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Real-world effectiveness of the Oxford /AstraZeneca COVID-19 vaccine in England

Submission date	Recruitment status	[_] Prospectively registered
22/06/2021	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
24/08/2021	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
19/04/2022	Infections and Infestations	[_] Record updated in last year

Plain English summary of protocol

Background and study aims
The Oxford/Astrazeneca COVID-19 vaccine has shown to be highly effective in studies before it used widely. This study aims to find the effectiveness of the vaccine in England.
The UK has been one of the most significantly affected countries, with over four million cases and over 150,000 deaths at the time of writing. Vaccines against COVID-19 are an important measure in reducing the ongoing spread and severity of the disease in England. The Oxford /Astrazeneca vaccine against COVID-19 has been widely used but limited data exists on its real-world effectiveness, particularly amongst different age groups. Also the impact of a single dose compared to two doses and the time interval between each dose will be studied.

Who can participate?
Data used for the study will include all the individuals in England.

What does the study involve?
During the study GP data will be combined with hospital data to get an understanding of hospitalisations and deaths due to COVID-19 in people who have received the Oxford /Astrazeneca vaccine compared to those who have not received the Oxford/Astrazeneca vaccine.

What are the possible benefits and risks of participating?
The results of the study will give a better understanding about how to administer the vaccine in the English population in the future.

Where is the study run from?
Nuffield Department of Primary Health Care Sciences of the University of Oxford (UK)

When is the study starting and how long is it expected to run for?
January 2021 to November 2022

Who is funding the study?
AstraZeneca (UK)

Who is the main contact?
Prof Simon de Lusignan, simon.delusignan@phc.ox.ac.uk

Study website
http://orchid.phc.ox.ac.uk/index.php/raven

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
300259

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
D8111R00007, IRAS 300259

Study information

Scientific Title
Real-world effectiveness of the Oxford/AstraZeneca COVID-19 vaccine in England: an observational retrospective cohort study using secondary databases to establish the effectiveness of the Oxford/AstraZeneca COVID-19 vaccine in England

Acronym
RAVEN

Study objectives
AZD1222 has been shown to be highly efficacious in pivotal randomized clinical trials (RCT), demonstrating 82% overall efficacy against symptomatic infection and 100% efficacy against severe infection. Recent unpublished data from the phase 3 pivotal trial in the US showed high efficacy (85%) in people 65 years of age or older, and again confirmed 100% efficacy in preventing severe cases. Although a high level of single-dose efficacy has been demonstrated in clinical trials between 3 and 12 weeks and confirmed in early effectiveness studies conducted in the UK, clinical trials and effectiveness study so far have not included detailed vaccine-specific analysis by age group, co-morbidities, nor have they assessed vaccine impact on critical care admission, mortality, and overall outcomes. Thus, it remains important to better understand vaccine effectiveness by ages, time intervals between doses, and also to determine if single-dose effectiveness may extend beyond 12 weeks. It's also important to assess vaccine effectiveness by age groups and comorbidities for best guidance for COVID-19 immunization programs.

The UK is one of the first countries that are introducing mass vaccination campaign for COVID-19 and is currently vaccinating the elderly population starting from the oldest age groups (JCVI advice 2020). Three COVID-19 vaccines were licensed and are being used including the Moderna, the BioNTech/Pfizer, and the Oxford/AstraZeneca vaccines. Vaccination with the BioNTech /Pfizer vaccine started in December 2020 and with the Oxford/AstraZeneca vaccine started in early January 2021. This study is to primarily assess the effectiveness of the Oxford/AstraZeneca COVID-19 vaccine. Given the known high efficacy of the Pfizer vaccine in RCT and RWE studies, the study is also to evaluate the Pfizer vaccine effectiveness as a validation of the study's methods.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 23/05/2021, London - Bromley Research Ethics Committee (Temple Quay House, 2 The Square, Temple Quay, Bristol, BS1 6PN, UK; +44 (0)207 104 8000; bromley.rec@hra.nhs.uk), ref: 21/HRA/1971

