Effectiveness of the Monovalent XBB.1.5 and of the 2024/2025 COVID-19 Vaccines
Living Evidence Synthesis #21
(Version 21.5: 7 March 2025)

Questions

What is the added protection (VE ≥7 days post vaccination and over time) conferred by any 2023/2024 monovalent XBB.1.5-containing vaccine or the 2024/2025 COVID-19 vaccines authorised in Canada against the following Omicron-related outcomes during XBB sublineage (and any future variant) predominance:

1. Symptomatic and medically attended COVID-19 infections;
2. COVID-19-related emergency department (ED) visits;
3. COVID-19-related hospitalisations;
4. COVID-19-related intensive care unit (ICU) admissions;
5. COVID-19-related deaths;
6. Multisystem inflammatory syndrome in children (MIS-C); and
7. Post-COVID Conditions
8. Other outcomes: e.g., COVID-19-related outpatient visits

compared with:

- Previous COVID-19 vaccines:
  - No COVID-19 vaccination and previous COVID-19 bivalent or monovalent vaccines;
  - Previous mRNA COVID-19 bivalent boosters;
  - Previous original monovalent COVID-19 vaccines;
- No COVID-19 vaccination; and
- Hybrid immunity.

This question is being explored in the following populations (where possible):

- General population;
- Healthcare workers;
- Older adults (≥65 years);
- Infants, children, and adolescents;
- Individuals with immunocompromising conditions; and
- Pregnant people and their newborns.

Box 1: Our approach

We retrieved candidate studies and updates to living evidence syntheses on vaccine effectiveness using the following mechanisms: 1) search on the National Institute of Health (NIH) iSearch COVID-19 portfolio, EMBASE and Medline; 2) systematic scanning of the Research Analysis (EXTRA) COVID-19 Titles from NACI / CCNI (PHAC/ASPC) and WHO weekly COVID-19 newsletter; and 3) exploration of citations of systematic reviews on this topic. We included studies and updates to living evidence syntheses identified up to seven days before the version release date. We did not include press releases unless a preprint was available. *A full list of included and excluded studies is provided in* ***Appendix 1 and 7****, respectively.*

Outcome measures: Symptomatic SARS-CoV-2 infections, COVID-19-related ED visits; hospitalisation due to COVID-19, ICU admission due to COVID-19, death due to COVID-19, MIS-C, and post-COVID conditions. Other outcomes (e.g., COVID-19- related outpatient visits)

Data extraction: We prioritised total population data over sub-groups. We extracted data from each study using a standard template with peer-review to confirm information (see ***Appendix 6***).

Critical appraisal: We assessed risk of bias in duplicate for individual outcomes using an adapted version of ROBINS-I (***Appendix 5***).

Summaries: Where data was insufficient to undertake meta-analyses, we provide an average (and range) of the available data or (point estimates and 95% CIs). Where there is enough data, we summarise the evidence by presenting meta-analysed pooled estimates with 95% CIs (see **Appendix 3** for details).

A glossary of terms is provided in ***Appendix 4****.*

This living systematic review was designed and executed by the Montreal Behavioural Medicine Centre, a joint Concordia University, Université du Québec à Montréal, and CIUSSS-NIM centre, and in collaboration with a network of evidence-support units supported by a secretariat housed at the McMaster Health Forum.

Visual representation of findings

1. The impact of any prior COVID-19 vaccination plus a 2023/2024 monovalent XBB.1.5 vaccine or the 2024/2025 COVID-19 vaccine vs. any prior COVID-19 vaccination against *SARS-CoV-2 infections* is presented in Table 1 and Figure 1.
2. The impact of any prior COVID-19 vaccination plus a 2023/2024 monovalent XBB.1.5 vaccine or the 2024/2025 COVID-19 vaccine vs. any prior COVID-19 vaccination against *COVID-19-related ED visits* is presented in Table 2.
3. The impact of any prior COVID-19 vaccination plus a 2024/2024 monovalent XBB.1.5 vaccine or the 2024/2025 COVID-19 vaccine vs. any prior COVID-19 vaccination against *COVID-19-related hospitalisations* is presented in Table 3.

Flow of included studies

To capture as many articles as possible, our initial search did not include date limits, meaning that all articles mentioning the keywords of interest prior to our first round (January 30th, 2024) were captured. On March 19th, 2024 (version 2), June 11th, 2024 (version 3), and October 1st, 2024 (version 4), a second, third and fourth round of searches were completed, respectively. By the fifth round (search date: February 28th, 2025) a total of 462 articles were title and abstract screened, 79 were full text appraised, with 37 initially included, 6 of these were excluded due to having a critical risk of bias (RoB; see **Appendix 1b)**, leaving 31 that were used to complete this summary. The reasons for excluding the 42 studies are reported in **Appendix 7b.** In addition, 192 records were identified through hand search, of which 92 were full text screened. Nine studies were first included but one was later excluded due to having a critical risk of bias (RoB; see **Appendix 1b),** leaving 8 included studies through hand search. The reasons for excluding the 83 studies are reported in **Appendix 7b** as well. Therefore, a total of 39 studies are included in this summary, including an update of a previously included study and 7 published version or corrections of previously included articles. Overall, the 39 included studies contributed 52 outcomes to this summary, with two outcomes being excluded for having a critical risk of bias (COVID-19 related hospitalisations from Link-Gelles and DeCuir; see **Appendix 1b**).

High level summary for COVID-19 outcomes

COVID-19-related infections

*XBB.1.5 vaccination **vs.** no XBB.1.5 vaccination (including individuals who have not received any COVID-19 vaccine)*

As shown in **Figure 1**, in the early (ca. 1-11 weeks) post vaccination period, overall incremental vaccine effectiveness [iVE] for **medically attended infections** is generally around 50%. In the mid (ca. 6-17 weeks) post vaccination period, iVE drops to 35-40%. There is a slight suggestion that younger (<65 years) adults have slightly better early protection compared to older (≥ 65 years) adults (54% vs. 48%), with consistent levels between the groups during the mid period (38% vs. 37%)

- Seven studies (six test-negative and one retrospective cohort study: five from the US, one from Canda, and one from South Korea) were included for **medically attended infections**.
    - One test-negative case-control study from US (Caffrey et al. (2024)) found that adults aged ≥18 years who had received the XBB.1.5 vaccine had a median 56-day iVE of 27% for medically attended COVID-19 infections, compared with those who had not received any XBB.1.5 vaccine (including unvaccinated individuals). Those who had immunocompromising conditions had a lower iVE vs. those without immunocompromising conditions (40% vs. 22%). Older individuals had a higher iVE compared to young individuals (18-64 years = 34% vs. ≥65 years = 24%). In addition, the vaccine seemed to provide better protection against XBB sublineages vs. JN.1 sublineages (14-60 days iVE = 50% vs. 31%, respectively). When compared to individuals who did not receive the XBB.1.5 variant-adapted vaccine but received at least one

BA.4/5 bivalent dose or receive 3 or more doses of original wild-type mRNA but no bivalent adapted vaccine, the iVE was 26% and 38%, respectively.

- One test-negative case-control study from the US (Lanièce Delaunay (2024)) found that individuals who had received an mRNA XBB.1.5 variant-adapted vaccine were less likely to have a medically attended infection compared with those who had not received the XBB.1.5 COVID-19 vaccine. After 7 to 41 days, the iVE was 48% for individuals aged ≥5 years, 69% for younger individuals (aged 5 to ≤50-64 years) and 45% for older individuals (≥50-65 years) while omicron sublineages were predominant (primarily XBB, EG.5.1 and JN.1). The effectiveness of the vaccine did wane through time, reaching 29% after 42 to 119 days for individuals aged ≥5 years, 28% for younger individuals, and 26% for older individuals.
- One test-negative case-control study from six university hospitals in South Korea (Lee et al. (2024)) found that adults aged ≥18 years who had received an mRNA XBB.1.5 COVID-19 vaccine were less likely to have a medically attended infection compared with those who had not received the XBB.1.5 COVID-19 vaccine. The authors found a moderate level of protection 7-59 days post vaccination (iVE= 57.7%) while omicron sub variants were predominant (primarily XBB, EG.5.1, HK.3 and JN.1). The iVE was slightly higher in older adults (≥65 years = 60.2%).
- One test-negative case-control study (Link-Gelles et al. (2024)) of US adults found a moderate level of protection ≥7 days post vaccination (iVE = 54%) while the XBB and JN.1 sublineages were predominant, compared with those who had not received any XBB.1.5 vaccine. When looking at specific periods of time, there was a drop in iVE from 58% at 7-59 days to 49% at 60-119 days. There was also a trend for the iVE to be higher in younger adults (18-49 years = 57%) compared with older adults (≥50 years = 46%).
- One test-negative case control study (Skowronski et al. (2024)) found that Canadian individuals aged ≥12 years who had received the XBB.1.5 COVID-19 vaccine were less likely to have a medically attended infection compared with those who had not received the XBB.1.5 COVID-19 vaccine. The authors found a moderate level of protection approximately 35 days post vaccination (iVE = 44%) during the period where XBB EG.5.1, HV.1, BA.2.75, BA.2.86 and JN.1 sublineages were predominant, compared with those who had not received any XBB.1.5 vaccine. This level of protection did not differ by age group (12-64 years = 46%; ≥65 years = 46%). When restricting the analysis to those who reported a prior NAAT- or RAT-confirmed SARS-CoV-2 infection and when excluding influenza cases from controls, the iVE increased to 72%.
- One test-negative case-control study (Tartof et al. (2023)*) of US adults found a moderate level of protection at a median of 30 days post vaccination (iVE = 58%) while the XBB sublineages were predominant and JN.1 was co-circulating, compared with those who had not received any XBB.1.5 vaccine. There was a trend for the iVE to be higher in older adults (≥65 years = 68%) compared with younger adults (18-64 years = 32%).
- One retrospective cohort (Wilson et al. (2024)) of US adults found an iVE against medically-attended infections of 25% when compared to individuals who had not received the XBB.1.5 variant adapted vaccine at a median of 84 days while omicron sublineages were predominant (primarily XBB, EG.5.1 and JN.1). The iVE was similar in all age groups, reaching 25% in individuals aged 18-49 years, 19% in individuals aged 50 to 64 years and 21% in individuals aged ≥65 years after at least 8 days. A similar iVE (28%) was observed for individuals with immunocompromising conditions after at least 8 days.

