**Supplementary Data**

**1. Review methodology**

*Study selection*

The International Vaccine Access Center (IVAC; Johns Hopkins Bloomberg School of Public Health, USA) and its online, VIEW-hub resource (<https://view-hub.org/covid-19/effectiveness-studies>) was selected as one of the most robust, independent systematic literature reviews of vaccine effectiveness data. The IVAC database only includes observational study effectiveness results that appeared in at least a detailed report/preprint. As per IVACs inclusion/exclusion criteria, observational studies were only eligible if the comparison group included concurrent individuals (e.g., modelled or historic controls were excluded), outcomes were laboratory-confirmed, the study design attempted to account for confounding, vaccination status was determined by self-report for <10% of participants, confidence intervals were reported, no significant bias was present as determined by expert opinion, controls were unvaccinated (e.g., excluded if “unvaccinated” included days 0-12 post-vaccination). Only studies comparing persons with and without the clinical outcome under investigation and with and without vaccination were included (**Supplementary Figure 1**).88

We extracted only VE against disease endpoints of interest, specifically symptomatic disease, severe disease (including “hospitalisation”), and death. We considered at least two doses necessary for full immunisation resulting in the exclusion of all 22 studies reporting VE for Ad26.COV2.S. Note that IVAC only includes results if at least one week had passed between the final dose and case detection, and they exclude effectiveness values for which the follow-up period after final dose was more than six months.88 Additionally, IVAC classifies effectiveness against specific SARS-CoV-2 variants if sequencing (or other molecular methods) either, i) confirmed the variant in all cases contributing to the estimate; or, ii) confirmed the variant caused the vast majority of cases in sample of study participants or of the larger population from which they came.88

To prevent skewing of vaccine comparisons, vaccines with less than five VE estimates were excluded from this review resulting in four vaccines (or combinations of) available for review, BNT162b2, mRNA-1273, AZD1222 and CoronaVac (**Supplementary Table 1, 2**). As there were only 5 VE studies reported for CoronaVac, it was also excluded from the formal review however study data is presented in **Supplementary Table 3** for completeness. Finally, as a number of mixed mRNA schedule studies were included, we elected to combine all mRNA VE data to provide a simpler “platform” view. This enabled a much simpler comparison of mRNA vaccines (BNT162b2 and mRNA-1273) to viral vector vaccines (represented by AZD1222).

In addition to the primary review of the IVAC database, we also performed a separate extraction of VE estimates from only those studies with comparative arms to assess the VE of AZD1222 and either BNT162b2 or mRNA-1273 or a heterologous mRNA schedule in the same settings (**Supplementary Figure 2**). This was intended to provide greater confidence in author comparability assessments attributed to these vaccines.

A parallel review of safety data from studies included in the IVAC database was not possible as this data is not currently captured. Any safety assessments discussed here are based on author consensus of existing safety literature.

*Data visualisation*

VE estimates for each vaccine platform were combined and stratified across VOC, age, study design and prior SARS-CoV-2 infection. To retain individual data clarity, VE point estimates are presented graphically from highest to lowest with their respective confidence intervals. Additionally, for studies where it was possible to extract a meaningful estimate of the time since vaccination, we attempted to assess potential waning of VE over time. Studies were stratified according to VE estimates recorded as “early” (14+ days post dose 2), “intermediate” (14-63 days post dose 2) and “late” (>140 days post dose 2). To enable expert discussions regarding platform comparisons, means and confidence intervals were calculated and provided for all figures. Statistical comparisons were conducted using two-tailed t-tests. P-values greater than 0.05 were considered as a non-significant difference.

*Non-IVAC data*

Following data extraction, a number of data gaps were apparent within the current IVAC dataset, primarily relating to VE in Asian populations, VE against the Omicron variant and VE for booster schedules. To enable expert discussion with a view to provide advice relevant for the current vaccination situations in Asia, we sourced local or international comparative datasets to address these data gaps as follows:

1. Asian data

A limited number of comparative VE studies after full vaccination are available in Asian settings. A recent Ministry of Health study from Malaysia26 provides primary schedule data for BNT162b2, CoronaVac and AZD1222. A number of VE studies have been conducted in different provinces in Thailand32 and are being collated by the Department of Disease Control.89 These provide both primary schedule VE data and data following a third booster dose (Table 1).