Study design
Observational retrospective cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Other

Study type(s)
Prevention

Participant information sheet
No participant information sheet available (retrospective study)

Health condition(s) or problem(s) studied
COVID-19 (SARS-CoV-2 infection)

Interventions
This is a retrospective cohort study using linked secondary databases in England accessed through the NHS Digital Trusted Research Environment (TRE). The primary care data will be linked with vaccination, hospitalization, COVID-19 test results, mortality data at the national level for the capture of key study variables. Individuals of all ages will be included. People in the vaccinated arm will be compared with two comparator cohorts:

a) The concurrent control arm (primary): People not vaccinated with any COVID-19 vaccine from January 2021 onward (for the Oxford/AstraZeneca arm) or from December 2020 onward (for the Pfizer arm)
b) The historical control arm (secondary): People during the period from July-December 2020 for primary outcomes or from March-December 2020 for secondary outcomes, before the COVID-19 vaccine was available in England

Only the first outcome event, i.e. hospitalization, ICU admission will be considered in the analysis.

Intervention Type
Biological/Vaccine

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Oxford/AstraZeneca COVID-19 vaccine

Primary outcome measure
Measured using linked secondary databases in England accessed through the NHS Digital Trusted Research Environment (TRE) at a single time point:
1. Rate of hospitalizations associated with COVID-19
2. Rate of admission to ICU associated with COVID-19
3. Rate of mortality associated with COVID-19

Secondary outcome measures
Measured using linked secondary databases in England accessed through the NHS Digital Trusted Research Environment (TRE) at a single time point:
1. Rate of any hospitalizations
2. Rate of any admission to ICU
3. Overall mortality rate

Overall study start date
01/01/2021

Completion date
30/11/2022

Eligibility

Key inclusion criteria
1. People in England who have received at least one dose of the Oxford/AstraZeneca COVID-19 vaccine (the AstraZeneca vaccine arm) or at least one dose of the Pfizer COVID-19 vaccine (the Pfizer vaccine arm)
2. People in England who were not vaccinated with any COVID-19 vaccine during the same time period (concurrent control arm) or during March-December 2020 (historical control arm) who were matched to the vaccinated individuals by age, gender, region, and comorbidity
3. All ages

Participant type(s)
All

Age group
All

Sex
Both

Target number of participants
All patients in England who are present in the integrated health records of NHS Digital TRE and /or Oxford Royal College of General Practitioners Clinical Informatics Digital Hub (ORCHID) database at the start of study period.

Key exclusion criteria
Primary analysis: People with a history of COVID-19 infection (confirmed by RT-PCR or not) prior to vaccination. This group of people is not excluded in the sensitivity analysis.

Date of first enrolment
01/05/2021

Date of final enrolment
30/08/2022

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Oxford
University Offices
The Chancellor, Masters and Scholars of the University of Oxford
Wellington Square
Oxford

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OX1 2JD

Sponsor information

Organisation
AstraZeneca (United States)

Sponsor details
Biopharmaceutical Medicine, Respiratory and Inflammation
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20878
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Sponsor type
Industry

Website
http://www.astrazeneca-us.com/home/

ROR
https://ror.org/043cec594

Funder(s)

Funder type
Industry

Funder Name
AstraZeneca

Alternative Name(s)
AstraZeneca PLC, Pearl Therapeutics

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location

United Kingdom

Results and Publications

Publication and dissemination plan
We anticipate to disseminate the study findings to the public in the format of abstract /poster / presentation at congresses, peer-reviewed scientific manuscripts, and press releases as appropriate. Results will also be shared with relevant public health bodies such as JCVI/PHE.

Intention to publish date
01/06/2023

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available. The participant level data will be securely hosted within the NHS Digital Trusted Research Environment. The data cannot be shared according to the data sharing agreement between NHS Digital and University of Oxford. Researchers interested in the participant data can obtain the data from NHS digital using their Data Access Request Service.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No