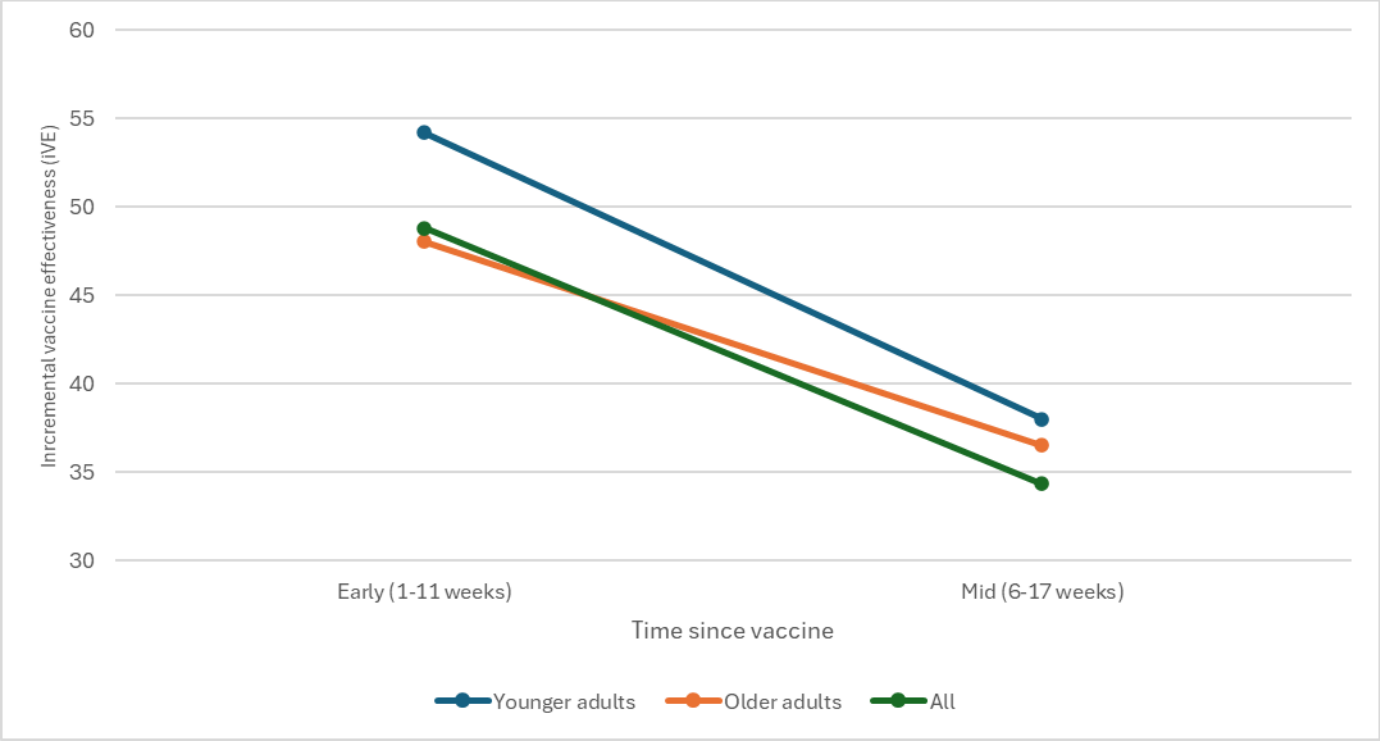

Figure 1: A visual representation of the trend in incremental vaccine effectiveness (iVE) for **medically attended infections** of the XBB.1.5 adapted COVID-19 vaccine over time (comparator = those who did not receive the XBB.1.5 vaccine, including unvaccinated individuals).

* The following categories consist of the data from the 7 included studies: The early time period covers the 7-77 days; the mid time period covers 42-119 days; the younger adults include cohorts with ages ranging from 12-65; the older adults include those who are ≥50 (though the majority are ≥65); and the whole samples generally included those ≥18 with 1 study included those ≥5. A simple averaging of data was applied across studies.

Five studies were included for **any SARS-CoV-2 infection**.

- One prospective cohort study measured *self-reported symptomatic SARS-CoV-2 infection.*
    - A study from the Netherlands (Huiberts et al. (2024)) found a lower level of protection ≥7 days post vaccination in younger adults (18-59 years, iVE = 34.7%) than older adults (60-85 years, iVE = 55.0%) while XBB sublineages and JN.1 were predominant.
- Two studies measured *PCR confirmed SARS-CoV-2 infection*, with the majority, but not all, being symptomatic.
    - A retrospective cohort study (Lin et al. (2024)) reported on individuals of all ages living in the US. Overall, the XBB.1.5 variant-adapted vaccine offered greater protection against the XBB.1.5 variant (iVE at 28-34 days = 64.4%) than the JN.1 variant (iVE at 28-34 days= 44.3%). The study also found that the iVE reached a peak at 4 weeks (iVE=52.2%) and waned after that (24-week iVE=16.4%).
    - A prospective cohort study in US adults (Shrestha et al. (2024)) found that the XBB.1.5 variant-adapted vaccine offered greater protection against infection before JN.1 became the dominant variant (iVE= 42%) than after it became dominant (iVE= 19%) when measured at least 7 days post vaccination.

- One retrospective cohort study measured *positive COVID-19 NAAT or antigen test*
    - A study from the US (Ioannou et al. (2025)) found that mRNA XBB.1.5 variant-adapted vaccines had an iVE of 14% after 60 days which waned to 3% by 120 days, while omicron sublineages were predominant (primarily XBB, EG.5.1 and JN.1). The iVE was lower in older individuals than in younger individuals (18 to 64 years: 9% vs ≥75 years: -13%).
- One retrospective cohort study measured COVID-19 from any electronic health records (EHR) or medical claim with either a COVID-19 diagnosis or positive laboratory test result
    - A study from the US (Kopel et al. (2024)) found that the Moderna mRNA XBB.1.5 variant-adapted vaccine offered some protection against infections in adults (iVE=33.1%) and in adults with medical conditions (iVE=34.5%) when measured at least 7 days post vaccination while omicron sublineages were predominant (primarily XBB, EG.5.1, and JN.1). The protection offered by the vaccine did not differ with age (≥18 years, ≥50 years, and ≥65 years).

*XBB.1.5 vaccination **vs.** variations in previous vaccination regimens*

- Two test-negative case-control studies were included for **medically attended infections**.
    - One study from six university hospitals in South Korea (Lee et al. (2024)) found that adults aged ≥18 years who had received an mRNA XBB.1.5 COVID-19 vaccine and at least one previous COVID-19 vaccine dose were less likely to have a medically attended infection compared with those who had not received the XBB.1.5 COVID-19 vaccine but had received at least one dose of a COVID-19 vaccine. The authors found a moderate level of protection 7-59 days post vaccination (iVE= 55.6%) while omicron sub variants were predominant (primarily XBB, EG.5.1, HK.3 and JN). The iVE was slightly higher in older adults (≥65 years = 57.6%). The protection was also higher in adults without immunocompromising conditions (iVE= 57.7%) than in adults with immunocompromising conditions (iVE= 47.6%).
    - The Tartof et al. (2023)* study explored a variety of vaccination comparator groups (adapted bivalent vaccine but no XBB1.5-adapted vaccine, ≥3 doses of wild-type vaccine but no variant-adapted vaccines of any kind, and ≥2 doses of wild-type vaccine but no variant-adapted vaccines of any kind). In general, the results were consistent with the median 30-day post-vaccination iVE being around 55% with younger individuals (18-64 years) having less protection (iVE = 22-40%) than older adults (≥65 years: iVE = 65-71%) while omicron sublineages were predominant (primarily XBB, EG.5.1and JN.1).

- One retrospective cohort study measured **PCR confirmed SARS-CoV-2 infections**, with the majority, but not all, being symptomatic.
    - A study (Chong et al. (2024)) from Singapore found an iVE of 41% against the JN.1 variant 8 to 120 days after the receival of an mRNA XBB.1.5 variant-adapted vaccine in individuals who received at least three previous mRNA doses when compared to individuals who had also received at least three mRNA vaccine doses but no XBB.1.5 variant-adapted vaccine.
- One prospective cohort study measured iVE against **PCR confirmed SARS-CoV-2 infection, including both symptomatic and mild/asymptomatic infections**.
    - A study (Kirwan et al. (2024)) found that in health care professionals (HCPs) the XBB.1.5 variant-adapted vaccine offered less protection against mild or asymptomatic infection (iVE= 12.0-17.8%) than symptomatic infection (iVE= 36.8-64.8%) in individuals who received at least three previous COVID-19 vaccine doses (but no more than five) when compared to individuals who have also received at least three COVID-19 vaccine doses (but no more than five) but not the XBB.1.5 variant-adapted vaccine while omicron sublineages were predominant (primarily XBB, EG.5.1, BA and JN.1).

