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

RAVEN study

(An observational retrospective cohort study using secondary databases to establish effectiveness of the Oxford/AstraZeneca COVID-19 vaccine in England)

Study dates: Start of data collection: 23 AUG 2021
End of data collection: 15 DEC 2022

Phase of development: Phase IV; Post Authorisation Safety Study

Principle Investigator:

PPD

Sponsor's Responsible Officer:

PPD

This study was performed in compliance with Good Clinical Practice, including the archiving of essential documents.

This submission /document contains trade secrets and confidential commercial information, disclosure of which is prohibited without providing advance notice to AstraZeneca and opportunity to object.

Publications

None at the time of writing this report.

Rationale and background

With the introduction into clinical practice of efficacious COVID-19 vaccines such as the Oxford/AstraZeneca COVID-19 vaccine (hereafter the AstraZeneca COVID-19 vaccine), it is important to assess the effectiveness of the vaccine in a real-world setting from a national perspective. The study sought to ascertain vaccine effectiveness against severe COVID-19 outcomes in England, with the aim to offer guidance for COVID-19 immunisation programs.

Research questions and objectives

The study's primary objective was to assess the overall effectiveness of at least one dose of the AstraZeneca COVID-19 vaccine by number of doses, by age groups, by comorbidity status (for comorbidities that are known to be associated with more severe COVID-19 infection and/or suboptimal response to the vaccine), by time periods after each dose and by interval between the doses.

The secondary objective was to assess the overall effectiveness of at least one dose of other COVID-19 vaccines, by number of doses, by age group, by comorbidity status, by time periods after each dose and by interval between doses. For this objective, the Pfizer COVID-19 vaccine was used to represent 'other' COVID-19 vaccines in use in England. This objective was intended purely as a validation of the methods used to evaluate vaccine effectiveness (VE).

All the above objectives were assessed against the outcome measures of hospitalisation associated with COVID-19, Intensive Care Unit (ICU) admissions associated with COVID-19, and mortality associated with COVID-19 as well as all-cause hospitalisation, ICU admissions and death. Note: outcomes were defined based on COVID-19 being the primary reason for admission in COVID-19 hospitalisations and ICU admissions, and COVID-19 as the underlying cause of death for COVID-19 mortality.

Study design

The objectives were addressed through a retrospective cohort study using linked primary care and secondary care electronic health record (EHR) data, and national COVID-19 datasets in England. Persons vaccinated with AstraZeneca COVID-19 vaccine or 'Other' (Pfizer) COVID-

19 vaccine were compared to matched persons not vaccinated with any COVID-19 vaccine for occurrence of study outcomes from initial roll-out of COVID-19 vaccines in England through 31 December 2021.

Setting

The study dataset was from England, UK.

Subjects and study size

The population for this study were individuals in England who had received at least one dose of the AstraZeneca COVID-19 vaccine from January 2021 onwards or at least one dose of 'other' COVID-19 vaccine from December 2020 onwards and individuals in England who were not vaccinated with any COVID-19 vaccine at the time of matching to an individual vaccinated with AstraZeneca or 'other' COVID-19 vaccine. Individuals were matched 1:1 using age group in years (16-24, 25-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84 and 85+), gender, National Health Service (NHS) region, and quartile of the Cambridge Multimorbidity Score. Any individuals who were subsequently vaccinated were censored at date of vaccination and were then eligible to re-enter the study as newly vaccinated individuals. Similarly, vaccinated individuals in the dose 1 cohort were censored at the date they received their second vaccine dose and were eligible to re-enter the study in the dose 2 cohort.

Variables and data sources

The main exposures in this study were (a) whether an individual was vaccinated with one or two doses of the AstraZeneca COVID-19 vaccine or (b) one or two doses of the 'other' COVID-19 vaccine.

The primary outcomes of this study were COVID-19 related hospitalisation, COVID-19 related ICU admission and COVID-19 related death. The secondary outcomes of this study were all-cause hospitalisation, all-cause ICU admission and all-cause mortality.