1. Omicron data

The authors felt that the most credible comparison of VE against the Omicron variant for mRNA and AZD1222 vaccines was available from the United Kingdom via Public Health England (PHE) surveillance.2,90 This provides both primary schedule and booster data.

1. Booster data

In addition to the booster data available from Thailand and PHE, a study with a schedule relevant for Asian countries is also available from Chile and evaluates AZD1222, BNT162b2 and CoronaVac VE following a third dose in individuals primed with two doses of CoronaVac (Table 1).18

| **Source** | **Country** | **Design** | **URL** |
| --- | --- | --- | --- |
| Abu-Raddad et al. 2022 | Qatar | Test-negative case control | <https://www.nejm.org/doi/10.1056/NEJMc2119432> |
| Alali et al. 2021 | Kuwait | Retrospective | <https://www.mdpi.com/2227-9032/9/12/1692/htm> |
| Amodio et al. 2021 | Italy | Retrospective  | <https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4001786> |
| Andrews et al. 2022 | England | Test-negative case control | <https://www.nejm.org/doi/pdf/10.1056/NEJMoa2115481?articleTools=true> |
| Andrews et al. 2022 | England | Test-negative case control | <https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1050236/technical-briefing-34-14-january-2022.pdf> |
| Angel et al. 2021 | Israel | Retrospective | <https://jamanetwork.com/journals/jama/fullarticle/2779853> |
| Arregoces et al. 2021 | Colombia | Matched- pair cohort study | <https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3944059> |
| Bajema et al. 2021 | USA | Test-negative case control | <https://www.cdc.gov/mmwr/volumes/70/wr/mm7049a2.htm?s_cid=mm7049a2_w> |
| Berec et al. 2021 | Czech Republic | Retrospective | <https://www.medrxiv.org/content/10.1101/2021.12.10.21267590v1.full.pdf> |
| Botton et al. 2022 | France | Retrospective  | <https://www.sciencedirect.com/science/article/pii/S0264410X21016170?via%3Dihub> |
| Bruxvoort et al. 2021 | USA | Matched prospective cohort | <https://www.sciencedirect.com/science/article/pii/S2667193X21001307> |
| Cerqueira-Silva et al. 2021 | Brazil | Test-negative case control | <https://www.medrxiv.org/content/10.1101/2021.12.21.21268058v1.full.pdf> |
| Cerqueira-Silva et al. 2022 | Brazil | Test-negative case control | <https://www.nature.com/articles/s41591-022-01701-w.pdf> |
| Chemaitelly et al. 2022 | Qatar | Test-negative case control | <https://www.medrxiv.org/content/10.1101/2022.02.07.22270568v1.full.pdf> |
| Chiew et al. 2022 | Singapore | Retrospective | <https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3996796> |
| Chung et al. 2021 | Canada | Test negative case control | <https://doi.org/10.1136/bmj.n1943> |
| Chung et al. 2022 | USA | Test-negative case control | <https://www.medrxiv.org/content/10.1101/2021.12.30.21267928v1.full.pdf> |
| Collie et al. 2021 | South Africa | Test-negative case control | <https://www.nejm.org/doi/full/10.1056/NEJMc2119270> |
| Emborg et al. 2021 | Denmark | Cohort | <https://www.medrxiv.org/content/10.1101/2021.05.27.21257583v1> |
| Flacco et al. 2021 | Italy | Retrospective | <https://doi.org/10.3390/vaccines9060628> |
| Florea et al. 2021 | USA | Prospective | <https://www.medrxiv.org/content/10.1101/2021.12.13.21267620v2> |
| Giansante et al. 2021 | Italy | Retrospective | <https://www.mattioli1885journals.com/index.php/actabiomedica/article/view/11896/10087> |
| Glatman-Freedman et al. 2021 | Israel | Retrospective | [https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00367-4/fulltext](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964%2821%2900367-4/fulltext) |
| Goldberg et al. 2021 | Israel | Prospective | <https://www.medrxiv.org/content/10.1101/2021.04.20.21255670v1> |