*XBB.1.5 vaccination **vs.** no COVID-19 vaccination*

- Two test-negative case-control studies were included for **medically attended infections**.
    - A study from six university hospitals in South Korea (Lee et al. (2024)) found that adults aged ≥18 years who had received an mRNA XBB.1.5 COVID-19 vaccine were less likely to have a medically attended infection compared with those who had not received any COVID-19 vaccine. The authors found a moderate level of protection 7-59 days post vaccination (aVE= 65.2%) while omicron sub variants were predominant (primarily XBB, EG.5.1, HK.3 and JN.1). The aVE was slightly higher in older adults (≥65 years = 67.2%). A median of 25.5 days post vaccination, the aVE was 71.0%.
    - The Tartof et al. (2023)* study in the US found that, compared to unvaccinated individuals, adults aged ≥18 years who had received the Pfizer-BioNTech XBB.1.5 COVID-19 vaccine were less likely to have a medically attended COVID-19 infection (median 30 day aVE = 43%) while omicron sublineages were predominant (primarily XBB, EG.5.1 and JN.1). What was notable was a large absolute difference between younger individuals (18-64 years: aVE = 17%) and older adults (≥65 years: aVE = 60%); however, the overlapping confidence intervals meant that this finding was not statistically significant.

* The Tartof et al. data reported here is from a pre-print that eventually became a published paper, but this data was not included in the final publication.

COVID-19-related emergency department (ED) or urgent care (UC) visits

XBB.1.5 vaccination ***vs.*** *no XBB.1.5 vaccination*

- Three test-negative case-control studies from the US were included.
    - One study (Caffrey et al. (2024)) found that adults aged ≥18 years who had received the XBB.1.5 vaccine had a median 56-day iVE of 39% for COVID-19-related ED or UC visits, compared with those who had not received any XBB.1.5 vaccine (including unvaccinated individuals). Those who had immunocompromising conditions had a lower iVE vs. those without immunocompromising conditions (34% vs. 42%). Older individuals had a lower iVE compared to young individuals (18-64 years = 48% vs. ≥65 years = 35%). In addition, the vaccine seemed to provide better protection against XBB sublineages vs. JN.1 sublineages (14-60 day iVE = 52% vs. 41%). When compared to individuals who did not receive the XBB.1.5 variant-adapted vaccine but received at least one BA.4/5 bivalent dose or received 3 or more doses of original wild-type mRNA but no bivalent adapted vaccine, the iVE was 44% and 41%, respectively.
    - One study (DeCuir et al. (2024)) found that XBB.1.5 variant-adapted vaccines provided some protection against COVID-related ED and UC visits in immunocompetent adults aged ≥18 years 7 to 119 days after receiving the vaccine, compared to those who did not receive the XBB.1.5 variant-adapted vaccine (including unvaccinated individuals), but that this protection diminished slightly over time (median 33 day iVE = 51% vs. median 74 day iVE = 39%) while omicron sublineages were predominant (primarily XBB, EG.5.1 and JN). In general, there were no differences in iVE by age group (e.g., iVE at median 74 days = 18-64 years: 45% vs. ≥65 years: 37%).
    - One study (Tartof et al. (2024)) found that adults aged ≥18 years who had received the Pfizer-BioNTech XBB.1.5 COVID-19 vaccine had a 14-60 day iVE of 52% for COVID-19-related ED or UC visits during the JN.1 sublineage dominant period that dropped notably between 60 and 156 days (iVE = 34%), compared with those who had not received any XBB.1.5 vaccine (including unvaccinated individuals). During the XBB sublineage predominant period, the iVE was 59% 14-60 days post vaccination, dropping to an iVE of 39% at 60-128 days post vaccination.
- One retrospective cohort study from the US was included.

- One study (Andersen et al. (2025)) found that that the Pfizer-BioNTech XBB1.5-adapted vaccine offered some protection against COVID-related ED and UC visits in adults aged ≥18 years after 14 days (iVE: 45%) while omicron sublineages were predominant (primarily XBB, EG.5.1 and JN.1). The protection was similar in older adults (≥65 years) with an iVE of 48%.

*XBB.1.5 vaccination **vs.** variations in previous vaccination regimens*

- One retrospective cohort study from Singapore was included.
  - The Chong et al. (2024) study, found an iVE of 50% against the JN.1 variant 8 to 120 days after the receival of an mRNA XBB.1.5 variant-adapted vaccine in adults aged ≥18 years who received at least three previous mRNA doses when compared to adults who had also received at least three mRNA vaccine doses but no XBB.1.5 variant-adapted vaccine.
- One retrospective cohort study from the US was included.
  - One study (Andersen et al. (2025)) found that that the Pfizer-BioNTech XBB1.5-adapted vaccine offered some protection against COVID-related ED and UC visits in adults aged ≥18 years after 14 days when compared to individuals who received at least one BA.4/5 bivalent dose (iVE: 48%) and when compared to individuals who received at least two doses of wild-type vaccine only (iVE: 45%) while omicron sublineages were predominant (primarily XBB, EG.5.1 and JN.1).

*XBB.1.5 vaccination **vs.** no COVID-19 vaccination*

- One retrospective cohort study from the US was included
  - One study (Andersen et al. (2025)) found that that the Pfizer-BioNTech XBB1.5-adapted vaccine offered some protection against COVID-related ED and UC visits in adults aged ≥18 years after 14 days (aVE: 39%) when compared to those who had never had a vaccine while omicron sublineages were predominant (primarily XBB, EG.5.1 and JN.1).

COVID-19-related hospitalisations

*XBB.1.5 vaccination **vs.** no XBB.1.5 vaccination*

As shown in **Figure 2**, overall, in the early (ca. 1-13 weeks) post vaccination period, incremental vaccine effectiveness [iVE] is generally between 45 and 55%. In the mid (ca. 8-26 weeks) post vaccination period, iVE drops slightly to around 45%. There is no consistent difference between younger (< 65 years) and older (≥ 65 years) adults, though it should be noted that there are limited studies that directly compare these groups and few studies that report on younger adults.

- Eight test-negative case-control studies (four from the US, one from England, one from South Korea one from Canada, and one multi-country study from Europe) were included.
  - One US study (Caffrey et al. (2024)) found that adults aged ≥18 years who had received the Pfizer-BioNTech XBB.1.5 vaccine had a median 53-day iVE of 43% for COVID-19-related hospitalisations, compared with those who had not received any XBB.1.5 vaccine (including unvaccinated individuals). Individuals with immunocompromising conditions had a lower iVE vs. those who did not have immunocompromising conditions (33% vs. 49%). iVE was lower in older individuals compared to young individuals (18-64 years = 58% vs. ≥65 years = 41%). In addition, the vaccine seemed to provide notably better protection against XBB sublineages vs. JN.1 sublineages (14-60 day iVE = 62% vs. 32%). When compared to individuals who did not receive the XBB.1.5 variant-adapted vaccine but received at least one BA.4/5 bivalent dose or receive 3 or more doses of original wild-type mRNA but no bivalent adapted vaccine, the iVE was 45% and 56%, respectively.
  - One study from Canada (Carazo et al. (2024)) found that, during the periods of high XBB predominance, older adults aged ≥60 years who received the mRNA XBB.1.5 variant adapted

vaccine were less likely to be hospitalised due to COVID-19 than those who did not (>7 days iVE = 54%). There seemed to be a slight improvement in the iVE from the first 30 days to the second 30 days (7-30 day iVE = 53%, 31-60 day iVE = 60%). There also seemed to be a marginal benefit in older individuals (≥70 years) compared to those between 60-70 years. During the high JN.1 predominance period, older adults aged ≥60 years individuals who received the mRNA XBB.1.5 variant adapted vaccine were still somewhat protected, after at least 7 days (iVE: 30.8%). During the high KP predominance period, older adults aged ≥60 years individuals who received two doses of mRNA XBB.1.5 variant adapted vaccine had no noted benefit against COVID-19 hospitalisations compared to individuals who did not get the vaccine (iVE: -1%).

- One US study (DeCuir et al. (2024)) found that the mRNA and Novavax XBB.1.5 variant-adapted vaccines provided protection against COVID-19-related hospitalisation in immunocompetent adults aged ≥18 years after receiving the vaccine, compared to those who did not receive the XBB.1.5 variant-adapted vaccine (including unvaccinated individuals), but that this protection diminished slightly over time (median 32 day iVE = 53% vs. median 73 day iVE = 50%) while omicron sublineages were predominant (primarily XBB, EG.5.1 and JN). In general, there were no differences in iVE by age group (e.g., iVE at median 74 days = 18-64 years: 45% vs. ≥65 years: 50%), though older adults had a 5-12% greater iVE than younger adults.
- One study from England (Kirsebom et al. (2024)) found that XBB.1.5 variant-adapted vaccines provided protection against COVID-related hospitalisations in adults aged ≥65 years, compared to those who did not receive the XBB.1.5 variant-adapted vaccine (including unvaccinated individuals). The 9-13 day post-vaccination iVE was 37%, increasing to around 55% 14-28 days post-vaccination, and then dropping to 42% at 64-98 days post-vaccination while omicron sublineages were predominant (primarily XBB, JN, EG.5.1 and BA).
- One study from six university hospitals in South Korea (Lee et al. (2024)) found that adults aged ≥18 years who had received an mRNA XBB.1.5 COVID-19 vaccine were less likely to be hospitalised because of COVID-19 compared with those who had not received the XBB.1.5 COVID-19 vaccine. The authors found a moderate level of protection 7-59 days post vaccination (iVE= 64.3%) while omicron sub variants were predominant (primarily XBB, EG.5.1, HK.3 and JN). The iVE was slightly higher in older adults (≥65 years = 66.5%)
- One US study (Link-Gelles et al. (2024)) found that the mRNA and Novavax XBB.1.5 variant-adapted vaccines provided some protection against COVID-related hospitalisations in adults aged ≥18 years with immunocompromising conditions ≥7 days after receiving the vaccine (iVE=36%), compared to those who did not receive the XBB.1.5 variant-adapted vaccine (including unvaccinated individuals) while the omicron XBB sublineages and JN.1 were predominant. The level of iVE seemed to be stable up to 119 days post vaccination (7–59-day iVE = 38% and 60-119 days iVE = 34%).
- One study from Belgium, Germany, Italy, and Spain (Nguyen et al. (2025)) found that in adults aged ≥18 years old, the Pfizer-BioNTech XBB1.5-adapted vaccine offered moderate protection against COVID-19-related hospitalisations ≥14 days after vaccination (median 63 day iVE= 53.8%) when compared to individuals who had not received an XBB.1.5 variant-adapted vaccine during the JN.1 predominance period. The iVE was similar in individuals who had immunocompromising conditions or had cancer (iVE= 56.0%) and varied slightly with age: 18 to <65 years (56.5%), 65 to 79 years (62.5%) and ≥80 years (48.8%). The protection was still moderate after 120 days in adults aged ≥18 years (median 126 day iVE= 59.5%). The iVE for individual who were previously infected and for those who were not was 58% vs 54%, respectively.
- One US study (Tartof et al. (2024)) found that adults aged ≥18 years who had received the Pfizer-BioNTech XBB.1.5 COVID-19 vaccine had a 14-60 day iVE of 50% for COVID-19-

