

SYNOPSIS

03/16/2021

Review of articles on BNT162b2 and ChAdOx1nCoV-19 COVID-19 vaccine effectiveness

Article citations:

Hyams C, Marlow R, Maseko Z, King J, Ward L, Fox K, et al. Assessing the effectiveness of BNT162b2 and ChAdOx1nCoV-19 COVID-19 vaccination in prevention of hospitalisations in elderly and frail adults: a single centre test negative case-control study. SSRN 3796835 [Preprint]. 2021 Mar 03 [cited 2021 Mar 16]. Available from: <https://doi.org/10.2139/ssrn.3796835>

Lopez Bernal J, Andrews N, Gower C, Stowe J, Robertson C, Tessier E, et al. Early effectiveness of COVID-19 vaccination with BNT162b2 mRNA vaccine and ChAdOx1 adenovirus vector vaccine on symptomatic disease, hospitalisations and mortality in older adults in England. medRxiv 21252652 [Preprint]. 2021 Mar 02 [cited 2021 Mar 16]. Available from: <https://doi.org/10.1101/2021.03.01.21252652>

One-minute summary

- **Background:** The United Kingdom (UK) Coronavirus Disease 2019 (COVID-19) vaccination programme started on December 8, 2020 with the BNT162b2 vaccine (Pfizer-BioNtech, mRNA vaccine), and prioritized vaccination of vulnerable groups, including the elderly. The ChAdOx1 vaccine (AstraZeneca, adenoviral vector vaccine) was added to the programme on January 4, 2021, although there was a small number of participants > 65 years old in the clinical trials. Soon after vaccine programme implementation, a new variant of concern (VOC) called VOC 202012/01 or B.1.1.7 was identified in the UK. This VOC was found to have increased transmissibility and mutations to the spike protein, which is the target of the BNT162b2 and ChAdOx1 vaccines. In response to evolving evidence on vaccine effectiveness and increasing incidence of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the UK Joint Committee on Vaccination and Immunisation (JCVI) advised that the dose interval for the BNT162b2 and ChAdOx1 vaccines could be extended up to 12 weeks, allowing more people to receive a first dose of a vaccine. The real-world data on vaccine effectiveness of one dose of BNT162b2 or ChAdOx1 vaccine on symptomatic COVID-19 disease, disease severity and hospitalizations in the elderly is needed to inform the COVID-19 vaccine strategy currently utilized in the UK and is actively being assessed for implementation in other jurisdictions.
- Hyams et al. report vaccine effectiveness of one dose of BNT162b2 or ChAdOx1 vaccine against **hospitalization of adults aged ≥80 years with comorbidities:**
 - **BNT162b2:** 18/135 (13.3%) cases with SARS-CoV-2 infection and 90/269 (33.5%) controls negative for SARS-CoV-2 received one dose, resulting in an unadjusted one-dose vaccine effectiveness of 69.4% (95% confidence interval [CI]: 47.7-82.9) and an

adjusted one-dose vaccine effectiveness of 71.4% (95% CI: 43.1-86.2) against COVID-19-associated hospitalization occurring ≥ 14 days after receipt of first dose. When the analysis was restricted to the time period covered by the ChAdOx1 analysis, the adjusted one-dose vaccine effectiveness was 79.3% (95% CI: 47.0-92.5)($p=0.0014$).