| Grannis et al. 2021 | USA | Test-negative case control | <https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e2.htm?s_cid=mm7037e2_w#suggestedcitation> |
| Haas et al. 2021 | Israel | Retrospective | [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00947-8/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2821%2900947-8/fulltext) |
| Hitchings et al. 2021 | Brazil | Test-negative case control | <https://www.nature.com/articles/s41467-021-26459-6> |
| Irizarry et al. 2021 | Puerto Rico | Retrospective | https://papers.ssrn.com/sol3/papers.cfm?abstract\_id=3957118 |
| Jara et al. 2022 | Chile | Prospective | <https://www.nejm.org/doi/10.1056/NEJMoa2107715> |
| Katikireddi et al. 2021 | Scotland | Retrospective | [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02754-9/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2821%2902754-9/fulltext) |
| Katz et al. 2021 | Israel | Prospective | <https://www.sciencedirect.com/science/article/pii/S0264410X21015802?via%3Dihub> |
| Kissling et al. 2021 | Croatia, France, Ireland, Netherlands, Portugal, Romania, Spain, and UK | Test-negative case control | <https://osf.io/3nhps/> |
| Lauring et al. 2022 | USA | Test-negative case control | <https://www.medrxiv.org/content/10.1101/2022.02.06.22270558v1.full.pdf> |
| Lin et al. 2021 | USA | Retrospective | https://www.medrxiv.org/content/10.1101/2021.10.25.21265304v1.full.pdf |
| Lopez Bernal et al. 2021 | UK | Test-negative case control | <https://www.nejm.org/doi/10.1056/NEJMoa2108891> |
| Lytras et al. 2022 | Greece | Retrospective | https://www.medrxiv.org/content/10.1101/2022.01.28.22270009v1.full.pdf |
| Machado et al. 2021 | Portugal | Retrospective | <https://www.medrxiv.org/content/10.1101/2021.12.10.21267619v1> |
| Martinez-Bas et al. 2021 | Spain | Prospective | <https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.21.2100438> |
| Martínez-Baz et al. 2021 | Spain | Prospective | <https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.39.2100894#html_fulltext> |
| Mason et al. 2021 | UK | Case control | <https://bmcmedicine.biomedcentral.com/track/pdf/10.1186/s12916-021-02149-4.pdf> |
| McLean et al. 2021 | USA | Prospective | <https://www.medrxiv.org/content/10.1101/2021.12.14.21267809v1> |
| Meyer et al. 2021 | Germany | Retrospective | <https://www.medrxiv.org/content/10.1101/2021.09.13.21262519v1.full.pdf> |
| Nasreen et al. 2021 | Canada | Test-negative case control | <https://www.medrxiv.org/content/10.1101/2021.06.28.21259420v3> |
| Nordström et al. 2021 | Sweden | Retrospective | <https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3949410> |
| Nordström et al. 2021 | Sweden | Retrospective | <https://www.sciencedirect.com/science/article/pii/S2666776221002350> |
| Olson et al. 2022 | USA | Case control | <https://www.nejm.org/doi/pdf/10.1056/NEJMoa2117995?articleTools=true> |
| Olson et al. 2021 | USA | Test-negative case control | <https://www.cdc.gov/mmwr/volumes/70/wr/mm7042e1.htm?s_cid=mm7042e1_w> |
| Ostropolets et al. 2021 | USA | Retrospective | <https://www.medrxiv.org/content/10.1101/2021.12.22.21268253v1.full-text> |
| Pawlowski et al. 2021 | USA | Retrospective | [https://www.cell.com/med/pdf/S2666-6340(21)00238-5.pdf?\_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS2666634021002385%3Fshowall%3Dtrue](https://www.cell.com/med/pdf/S2666-6340%2821%2900238-5.pdf?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS2666634021002385%3Fshowall%3Dtrue) |
| Petrás et al. 2021 | Czech Republic | Retrospective | <https://www.mdpi.com/2076-393X/10/1/9/htm> |
| PHE 2021 | UK | Test-negative case control | <https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/990089/Vaccine_surveillance_report_-_week_20.pdf> |