related hospitalisations during the JN.1 sublineage dominant period. Protection remained relatively stable between 60 and 156 days post vaccination (iVE = 57%) compared with those who had not received any XBB.1.5 vaccine (including unvaccinated individuals). During the XBB sublineage predominant period, the iVE was 74% 14-60 days post vaccination.

- Five retrospective cohort studies from the US were included.
  - One study (Andersen et al. (2025)) found that that the Pfizer-BioNTech XBB1.5-adapted vaccine offered some protection against hospitalisation in adults aged ≥18 years after 14 days (iVE = 36%) while omicron sublineages were predominant (primarily XBB, EG.5.1 and JN.1). The protection was slightly higher in older adults (≥65 years) with an iVE of 47%.
  - One study that used an emulated RCT (Ioannou et al. (2025)) found that the mRNA XBB.1.5 variant-adapted vaccine offered some protection against COVID-19 related hospitalisations in adults 18-64 years, 65-74 years, and ≥75 years (iVEs=29.7%, 15.7%, and 14.4%, respectively) when measured at least 10 days post vaccination while omicron sublineages were predominant (primarily XBB, EG.5.1 and JN). The protection offered by the vaccine in all adults (≥18 years) tended to wane overtime, 60 day iVE = 37.6% vs. 120 day iVE = 16.6%.
  - One study (Kopel et al. (2024)) found that the Moderna mRNA XBB.1.5 variant-adapted vaccine offered a moderate level of protection against COVID-19 related hospitalisations in adults (iVE=60.2%) and in adults with medical conditions (iVE=58.7%) when measured at least 7 days post vaccination while omicron sublineages were predominant (primarily XBB, EG.5.1 and JN). The protection offered by the vaccine did not differ with age (≥18 years: 58.7%, ≥50 years: 61.1%, and ≥65 years: 60.5%).
  - One study (Lin et al. (2024)) reported on individuals of all ages living in the US. Overall, the XBB.1.5 variant-adapted vaccine offered greater protection against the XBB.1.5 variant (iVE at 28-34 days: 73.7%) than the JN.1 variant (iVE at 28-34 days: 60.1%) when compared to individuals who had not received the XBB.1.5 variant-adapted vaccine. The study also found that protection waned over time and that it took four weeks to reach peak protection.
  - One study (Wilson et al. (2024)) found that the Moderna mRNA XBB.1.5 variant-adapted vaccine offered a moderate level of protection against COVID-19 related hospitalisations in adults ≥18 years (median 84 day iVE=51%) when compared to individuals who have not received the XBB.1.5 variant adapted vaccine while omicron sublineages were predominant (primarily XBB, EG.5.1 and JN.1). The iVE was similar in all age groups, reaching 51% in individuals aged 18-49 years, 47% in individuals aged 50 to 64 years and 56% in individuals aged ≥65 years after at least 8 days. A similar iVE (46%) was observed for individuals with immunocompromising conditions after at least 8 days.

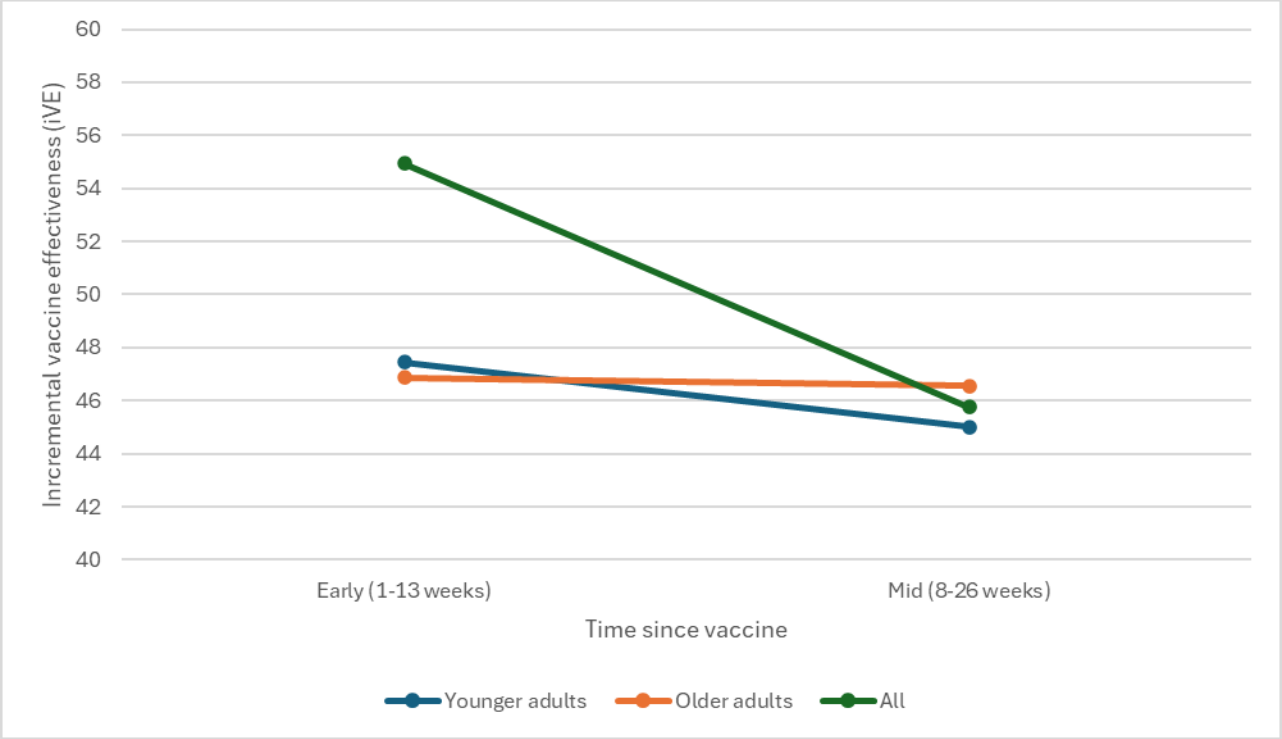

Figure 2: A visual representation of the trend in incremental vaccine effectiveness (iVE) for **COVID-19-related hospitalisations** of the XBB.1.5-adapted COVID-19 vaccine over time (comparator = those who did not receive the XBB.1.5 vaccine, including unvaccinated individuals).

* The following categories consist of the data from 18 included studies: The early time period covers 7-91 days, as well as 7+ and 14+ days; the mid time period covers 44-179 days; the younger adults include those who are 18-64; and the older adults include those who are ≥50. A simple averaging of data was applied across studies.

*XBB.1.5 vaccination **vs.** bivalent vaccine but no XBB.1.5 vaccination*

- Five studies found that individuals who had received the XBB.1.5 COVID-19 vaccine were less likely to be hospitalised for COVID-19 compared with those who had not received the XBB.1.5 vaccine.
    - One retrospective cohort study from the US (Andersen et al. (2025)) found that that the Pfizer-BioNTech XBB1.5-adapted vaccine offered some protection against COVID-related hospitalisation in adults aged ≥18 years after 14 days when compared to individuals who received at least one BA.4/5 bivalent dose (iVE: 40%) while omicron sublineages were predominant (primarily XBB, EG.5.1 and JN).
    - One test-negative case control study from Canada (Lee et al. (2024)) found that the mRNA XBB.1.5 variant-adapted vaccines offered a moderate level of protection against COVID-19-related hospitalisations 91-182 days after (iVE= 43%) during the JN an KP predominance period when compared to individuals who had not received an XBB.1.5 variant-adapted vaccine but received at least one bivalent mRNA vaccine.
    - One retrospective cohort study (Hansen et al. (2024)) of individuals aged ≥65 years in Denmark found a high level of protection ≥7 days post mRNA XBB.1.5 vaccination during XBB sublineage and EG.5.1 predominance (iVE = 76.1%) when compared to individuals who had not received an XBB.1.5 variant-adapted vaccine but previously received the seasonal booster the previous winter (2022/2023).
    - One test negative case-control study from Belgium, Germany, Italy, and Spain (Nguyen et al. (2025)) found that in adults aged ≥18 years old, the Pfizer-BioNTech XBB1.5-adapted vaccine offered moderate protection against COVID-19-related hospitalisations ≥14 days after (iVE=

61.0%) when compared to individuals who had not received an XBB.1.5 variant-adapted vaccine but received at least one BA.4/5 bivalent dose during the JN.1 predominance period.