- **ChAdOx1:** 9/36 (25%) cases with SARS-CoV-2 infection and 53/90 (58.9%) controls received one dose, resulting in an unadjusted one-dose vaccine effectiveness of 76.7% (95% CI: 46.5-90.6) and an adjusted one-dose vaccine effectiveness of 80.4% (95% CI: 36.4-94.5) against COVID-19-associated hospitalization occurring ≥ 14 days after receipt of first dose.
- **One dose of either BTN162b2 or ChAdOx1 vaccine reduces the risk of COVID-19-related hospitalization in the frail elderly with co-morbidities ≥ 80 years.**
- Lopez Bernal et al. report vaccine effectiveness with one or two doses of BTN162b2 or ChAdOx1 vaccine against **symptomatic lab-confirmed COVID-19 disease** in adults aged ≥ 70 years:
 - **Adults aged ≥ 80 years, pre-January 4, 2021** (relative to the higher baseline post-vaccination period seen in vaccinated individuals)
 - **BNT162b2:** Vaccine effectiveness was 70% (95% CI: 59-78%) and odds ratio (OR) for testing positive for COVID-19 disease was 0.30 (95% CI: 0.22-0.41) from days 28-34 after vaccination with a single dose, and then remained stable. Vaccine effectiveness was 89% (95% CI: 85-93%) and the OR for testing positive was 0.11 (95% CI: 0.07-0.15) from 14 days after the second dose.
 - **Adults aged ≥ 70 years, January 4, 2021 onwards**
 - **BNT162b2:** One-dose vaccine effectiveness reached 61% (95% CI: 51-69%) and the adjusted OR for testing positive for COVID-19 disease was 0.39 (95% CI: 0.31-0.49) from days 28-34 after vaccination, and then remained stable.
 - **ChAdOx1:** One-dose vaccine effectiveness reached 60% (95%CI: 41-73%) and the adjusted OR for testing positive for COVID-19 disease was 0.40 (95% CI: 0.27-0.59) from days 28-34 post-vaccination, further increasing to 73% (95%CI: 27-90%) one-dose vaccine effectiveness and adjusted OR 0.27 (95% CI 0.10-0.73) from day 35 onwards. One dose vaccine-effectiveness had not yet levelled off during the study period.
- **A single dose of the BNT162b2 vaccine is approximately 60-70% effective at preventing symptomatic COVID-19 disease in adults aged ≥ 70 years, and a single dose of the ChAdOx1 vaccine is approximately 60-75% effective against symptomatic COVID-19 disease.**
- Lopez Bernal et al. report vaccine effectiveness with one dose of BTN162b2 or ChAdOx1 against **hospitalization and mortality of adults aged ≥ 80 years:**
 - One dose **BNT162b2:** Within 14 days of a positive test, cases had an additional 43% (95% CI: 33-52%) lower risk and a hazards ratio of 0.57 (95% CI: 0.48-0.67) for emergency hospitalization, and an additional 51% (95% CI: 37-62%) lower risk of death within 21 days of a positive test.
 - One dose **ChAdOx1:** Within 14 days of a positive test, cases had an additional 37% (95% CI: 3-59%) lower risk and a hazards ratio of 0.63 (95% CI: 0.41-0.97) for emergency hospitalization.
- **A single dose of either BNT162b2 or ChAdOx1 vaccine is approximately 80% effective at preventing hospitalization in older adults. A single dose of BNT162b2 is 85% effective at preventing death with SARS-CoV-2.**

- **Both of these studies use a test-negative study design and demonstrate that a single dose of BNT162b2 or ChAdOx1 vaccine provides effective protection from COVID-19-related hospitalization in the elderly (approximately 80% effective). The testing period for both studies overlapped with the circulation of B.1.1.7 in the UK population, suggesting that these vaccines are effective against the B.1.1.7 VOC.**

Additional information

Hyams et al.

- This was a prospective test-negative case-control study of adults aged ≥ 80 years hospitalized with signs and symptoms of respiratory disease between December 18, 2020 (10 days after the first BNT162b2 administration) and February 26, 2021 inclusive.
- Eligible cases and controls were selected from the hospital admissions list. Cases were defined by having symptomatic respiratory disease and a positive lab-confirmed SARS-CoV-2 test result. Controls had respiratory disease and a negative SARS-CoV-2 test result.
- The exposure was having received a single dose of either vaccine between December 8, 2020 (BNT162b2) or January 4, 2021 (ChAdOx1) and February 12, 2021, with maximum follow-up time censored at February 26, 2021 – the latest event date. Vaccination records were from linked hospital and general practitioner records and included vaccine brand name and vaccine administration date.
- Follow-up period from vaccination to data cut on February 26, 2021 for the analysis ranged between 34-80 days for BNT162b2 and 19-64 days for ChAdOx1nCoV-19, respectively.
- Vaccine effectiveness of first dose was assessed ≥ 14 days after receipt of first vaccine dose. It was defined as $1 - \text{OR}$ of receipt of one dose.
- The logistic regression controlled for time (week), gender, index of multiple deprivations (IMD), and care residency status (CRS). Sensitivity analyses matched for time and gender using a conditional logistic model, adjusting for IMD and CRS.
- Matched conditional sensitivity analysis generated slightly lower effectiveness estimates for both vaccines, with wider confidence intervals which crossed zero.
- Strengths of the study include:
 - Test-negative design case-control study allowed for the effect of one dose of BNT162b2 or ChAdOx1nCoV-19 vaccine against hospitalisation to be examined in elderly, frail patients.
 - Using the date of symptom-onset to define the start of illness and assess time from vaccination and time to hospitalization increased the accuracy when estimating one-dose vaccine effectiveness.
 - Patients were excluded if their symptoms started more than 10 days before admission, removing bias from false negative SARS-CoV-2 test results.
 - Adjusting for week of symptom-onset reduced the risk of bias in the results attributable to any prioritisation that may have occurred in vaccination strategy or changes in background SARS-CoV-2 rates and therefore exposure to infection.
- Limitations to the data reported by the authors include:
 - Larger proportion of care home residents and frailty among the ChAdOx1 group compared to the BNT162b2 group.
 - Individuals with previous SARS-CoV-2 infection; thus, some degree of protection, may have been included in the study.