| PHE 2021 | UK | Screening Method | <https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/963532/COVID-19_vaccine_effectiveness_surveillance_report_February_2021_FINAL.pdf> |
| Poukka et al. 2022 | Finland | Retrospective | <https://www.sciencedirect.com/science/article/pii/S0264410X21016406?via%3Dihub> |
| Pritchard et al. 2021 | UK | Prospective | https://www.nature.com/articles/s41591-021-01410-w |
| Prunas et al. 2022 | Israel | Matched case-control | <https://www.medrxiv.org/content/10.1101/2022.01.04.22268776v1.full.pdf> |
| Puranik et al. 2021 | USA | Retrospective | <https://www.medrxiv.org/content/10.1101/2021.08.06.21261707v2.full.pdf> |
| Ranzani et al. 2021 | Brazil | Test-negative case control | <https://doi.org/10.1136/bmj.n2015> |
| Reis et al. 2021 | Israel | Retrospective | <https://www.nejm.org/doi/10.1056/NEJMc2114290> |
| Roberts et al. 2022 | USA | Test-negative case control | <https://www.medrxiv.org/content/10.1101/2022.01.29.22269971v1.full.pdf> |
| Saciuk et al. 2021 | Israel | Retrospective | <https://www.sciencedirect.com/science/article/pii/S009174352100520X?via%3Dihub> |
| Self et al. 2021 | USA | Test-negative case control | <https://www.cdc.gov/mmwr/volumes/70/wr/mm7038e1.htm?s_cid=mm7038e1_w> |
| Sheikh et al. 2021 | Scotland | Retrospective | <https://www.nejm.org/doi/10.1056/NEJMc2113864> |
| Skowronski et al. 2021 | Canada | Test-negative case control | <https://www.medrxiv.org/content/10.1101/2021.10.26.21265397v1> |
| Stowe et al. 2021 | UK | Test-negative case control | https://khub.net/web/phe-national/public-library/-/document\_library/v2WsRK3ZlEig/view/479607266 |
| Suryatma et al. 2022 | Indonesia | Test-negative case control | <https://www.medrxiv.org/content/10.1101/2022.02.02.22270351v1.full.pdf> |
| Tang et al. 2021 | Qatar | Test-negative case control | https://www.nature.com/articles/s41591-021-01583-4#Tab4 |
| Tartof et al. 2021 | USA | Retrospective | <https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3989856> |
| Tartof et al. 2022 | USA | Test-negative case control | <https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4011905> |
| Tenforde et al. 2021 | USA | Test-negative case control | <https://jamanetwork.com/journals/jama/fullarticle/2786039> |
| Tenforde et al. 2021 | USA | Test-negative case control | <https://doi.org/10.1093/cid/ciab687> |
| Tenforde et al. 2021 | USA | Test-negative case control | <https://www.cdc.gov/mmwr/volumes/70/wr/mm7018e1.htm?s_cid=mm7018e1_x> |
| Tenforde et al. 2022 | USA | Test-negative case control | <https://www.cdc.gov/mmwr/volumes/71/wr/mm7104a2.htm?s_cid=mm7104a2_w> |
| Thompson et al. 2022 | USA | Test-negative case control | <https://www.cdc.gov/mmwr/volumes/71/wr/mm7104e3.htm?s_cid=mm7104e3_w> |
| Tseng et al. 2022 | USA | Test-negative case control | <https://www.medrxiv.org/content/10.1101/2022.01.07.22268919v2> |
| UKHSA 2022 | England | Test-negative case control | <https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1050721/Vaccine-surveillance-report-week-4.pdf> |
| Vokó et al. 2021 | Hungary | Retrospective | https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(21)00639-X/fulltext |
| Whitaker et al. 2022 | UK | Prospective | [https://www.journalofinfection.com/article/S0163-4453(21)00664-2/fulltext](https://www.journalofinfection.com/article/S0163-4453%2821%2900664-2/fulltext) |
| Young-Xu et al. 2021 | USA | Test-negative case control | <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2784769> |
| Young-Xu et al. 2022 | USA | Matched test-negative case control | <https://www.medrxiv.org/content/10.1101/2022.01.15.22269360v1.full.pdf> |