- One test-negative case-control study (UK Health Security Agency (2024)) conducted among individuals aged ≥65 years in England found consistent levels of protection between 14 and 63 days post Pfizer-BioNTech XBB.1.5 vaccination during XBB sublineage predominance (iVE = 50.9-55.4%) when compared to individuals who had not received an XBB.1.5 variant-adapted vaccine but previously received at least one BA.1 bivalent dose .

*XBB.1.5 vaccination **vs.** variations in previous vaccination regimens*

- Four test-negative case-control studies (two from Canada, one from South Korea, and one multi-country study from Europe) found that individuals who had received the XBB.1.5 COVID-19 vaccine were less likely to be hospitalised for COVID-19 compared with those who had not received the XBB.1.5 vaccine.
    - One study from Canada (Carazo et al. (2024)) found that, during XBB predominance older adults aged ≥60 years who received the mRNA XBB.1.5 variant adapted vaccine were less likely to be hospitalised due to COVID-19 than individuals who did not but received an ancestral mRNA monovalent or bivalent vaccine dose during Quebec's prior vaccination campaign from July to December 2022, after at least 7 days (iVE: 54%). The protection was lower in younger individuals than in older individuals (60-69 years: 48% vs. 70-79 years: 56% vs. ≥ 80 years: 55%) and was slightly higher in individuals who had a prior infection (iVE: 73.6%). During JN.1 predominance, older adults aged ≥60 years who received the mRNA XBB.1.5 variant adapted vaccine were still somewhat protected, after at least 7 days (iVE: 23%). The protection was lower in younger individuals than in older individuals with (60-69 years: -7% vs. 70-79 years: 26% vs. ≥ 80 years: 29%) and was slightly higher in individuals who had a prior infection (iVE: 41%). The protection waned over time. During KP.2/KP.3 predominance, older adults aged ≥60 years who received two doses of mRNA XBB.1.5 variant adapted vaccine were less likely to be hospitalised due to COVID-19 than individuals who only received an ancestral mRNA monovalent or bivalent vaccine dose during Quebec's prior vaccination campaign from July to December 2022, after at least 7 days (iVE: 39%). This was not the case for those who received one dose (iVE: -4%); however, after 7 to 60 days, individuals who received one or two doses of XBB.1.5 variant adapted vaccine had an iVE of 70% and 57%, respectively. The effectiveness waned over time and was slightly lower in younger individuals than older individuals after 7 to 60 days (60-69 years: 53% vs. 70-79 years: 56% vs. ≥ 80 years: 63%).
    - One study from Canada (Lee et al. (2024)) found that the mRNA XBB.1.5 variant-adapted vaccines offered a moderate level of protection against COVID-19-related hospitalisations 91-182 days after vaccination (iVE= 44%) during the JN and KP predominance period when compared to individuals who had not received an XBB.1.5 variant-adapted vaccine but received at least two doses of a non XBB.1.5 mRNA vaccine. This effect waned after 183-274 days (iVE: 21%). When compared to individuals who did not receive an XBB.1.5 variant-adapted vaccine but received an original monovalent XBB.1.5 vaccine, iVE was 53%.
    - One study from six university hospitals in South Korea (Lee et al. (2024)) found that adults aged ≥18 years who had received an mRNA XBB.1.5 COVID-19 vaccine and at least one previous COVID-19 vaccine dose were less likely to have a medically attended infection compared with those who had not received the XBB.1.5 COVID-19 vaccine but had received at least one dose of a COVID-19 vaccine. The authors found a moderate level of protection 7-59 days post vaccination (iVE= 61.2%) while omicron sub variants were predominant (primarily XBB, EG.5.1, HK.3 and JN.1). The iVE was slightly higher in older adults (≥65 years = 64.1%). The protection was also higher in individuals with immunocompromising conditions (iVE= 79.4%) than in those without (iVE= 56.4%).

- One study from Belgium, Germany, Italy, and Spain (Nguyen et al. (2025)) found that in adults aged ≥18 years old the Pfizer-BioNTech XBB1.5-adapted vaccine offered moderate protection against COVID-19-related hospitalisations ≥14 days after vaccination (rVE= 48.8%) when compared to individuals who had not received an XBB.1.5 variant-adapted vaccine but received two mRNA wild-type doses only during the JN.1 predominance period.

- Six retrospective cohort studies (two from the US, one from Singapore, and three multi-country studies) also found that individuals who had received the XBB.1.5 COVID-19 vaccine were less likely to be hospitalised for COVID-19 compared with those who had not received the XBB.1.5 vaccine.
  - One study from the US (Andersen et al. (2025)) found that that the Pfizer-BioNTech XBB1.5-adapted vaccine offered some protection against COVID-related hospitalisation in adults aged ≥18 years after 14 days when compared to individuals at least two doses of wild-type vaccine only (iVE: 34%) while omicron sublineages were predominant (primarily XBB, EG.5.1 and JN.1).
  - A multicounty European study (Andersson et al. (2024)) of older individuals (≥65 years) found that the mRNA XBB.1.5 variant-adapted vaccines provided additional protection 8-168 days post-vaccination compared to having had four (rVE=55%), five (rVE=57%), or six (rVE=57%) prior doses of a non-XBB.1.5 variant-adapted vaccine while omicron sublineages were predominant (primarily XBB, EG.5.1, HK.3 and JN.1). The iVE was 75% and 56% during the XBB and BA.2.86 sublineages predominance, respectively in individuals who received at least 4 doses of a non-XBB.1.5 variant-adapted vaccine.
  - The Chong et al. (2024) study from Singapore found an iVE of 42% against the JN.1 variant 8 to 120 days after the receival of an mRNA XBB.1.5 variant-adapted vaccine in individuals who received at least two previous mRNA doses when compared to individuals who have also received at least three mRNA vaccine doses but no XBB.1.5 variant-adapted vaccine.
  - One study from the US (Ioannou et al. (2025)) found that mRNA XBB.1.5 variant adapted vaccine provides some protection against COVID-19 related hospitalisation with an iVE of 38% after 60 days which waned over time while omicron sublineages were predominant (primarily XBB, EG.5.1 and JN). The iVE was lower in older individuals than in younger individuals (18 to 64 years: 29.7% vs ≥75 years: 14%).
  - A multinational study by (Monge (2024)) found that mRNA XBB.1.5 variant adapted vaccine provides a moderate level of protection against COVID-19 related hospitalisation in older individuals after 14 days when compared to individuals who have received at least a complete primary series (iVE: 65-79 years: 67% vs. ≥80 years: 66%) while omicron sublineages were predominant (primarily XBB, EG.5.1, BA.2.86 and JN.1).
  - A multi-country European study by Nunes et al. (2024) found an iVE of any XBB.1.5 vaccine (>95% Pfizer-BioNTech) of 50.2% in 65-79 year olds and 40.7% in ≥80-year-olds after at least 14 days when compared to individuals who had received at least two COVID-19 vaccine doses while BA.2.86 and JN.1 sublineages were predominant. The protection waned over time and was lower for older individuals.

XBB.1.5 vaccination ***vs.*** *no COVID-19 vaccination*

- Four test-negative case-control studies found that individuals who had received the XBB.1.5 COVID-19 vaccine were less likely to be hospitalised for COVID-19 compared with those who had not received any COVID-19 vaccines.
  - One study from Canada (Carazo et al. (2024)) found that in older adults aged ≥60 years individuals who received the mRNA XBB.1.5 variant adapted vaccine were less likely to be hospitalised due to COVID-19 than unvaccinated individuals after at least 7 days (aVE: 30%) while omicron subvariants were predominant (primarily XBB, EG.5.1, HK.3 and JN.1). During the XBB predominance, older adults aged ≥60 years who received the mRNA XBB.1.5 variant

adapted vaccine were less likely to be hospitalised due to COVID-19 after at least 7 days (aVE: 54%). During JN.1 predominance, older adults aged ≥60 years who received the mRNA XBB.1.5 variant adapted vaccine were still somewhat protected, after at least 7 days (aVE: 30.8%). This was not the case during KP.2/KP.3 predominance (aVE: 7%).
    - One study from six university hospitals in South Korea (Lee et al. (2024)) found that adults aged ≥18 years who had received an mRNA XBB.1.5 COVID-19 vaccine were less likely to be hospitalised due to COVID-19 compared with those who never received a COVID-19 vaccine. The authors found a good level of protection 7-59 days post vaccination (aVE= 77.3%) while omicron subvariants were predominant (primarily XBB, EG.5.1, HK.3 and JN.1). The aVE was slightly lower in older adults (≥65 years = 72.8%).
    - One study from Belgium, Germany, Italy, and Spain (Nguyen et al. (2025)) found that in adults aged ≥18 years, the Pfizer-BioNTech XBB1.5-adapted vaccine offered some protection against COVID-19-related hospitalisations after ≥14 days (aVE= 51.1%) when compared to individuals who never received a COVID-19 vaccine during the JN.1 predominance period.
- One retrospective cohort study from the US was included.
    - One study (Andersen et al. (2025)) found that that the Pfizer-BioNTech XBB1.5-adapted vaccine offered some protection against COVID-related hospitalisations in adults aged ≥18 years after 14 days (aVE: 33%) while omicron sublineages were predominant (primarily XBB, EG.5.1 and JN.1).