Data sources were: primary care EHR data curated within the Oxford-Royal College of General Practitioners' Clinical Informatics Digital Hub (ORCHID) dataset and NHS Digital data including secondary care EHR data and national COVID-19 datasets (National Immunisation Management System [NIMS]), Hospital Episode Statistics [HES], Office for National Statistics [ONS] Civil Registration of Deaths, COVID-19 Second Generation Surveillance System (SGSS), COVID-19 UK Non-hospital Antigen Testing Results including National Pathology Exchange (NPEx)).

Summary of results

The final matched-analysis cohorts included: 2,832,126 individuals vaccinated with one dose of AstraZeneca COVID-19 vaccine, 2,765,609 individuals vaccinated with one dose of the 'Other' COVID-19 vaccine, 4,515,315 individuals vaccinated with two doses of AstraZeneca COVID-19 vaccine and 3,554,893 individuals vaccinated with two doses of then 'Other' COVID-19 vaccine. All vaccinated individuals were matched 1:1 to an unvaccinated individual.

During 2021, where circulating SARS-CoV-2 variants included Alpha, Delta and Omicron, overall vaccine effectiveness with one dose of the AstraZeneca COVID-19 vaccine ranged from 71.5 - 81.2% for severe COVID-19 outcomes, including hospitalisation, ICU admission and death. The overall vaccine effectiveness with two doses of the AstraZeneca COVID-19 vaccine increased to 84.1 - 90.7% for the three severe disease outcomes.

During the same year, the overall vaccine effectiveness of the 'Other' COVID-19 vaccine against severe disease outcomes ranged from 79.8 - 85.6% with 1 dose and from 89.7- 95.0% with two doses. These estimates only reflect effectiveness in the populations that received one, or two doses of the AstraZeneca and 'Other' COVID-19 vaccines.

The characteristics of the AstraZeneca and the 'Other' vaccinated populations are different, specifically with respect to clinical and demographic characteristics known to influence response to vaccination (e.g. age and calendar time of vaccination). For both vaccines, effectiveness was impacted by age, co-morbidity score, frailty score, and time since vaccination. The age distribution of the AstraZeneca and the 'Other' COVID-19 vaccine cohorts were different. The AstraZeneca COVID-19 vaccine cohort mean age was 51.8 and 56.5 years old for dose 1 and dose 2 cohorts, respectively; and the 'Other' COVID-19 vaccine cohort mean age was 41.4 and 49.7 years old for dose 1 and dose 2 cohorts, respectively. Although in England the AstraZeneca COVID-19 vaccine was first rolled out on 04 January 2021, almost a month after the 'Other' (Pfizer) COVID-19 vaccine was rolled-out on 08 December 2020, the age difference of these two cohorts can partially be explained by the younger populations being preferentially vaccinated with the 'Other' COVID-19 vaccine which was available later to the younger population compared to the AstraZeneca COVID-19 vaccine which was predominantly administered to the older population. In addition, the mean follow-up times were different between the two vaccines cohorts: 44.6 days since vaccination with one dose and 156.5 days with two doses for the AstraZeneca COVID-19 vaccine and 42.3 days since vaccination for one dose and 130.8 days for two doses for the 'Other' COVID-19 vaccine. Hence, the AstraZeneca COVID-19 vaccine cohort was followed-up for an additional month compared to the 'Other' COVID-19 vaccine cohort. It has been shown in previously published literature that vaccine effectiveness wanes over time, therefore the vaccine effectiveness results of the AstraZeneca COVID-19 vaccine are impacted by this extra month of follow-up. Altogether, this informs that

the effectiveness results for AstraZeneca and the 'Other' COVID-19 vaccines should not be interpreted as direct comparisons.

Conclusion(s)

Our study confirms the real-world overall vaccine effectiveness against severe disease outcomes from SARS-CoV-2 infection including hospitalisation, ICU admission and death for the AstraZeneca COVID-19 vaccine as a primary series. Estimates of effectiveness of the AstraZeneca COVID-19 vaccine in RAVEN are consistent with the literature. Estimates for the 'Other' COVID-19 vaccine effectiveness are also consistent with those from other real-world studies, and therefore confirms the validity of the RAVEN data sources and methods for evaluating vaccine effectiveness.

We also present data on vaccine effectiveness by number of doses, by age groups, by comorbidity status, by time since each dose and by interval between the doses to guide vaccination policy and implementation of COVID-19 immunisation programs.