository (CDR) will be set up and used to store the pseudonymised data collected from POS-ARI-PC sites via the CASTOR electronic case report forms(eCRFs) and sample related data from University of Antwerp laboratory of Medical Microbiology's System ClinSLIMS. Pseudonymised data will be stored in the ECRAID-Base CDR for a maximum of 25 years. Data in the ECRAID-Base-CDR is directly accessible by the business intelligence tool Microsoft Power BI.

Reports and visualisations related to study and network data will be created and made available to authorised users such as the Sponsor, POS-ARI-PC project managers, and study monitors. Participant-level pseudonymised data in the CDR will be made available to members of the ECRAID-Base Consortium using the Digital Research Environment (DRE) which is a safe, secure and GDPR-compliant research platform. Data can be analysed in the DRE using R, SAS, or SPSS or can be downloaded to a researcher's own environment after a download request approval. Those outside of the ECRAID-Base Consortium will have access to pseudonymised data (access and governance mechanisms for this have not yet been decided). Participants in POS-ARI-PC provide informed consent allowing their pseudonymised data to be stored in the CDR for 25 years, pseudonymised data to be shared for future health, medical or biomedical research within the ECRAID-Base Consortium, and with those outside the Consortium. In the future, data will also be made available in a publicly available repository, however, the details of which repository etc. have not yet been decided.

IPD sharing plan summary
Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	ECRAID-Base POS-ARI-PC version 3.0	05/05/2023	27/06/2023	No	Yes
Protocol file	ECRAID-Base POS-ARI-PC version 2.0	05/04/2023	27/06/2023	No	No
Protocol file	ECRAID-Base POS-ARI-PC version 2.0	05/04/2023	27/06/2023	No	No
HRA research summary			20/09/2023	No	No
Other files	Study specific appendix 1 version 1.0	22/11/2023	28/02/2024	No	No
Protocol file	version 4.0	17/01/2024	28/02/2024	No	No