COVID-19-related emergency department (ED) / urgent care (UC) visits or hospitalisations

*XBB.1.5 vaccination **vs.** no XBB.1.5 vaccination*

- One test-negative case-control study from the US was included.
    - One study (Tartof et al. (2024)) found that the Pfizer-BioNTech XBB1.5-adapted vaccine provided a moderate level of protection after 14 days against COVID-related ED and UC visits and hospitalisations in children aged 5 to 17 years when compared to individuals who have not received an XBB.1.5 variant adapted vaccine (iVE: 65%) while omicron sublineages were predominant (primarily XBB, EG.5.1 and JN.1). The level of protection was similar in older and younger children (12-17 years: 63% vs. 5-11 years: 68%).

COVID-19-related intensive care unit (ICU) admissions

- There were no studies which reported data for this outcome.

COVID-19-related deaths

As shown in **Figure 3**, in the early (ca. 1-13 weeks) post vaccination period, overall incremental vaccine effectiveness [iVE] is generally between 60 and 65%. In the mid (ca. 10-20 weeks) post vaccination period, there is a notable drop in protection to 30-35%. There were no available data for a younger population (18-64 years). These patterns need to be interpreted with caution given the limited available data (e.g., there is only one study in the general population).

*XBB.1.5 vaccination **vs.** no XBB.1.5 vaccination (including individuals who had not received any COVID-19 vaccine)*

- One retrospective cohort study in the US reported on this outcome.
    - (Lin et al. (2024)) reported on individuals of all ages living in the US. Overall, the mRNA XBB.1.5 variant-adapted vaccines offered greater protection against the XBB.1.5 variant (iVE at 28-34 days = 86.2%) than the JN.1 variant (iVE at 28-34 days = 59.8%) when compared to individuals who had not received the XBB.1.5 variant-adapted vaccine. The study also found that the iVE waned overtime and took a few weeks before reaching peak protection at week 4.

*XBB.1.5 vaccination **vs.** at least 4 prior doses*

- One retrospective cohort study from Europe reported on this outcome.
    - A multicountry European study (Andersson et al. (2024)) of older individuals (≥65 years) found that the XBB.1.5 variant-adapted vaccine provided additional protection against COVID-19-related mortality 8-168 days post vaccination compared to having received at least four prior doses of COVID-19 vaccine (iVE = 75%). iVE slowly declined across the post-vaccination period (8–27-day iVE = 82% and 70-90 days iVE = 70%) while omicron sublineages were predominant (primarily XBB, EG.5.1, HK.3 and JN.1). The iVE was 86% and 78% during XBB and BA.2.86 predominance, respectively.

*XBB.1.5 vaccination **vs.** variations in previous vaccination regimens*

- Five retrospective cohort studies (three European, one from Australia, and one from the US) reported on this outcome.
    - A European study (Andersson et al. (2024)) found that the XBB.1.5 variant-adapted vaccine provided additional protection against COVID-19-related mortality 8-168 days post-vaccination compared to having had four (rVE=75%), five (rVE=76%), or six (rVE=66%) prior doses of a non-XBB.1.5 variant-adapted vaccine while omicron sublineages were predominant (primarily XBB, EG.5.1, HK.3 and JN.1).
    - A study using an emulated RCT design from the US (Ioannou et al. (2025)) found that, in individuals aged ≥18 years who received at least one prior dose of earlier formulation COVID-19 vaccine, an mRNA XBB.1.5 variant-adapted vaccine offered additional protection against COVID-19-related mortality after at least 10 days in 18 to 64 years old (iVE: 84%). The protection was lower in older individuals (65 to 74 years: 27%, ≥75 years: 23%) and waned over time, going from 54% after 60 days to 27% at the end of the study in individuals aged ≥18 years.
    - An Australian study (Liu et al. (2024)) found that in individuals aged ≥65 years who received at least one COVID-19 vaccine booster dose, an mRNA XBB.1.5 variant-adapted vaccine offered additional protection against COVID-19-related mortality 8-90 days post vaccination (iVE= 74.7%) compared to having received a booster vaccine at least one year earlier and no XBB.1.5 vaccine. The protection offered did not differ during the JN.1 period (iVE= 74.6%) and was slightly higher in older individuals ≥75 years (iVE= 76.7%).
    - A multinational European study (Monge et al. (2024)) found that in individuals aged ≥65 years who completed at least a primary series, an mRNA XBB.1.5 variant-adapted vaccine offered additional protection against COVID-19-related mortality after at least 14 days, reaching an iVE of 67% and 72% in younger (65 to 79 years) and older (≥ 80 years) individuals, respectively.
    - A multi-country European study by Nunes et al. (2024) found an iVE of 57.5% in individuals 65-79 years old and 48.4% in individuals ≥80 years old after at least 14 days when compared to individuals who had received at least two COVID-19 vaccine doses while BA.2.86 and JN.1 sublineages were predominant. This protection waned over three to six months and was lower for older individuals.

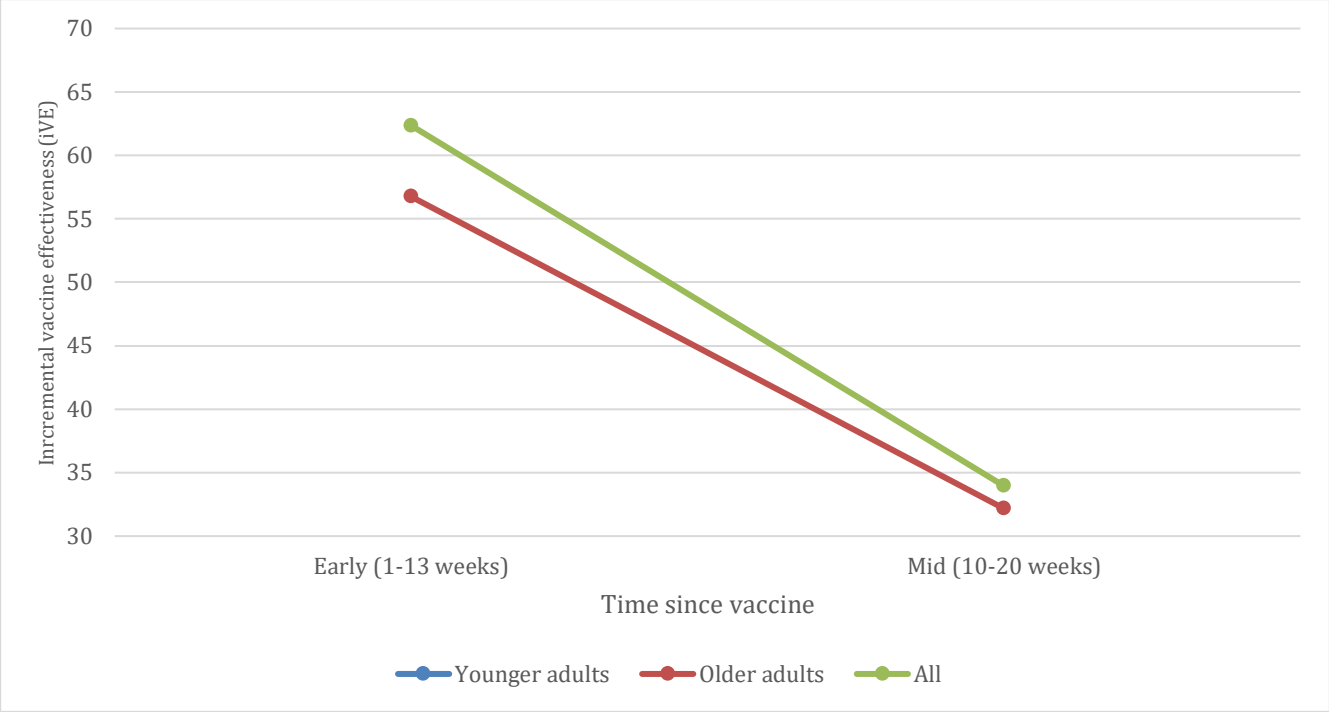

Figure 3: A visual representation of the trend in incremental vaccine effectiveness (iVE) for **COVID-19-related deaths** of the XBB.1.5 adapted COVID-19 vaccine over time (comparator = those who did not receive the XBB.1.5 vaccine, including unvaccinated individuals).

* The following categories consist of the data from 6 included studies: The early time period covers 8-91 days; the mid time period covers 71-139 days; the older adults include those who are ≥65, there was one study of younger adults (18-64), which found a ≥10 day post-vaccination iVE = 83.6%. A simple averaging of data was applied across studies.

Multisystem inflammatory syndrome in children (MIS-C)

- There were no studies that reported data for this outcome.

Post-COVID Conditions

- There were no studies that reported data for this outcome.

Impact of the 2024/2025 variant-adapted COVID-19 vaccine on symptomatic and medically attended COVID-19 infections compared to no 2024/2025 variant-adapted COVID-19 vaccine

- Two test-negative case control studies from the US reported on this outcome.
    - One study in adults aged ≥18 years (Appaneal et al. (2024)) found that the Pfizer-BioNTech KP.2 variant-adapted vaccine provided a moderate level of protection against medically attended infections at a median of 31 days post vaccination (iVE: 56%) while Omicron KP.2, KP.3, JN.1, and XEC were the predominant variants. The protection level was similar in individuals aged ≥65 years (iVE: 58%).
    - One study in adults aged ≥18 years (Rudolph et al. (2024)) found that the Pfizer-BioNTech KP.2 variant-adapted vaccine provided a moderate level of protection against medically attended infections at least 14 days post vaccination (iVE: 48%) while Omicron KP.2, KP.3, JN.1, and XEC were the predominant variants. The protection level slightly decreased with age; individuals aged 18-49 years had the highest protection (iVE: 59%) and individuals aged ≥65 years, the lowest (iVE: 24%).