**Supplementary Table 1.** All studies extracted from the IVAC database reporting VE for either symptomatic infection, hospitalisations or death that were used in our analyses.

|  |  |
| --- | --- |
| **Study characteristic** | **Number of Studies** |
| 1. **COVID-19 vaccine(s) studied**
 |
| BNT162b2 | 58 |
| mRNA-1273 | 34 |
| Heterologous mRNA | 14 |
| AZD1222 | 25 |
| CoronaVac (Sinovac) | 5 |
| 1. **Study design**
 |
| Retrospective | 30 |
| Prospective | 10 |
| Test-negative case-control | 34 |
| Other | 5 |
| 1. **Sample size**
 |
| <1,000 | 2 |
| 1,000-10,000 | 13 |
| 10,000-100,000 | 20 |
| 100,000-1,000,000 | 21 |
| 1,000,000-10,000,000 | 17 |
| >10,000,000 | 2 |
| N/A | 4 |
| 1. **Age ranges**
 |
| 12-18 | 5 |
| >12 | 4 |
| >15 | 1 |
| >16 | 40 |
| 16-89 | 1 |
| >60 | 8 |
| 80-83 | 1 |
| N/A | 19 |
| 1. **Geographical region of study**
 |
| Northern America (US, Canada) | 28 |
| Continental Europe | 19 |
| Middle East | 12 |
| United Kingdom | 11 |
| Central & Southern America | 6 |
| Asia-Pacific | 2 |
| South Africa | 1 |

**Supplementary Table 2. Characteristics of studies included in our review**. On February 10, 2022, we extracted and analysed publicly-available data in 79 studies compiled by IVAC which reported data on effectiveness of vaccines against SARS-CoV-2 infection, COVID-19-related hospitalisations and deaths). Our analysis was conducted in accordance with PRISMA recommendations. Most studies were test-negative case-control or retrospective in nature and had a sample size of 100,000 to 1,000,000 individuals aged 16 years and older.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Source** | **Country** | **Study Design** | **Age (Years)** | **Variant** | **Outcome** | **2nd Dose VE (95% CI)** |
| Cerqueira-Silva et al. 2021 | Brazil | Test-negative case control | > 18 | Non-VOC, Gamma, Delta | Symptomatic reinfection | 39 (36-43) |
| Hospitalization or death | 81 (75-86) |
| Jara et al. 2022 | Chile | Prospective | > 18 | Alpha, Gamma | Hospitalization | 88 (87-88) |
| Death | 86 (85-88) |
| Ranzani et al. 2021 | Brazil | Test-negative case control | > 70 | Gamma | Symptomatic Infection | 47 (39-54) |
| Hospitalization | 56 (47-63) |
| Death | 61 (49-71) |
| Cerqueira-Silva et al. 2022 | Brazil | Test-negative case control | na | Gamma. Delta | Hospitalization | 82 (81-83) |
| Death | 83 (82-84) |
| Suryatma et al. 2022 | Indonesia | Test-negative case control | > 18 | Non-VOC, Alpha | Hospitalization | 71 (63-78) |
| Death | 87 (65-95) |

**Supplementary Table 3. CoronaVac studies included in the IVAC database reporting VE for either symptomatic infection, hospitalisations or death.**



**Supplementary Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) diagram.** Inclusion and exclusion criteria applied by IVAC facilitated our extraction of relevant studies and data from the database.

### Diagram  Description automatically generated

## Supplementary Figure 2. Comparability of VE in individual studies. Studies with comparative arms to assess the VE of AZD1222 and either BNT162b2 or mRNA-1273 or a heterologous mRNA schedule in the same settings. Within the larger dataset of 79 studies, 18 studies reported VE against relevant outcomes for AZD1222 in parallel with an mRNA vaccine and inactivated vaccine (1 study). Studies were further stratified by a) symptomatic infection, b) hospitalisation, and c) death due to Delta in addition to VE for each outcome in older adults.