Lopez Bernal et al.

- This was a test-negative case-control study using adults aged ≥ 70 years in England.
- The analysis included all COVID-19 testing in the community among eligible individuals who reported symptoms between December 8, 2020 and February 19, 2021. SARS-CoV-2 test results were taken from a community testing database. Vaccination data (the exposure) were obtained from the national vaccination registry hospitalization data were obtained from the Emergency Care Dataset, and deaths data from National Health Service (NHS) records.
- Cases were defined as symptomatic and polymerase chain reaction (PCR) test-positive for SARS-CoV-2 from community testing. Controls were symptomatic and PCR-negative for SARS-CoV-2.
- **Individuals were excluded from primary analyses if they had a previous positive PCR or antibody test for SARS-CoV-2.**
- The maximum duration of follow-up after one dose of BNT162b2 and ChAdOx1 was 56 and 41 days, respectively.
- The logistic regression controlled for age, gender, ethnicity, NHS region, IMD, whether they were a care home resident and week of symptom-onset.
- Between the weeks of December 7, 2020 and January 25, 2021, B.1.1.7 accounted for between 98 and 100% of S gene target failure (SGTF) in PCR testing for SARS-CoV-2 in England. SGTF was used as a proxy for identification of the B.1.1.7 variant.
- The authors used narrow post-vaccination windows of time, which can help identify when vaccine first takes effect, reaches full effect, and reduce potential bias in analyses.
- Adults aged ≥ 80 years vaccinated with BNT162b2 had higher odds of a PCR-positive SARS-CoV-2 test result in the 9 days after vaccination (OR up to 1.48, 95% CI: 1.23-1.77), suggesting individuals receiving vaccine were at higher risk of infection and were therefore likely targeted for vaccination.
- With BNT162b2, the odds of testing positive among vaccinees began to decline from 10-13 days after the first dose. For ChAdOx1, the odds of testing positive among vaccinees began to decline after 14-20 days.
- Strengths of the study include:
 - Record linkage using large datasets (i.e. vaccination data and clinical data) provided a large sample size to estimate vaccine effectiveness on severe outcomes.
- Limitations to the data reported by the authors include:
 - Used routine test and vaccination data, which were not being collected specifically for the study purposes.
 - There were differences between the adjusted and unadjusted OR in the analysis of adults aged ≥ 70 years (January 4 onwards), due to confounding by age and care home status.
 - There were a relatively small number of subjects included in the ChAdOx1 vaccine analysis at later time points (i.e. time points of ≥ 35 days after vaccination) due to the later vaccine roll-out date for the ChAdOx1AZ vaccine.

PHO reviewer's comments

- Both studies used a study design that is considered powerful when estimating real-world vaccine effectiveness, has high concordance with randomized controlled trials, and helps to control for factors such as health-seeking behaviour, access to testing, and case ascertainment, which can be difficult to estimate in observational studies.

- The authors attempted to address biases through their analyses.
- The one-dose vaccine effectiveness estimates for the two vaccines should not be compared, for a number of reasons, including temporal differences in vaccine rollout, eligibility, background rates of exposure to infection, prevalence of VOCs, and the reproductive number (R) at the time.
- Hyams et al. disclose that their study was an investigator-led project funded under a collaborative agreement by Pfizer, the manufacturer of vaccine BNT162b2. Pfizer collaborated in the design of the study and commented on the manuscript but were not involved in data collection or analysis.
- Lopez Bernal et al. claim their findings demonstrate good effectiveness of the vaccines against VOC B.1.1.7. The analysis by SGTF status is within the Supplementary data, and the numbers of non-VOC cases are very small and the confidence intervals overlap throughout. Their claim is based on the fact that B.1.1.7 was the dominant strain during the study period, which seems reasonable.
- New VOCs may become prevalent that challenge the effectiveness of these vaccines.
- Evidence is still needed on the duration of protection, asymptomatic infection, viral transmission and safety in the elderly.
- The rapidly evolving epidemiology, vaccination strategies, public health interventions, and individual behaviours are a challenge for COVID-19 real-world vaccine effectiveness studies. Statistical adjustments and sensitivity analyses attempt to address the resulting biases and covariates.

Citation

Ontario Agency for Health Protection and Promotion (Public Health Ontario). Review of articles on BNT162b2 and ChAdOx1nCoV-19 COVID-19 vaccine effectiveness. Toronto, ON: Queen's Printer for Ontario; 2021.

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