Impact of the 2024/2025 variant-adapted COVID-19 vaccine on COVID-related ED or UC visits compared to no 2024/2025 variant-adapted COVID-19 vaccine

- One test negative case control study from the US in adults aged ≥18 years (Appaneal et al. (2024)) found that the Pfizer-BioNTech KP.2 variant-adapted vaccine provided a moderate level of protection against COVID-19 related ED or UC visits at a median of 35 days post vaccination (iVE: 57%) while Omicron KP.2, KP.3, JN.1, and XEC were the predominant variants.
- One retrospective cohort from the US (Link-Gelles et al. (2025)) found that in adults aged ≥18 years the Pfizer-BioNTech KP.2 variant-adapted vaccine provided some level of protection against COVID-19 related ED or UC visits at a median of 55 days post-vaccine (iVE: 33%) while Omicron KP.2, KP.3, JN.1, and XEC were the predominant variants. The protection waned slightly with time but did not seem to vary much with age.

Impact of the 2024/2025 variant-adapted COVID-19 vaccine on hospitalisations related to COVID-19 compared to no 2024/2025 variant-adapted COVID-19 vaccine

- One test-negative case control study in adults aged ≥18 years from the US (Appaneal et al. (2024)) found that the Pfizer-BioNTech KP.2 variant-adapted vaccine provided a moderate level of protection against COVID-19 related hospitalisation at a median of 30 days post vaccination (iVE: 57%) while Omicron KP.2, KP.3, JN.1, and XEC were the predominant variants. The protection level was similar in individuals aged ≥65 years (iVE: 56%).

Potential implications for health systems decision-making

The limited initial evidence from seven studies from different countries, including one study from Canada, suggests a **moderate benefit of the XBB.1.5 vaccine** against COVID-19-related **medically attended infections**, which tends to wane over time. The raw average iVE was around 48% during the early phases post vaccination (up to 11 weeks), with younger patients seeming to have better protection than older adults. However, there was a reduction in effect during the mid-term post vaccination period (up to 17 weeks), with a reduction to around 34-38%, with consistency between age groups.

The initial evidence from 18 studies from a variety of different countries, including one study from Canada, suggests a **moderate benefit of the XBB.1.5 vaccine** against COVID-19-related **hospitalisations**. Initial iVE was around 45-55% (up to 13 weeks post-vaccination) which dropped to about 45% (up to 26 weeks post-vaccination). Overall, there seemed to be no differences between younger and older adults.

The limited initial evidence from six studies from a variety of different countries (though there was no Canadian data) suggests a **moderate-to-strong initial benefit of the XBB.1.5 vaccine** against COVID-19-related **deaths**. Initial iVE was around 55-65% (up to 13 weeks post-vaccination). However, there was a drastic drop in effectiveness over time with an iVE of ca. 33% by 20 weeks post vaccination. It should be noted that there was only one study which assessed younger adults (18-65 years), finding that the iVE against COVID-19 related deaths was 83.6% (data was from 10+ days post vaccination).

These findings were relatively consistent regardless of the comparator group, meaning that the XBB.1.5 vaccines seem to provide notable benefit no matter what an individual's previous vaccination or infection pattern is. Unsurprisingly, there may be additional benefit against XBB sublineages vs. JN.1 sublineages, with a poorer performance than for the KP sublineages, though there is limited comparative data.

As such, **this initial evidence supports the use of the XBB.1.5 vaccine** to protect all age groups against **COVID-19-related medically attended infections, hospitalisations, and deaths**. However, the notable drops in effectiveness in medically attended infections and death by around 16-20 weeks might suggest that **additional doses could be needed** in that time window.

The **limited evidence around the KP.2 vaccine** seems to be aligned with that of the XBB.1.5 vaccine, where there is early protection against **COVID-19-related medically attended infections and hospitalisations.** However, more studies and longer follow-up are need to see if there is consistency in the finding and how long this protection might last.

Though positive, it should be noted that this data is drawn from only a small number of studies, all with slightly different methodologies, and most of which were not conducted in Canada. Also, these were not randomised controlled studies, so individuals chose to get vaccinated. It is possible that those individuals may have engaged in more COVID-19 preventative behaviours (e.g., wearing masks, physical distancing, hand washing, etc.), so we can't be sure that the benefits of the XBB.1.5 vaccine or the KP.2 vaccine were totally due to the vaccine and not these other factors.

Visual representation of data

- For Tables 1 through 9 **the number** indicates the *level of effectiveness* of the XBB.1.5 COVID-19 vaccine compared to individuals who did not receive the vaccine. A value of 0% indicates no protection and a value of 100% indicates that the vaccine maximally prevents COVID-19 outcomes (e.g., hospitalisations).
- **Colour** indicates **Level of Certainty** based on the evidence (see note after the table about colourations of previous versions).
- In all tables, **days** refers to time since the administration of the vaccine.

High certainty evidence	Moderate certainty evidence	Low certainty evidence	Not enough evidence
Pooling of sufficient observational studies (including RCTs with follow-up data) with consistent findings	Pooling of sufficient observational studies (including RCTs with follow-up data) with some consistency in findings	Pooling of sufficient observational studies (including RCTs with follow-up data) but *inconsistent* findings	Pooling of insufficient observational studies (including RCTs with follow-up data) to be able to draw conclusions
At least 10 cohorts represented with at least one CI within 10% of the point estimate	At least 4 cohorts represented with at least one CI within 15% of the point estimate	At least 4 cohorts represented	Less than 4 cohorts reported

Question 1: Impact of the XBB.1.5 COVID-19 vaccine on symptomatic and medically attended COVID-19 infections

Table 1: VE of the XBB.1.5 variant-adapted COVID-19 vaccine against symptomatic and medically attended COVID-19 infections compared with those who have not received the XBB.1.5 variant-adapted COVID-19 vaccine (n=7).

Author (date) - Country Type of publication	Population	Predominant variant	Intervention	Comparator group (reference)	Time since last dose (days)	VE (%) (95% CI)
Test-negative case control						
Caffrey et al. (2024) – United States Peer-reviewed	113,174 respiratory infection episodes in adults aged 18+ and diagnosed with an acute respiratory infection in hospital, emergency department, urgent care or outpatient setting from the US Veterans Affairs Healthcare system	Omicron (primarily XBB and JN.1 sublineages)	Received a Pfizer-BioNTech XBB1.5-adapted vaccine	Did not receive the XBB.1.5 variant-adapted vaccine (includes unvaccinated individuals)	Median (IQR): 56 (36-76)	**Medically attended infections:** ≥18 years: 27 (16-37)
					Median (IQR): 55 (35-74)	**Medically attended infections:** Immunocompromised: 40 (19-55)
					Median (IQR): 56 (36-77)	**Medically attended infections:** Immunocompetent: 22 (8-34)
					Median (IQR): 54 (35-74)	**Medically attended infections:** 18 to 64 years: 34 (14-50)
					Median (IQR): 56 (36-77)	**Medically attended infections:** ≥65 years: 24 (9-36)
		XBB sublineages and JN.1			Median (IQR): 53 (38-67)	**Medically attended infections:** ≥18 years: 29 (9-44)
		XBB sublineages			Median (IQR): 31 (22-40)	**Medically attended infections:** ≥18 years: 51 (27-67)

					14 to 60	**Medically attended infections:** ≥18 years: 50 (25-66)
		JN.1			14 to 60	**Medically attended infections:** ≥18 years: 31 (1-52)
					61 to 133 days	**Medically attended infections:** ≥18 years: 20 (-4-38))
					Median (IQR): 75 (55-90)	**Medically attended infections:** ≥18 years: 24 (5-39)
		Omicron (primarily XBB and JN.1 sublineages)		Did not receive the XBB.1.5 variant-adapted vaccine but received at least one BA.4/5 bivalent dose	At least 14 days	**Medically attended infections:** ≥18 years: 26 (11-39)
				Did not receive the XBB.1.5 variant-adapted vaccine but received 3 or more doses of original wild-type mRNA but no bivalent-adapted vaccines	At least 14 days	**Medically attended infections:** ≥18 years: 38 (11-57)
Lanièce Delaunay (2024) - Croatia, France, Germany, Hungary, Ireland, Portugal, The Netherlands, Romania, Spain, national, Spain, Navarre region, Sweden	Patients consulting their primary care physicians or paediatricians with acute respiratory infection (N=5,454)	Omicron (primarily XBB, EG.5.1 and JN.1)	Received an mRNA XBB.1.5 variant-adapted vaccine (mostly Pfizer-BioNTech)	Did not receive the XBB.1.5 variant-adapted vaccine (including unvaccinated individuals)	≥7	**Medically attended infections:** • ≥ 5 years: 40 (26-53) • <50-65 years: 59 (18-82) • >50-65 years: 37 (19-51)
					7 to 41	**Medically attended infections:**

Published						• ≥ 5 years: 48 (31-61) • <50-65 years: 69 (28-90) • >50-65 years: 45 (26-60)
					42 to 119	**Medically attended infections:** • ≥ 5 years: 29 (3-49) • <50-65 years: 28 (-128-84) • >50-65 years: 26 (-3-48)
					≥14	**Medically attended infections:** • ≥ 5 years: 40 (24-54) • <50-65 years: 70 (30-90) • >50-65 years: 36 (16-51)
					14 to 41	**Medically attended infections:** • ≥ 5 years: 51 (33-66) • >50-65 years: 45 (22-62)
					42 to 119 (when considering at least 14 days post vaccination)	**Medically attended infections:** • ≥ 5 years: 26 (-2-47) • <50-65 years: 21 (-150-82) • >50-65 years: 24 (-6-47)
		XBB.1.5			≥7	**Medically attended infections:** • ≥ 5 years: 50 (-17-82)

						• >50-65 years: 63 (6-88)
					7 to 41	**Medically attended infections:** • ≥ 5 years: 46 (-32-82) • >50-65 years: 63 (-2-90)
Lee et al. (2024) – South Korea Peer-reviewed	Adults aged ≥18 year who underwent PCR testing or rapid antigen testing in the emergency department, outpatient clinics, general wards, or intensive care units of each hospital were included in the study. (N=5,516)	Omicron (primarily XBB, EG.5.1, HK.3 and JN.1 sub variants)	Received an mRNA XBB.1.5 variant-adapted vaccine	Did not receive the XBB.1.5 vaccine (includes unvaccinated individuals)	7 to 59	**Medically attended infections** • ≥18 years: 57.7 (34.7-72.6) ≥ 65 years: 60.2 (35.6-75.4)
				Unvaccinated individuals	7 to 59	**Medically attended infections:** • ≥18 years: 65.2 (36.1-81.0) • ≥ 65 years: 67.2 (34.3-83.6)
					Median of 25.5	**Medically attended infections** • ≥18 years: 71.0 (44.6-84.8)
				Did not receive the XBB.1.5 vaccine but have received at least one dose of COVID-19 vaccine	7 to 59	**Medically attended infections** • ≥18 years: 55.6 (31.2-71.3) • Immunocompromised: 47.6 (-43.6-80.9) • Immunocompetent: 57.7 (31.0-74.1) • ≥ 65 years: 57.6 (30.9-74.0)

Link-Gelles et al. (2024) - US Peer-reviewed	≥18 years who had at least one symptom and had a COVID-19 test conducted at a participating CVS Pharmacy or Walgreens (N=9,222)	Omicron XBB sublineages and JN.1	Received an mRNA XBB.1.5 variant-adapted vaccine (Moderna, Pfizer-BioNTech or Novavax)	Did not receive the XBB.1.5 vaccine (includes unvaccinated individuals)	≥7	**Medically attended infections:** • ≥18 years: 54 (46-60) • 18-49 years: 57 (48-65) • ≥50 years: 46 (31-58)
					7-59	**Medically attended infections:** • ≥18 years: 58 (48-65) • 18-49 years: 64 (53-73) • ≥50 years: 45 (26-60)
					60-119	**Medically attended infections:** • ≥18 years: 49 (36-58) • 18-49 years: 48 (31-60) • ≥50 years: 47 (24-62)
Skowronski et al. (2024) – Canada Peer-reviewed	2,176 individuals with respiratory infection symptoms, aged 12+ and recruited from community-based sentinel practitioners (Canadian Sentinel Surveillance Network) in British Columbia, Ontario and Quebec	XBB sublineages, EG.5.1, HV.1, BA.2.75, BA.2.86 and JN.1	Received an mRNA XBB.1.5 variant-adapted vaccine (Moderna, Pfizer-BioNTech)	Did not receive the XBB.1.5 vaccine (includes unvaccinated individuals)	Median (IQR): 35 (21-49)	**Medically attended infections:** ≥12 years: 44 (14-63)
					Median (IQR): 42 (21-56)	**Medically attended infections:** 12-64 years: 46 (2-70)
					Median (IQR): 35 (21-56)	**Medically attended infections:** ≥65 years: 46 (-3-72)
			Received an mRNA XBB.1.5 variant-adapted vaccine (Moderna, Pfizer-BioNTech) and received their previous dose (non-XBB.1.5)	Did not receive the XBB.1.5 vaccine and received their last dose more than 12 weeks ago	Median (IQR): 35 (21-56)	**Medically attended infections:** ≥12 years: 41 (13-60)

			more than 12 weeks ago			
			Received an mRNA XBB.1.5 variant-adapted vaccine (Moderna, Pfizer-BioNTech) and received their previous dose (non-XBB.1.5) more than 24 weeks ago	Did not receive the XBB.1.5 vaccine and received their last dose more than 24 weeks ago	Median (IQR): 35 (21-56)	**Medically attended infections:** ≥12 years: 47 (21-65)
			Received an mRNA XBB.1.5 variant-adapted vaccine (Moderna, Pfizer-BioNTech) – Excluding influenza positive cases from the COVID-19 control group	Did not receive the XBB.1.5 vaccine – Excluding influenza positive cases from the COVID-19 control group (includes unvaccinated individuals)	Median (IQR): 35 (21-56)	**Medically attended infections:** ≥12 years: 54 (31-70)
			Received an mRNA XBB.1.5 variant-adapted vaccine (Moderna, Pfizer-BioNTech) and had a previous COVID-19 infection	Did not receive the XBB.1.5 vaccine and had a previous COVID-19 infection (includes unvaccinated individuals)	Median (IQR): 42 (21-56)	**Medically attended infections:** ≥12 years: 67 (28-85)

			Received an mRNA XBB.1.5 variant-adapted vaccine (Moderna, Pfizer-BioNTech) and had a previous COVID-19 infection – Excluding influenza positive cases from the COVID-19 control group	Did not receive the XBB.1.5 vaccine and had a previous COVID-19 infection – Excluding influenza positive cases from the COVID-19 control group (includes unvaccinated individuals)	Median (IQR): 42 (21-56)	**Medically attended infections:** ≥12 years: 72 (39-87)
*Tartof et al. (2023) – United States Preprint This outcome was not reported in the updated article Tartof et al. (2024)	≥18 years who have been at Kaiser Permanente Southern California (KPSC) for at least a year (N=24,007)	Omicron (primarily XBB, EG.5.1 and JN.1)	Received a BNT162b2 XBB1.5-adapted vaccine	Did not receive the XBB.1.5 vaccine (includes unvaccinated individuals)	Median (range): 30 (14 to 73)	**Medically attended infections:** • ≥18 years: 58 (34 to 73) • 18-64 years: 32 (-1 to 54) • ≥65 years: 68 (49 to 79)
				Received BA.4/5-adapted bivalent vaccine but no XBB1.5-adapted vaccine		**Medically attended infections:** • ≥18 years: 51 (32 to 65) • 18-64 years: 22 (-21 to 50) • ≥65 years:71 (53 to 82)
				≥3 doses of wild-type vaccine but no variant-adapted vaccines of any kind		**Medically attended infections:** • ≥18 years: 56 (40 to 67) • 18-64 years: 40 (10 to 60)

						• ≥65 years:65 (45 to 78)
				≥2 doses of wild-type vaccine but no variant-adapted vaccines of any kind		**Medically attended infections:** • ≥18 years: 54 (38 to 66) • 18-64 years: 35 (3 to 57) • ≥65 years: 67 (47 to 79)
				Unvaccinated		**Medically attended infections:** • ≥18 years: 43 (16 to 61) • 18-64 years: 17 (-33 to 48) • ≥65 years: 60 (13 to 82)
Retrospective cohort						
Wilson et al. (2024) - United States Peer-reviewed	Observational matched cohort of adults aged ≥ 18 years who had continuous medical and pharmacy enrollment (with 45-day allowable gaps) from 365 days prior to index date through cohort entry date	Omicron (primarily XBB, EG.5.1 and JN.1)	Received a Moderna mRNA XBB.1.5 variant-adapted vaccine	Did not receive any XBB.1.5 variant adapted vaccine (including unvaccinated individuals)	Median (IQR): 84 (58-101)	**Medically attended infections:** • ≥18 years: 25 (24-27)
					≥8	**Medically attended infections:** • Immunocompromised: 28 (25-30) • 18-49 years: 25 (23-27) • 50 to 64 years: 19 (16-22) • ≥65 years: 21 (18-24)

*The primary article presented outcomes in the form of odds ratio (OR) data, subsequently translated into vaccine effects (VE)

Table 2: VE of the XBB.1.5 variant-adapted COVID-19 vaccine against COVID-19 infections compared with those who have not received the XBB.1.5 variant-adapted COVID-19 vaccine (n=7).

Author (date) - Country Type of publication	Population	Predominant variant	Intervention	Comparator group (reference)	Time since last dose (days)	VE (%) (95% CI)
Prospective cohort						
Huiberts et al. (2024) – Netherlands Peer-reviewed This study was not included in the figure above as it reports on self-reported infections.	18- to 85-year-old community dwelling Dutch participating to the VAccine Study COvid-19 (VASCO) (N=23,895)	XBB sublineages and JN.1	Received a booster dose and a dose of the Pfizer-BioNTech XBB.1.5 variant-adapted vaccine	Received a booster dose but did not receive an XBB.1.5 variant-adapted vaccine	≥7	**Self-reported infections** • 18 to 59 years: 41.3 (22.6-55.5) • 60 to 85 years: 50.3 (43.8-56.1) **Self-reported symptomatic infections** • 18 to 59 years: 34.7 (10.4-52.4) • 60 to 85 years: 55.0 (47.6-61.4)
					7-42	**Self-reported infections** • 18 to 59 years: 40.2 (19.6-55.5) • 60 to 85 years: 52.1 (45.4-57.9)
					49-84	**Self-reported infections** • 18 to 59 years: 46.7 (-5.7-73.1) • 60 to 85 years: 40.6 (25.7-52.4)
			Didn't have any prior infection and received a booster dose and the	Did not have any prior infection and received a booster dose but	≥7	**Self-reported infections**

			Pfizer-BioNTech XBB.1.5 variant-adapted vaccine	did not receive an XBB.1.5 variant-adapted vaccine		• 18 to 59 years: 11.7 (-60.9-51.6) • 60 to 85 years: 48.8 (36.4-58.8)
			Had prior infection <1 year ago, received a booster dose and the Pfizer-BioNTech XBB.1.5 variant-adapted vaccine			**Self-reported infections** • 18 to 59 years 49.7 (22.8-67.2) • 60 to 85 years: 67.7 (61.2-73.1)
			Had prior infection > 1 year ago, received a booster dose and the Pfizer-BioNTech XBB.1.5 variant-adapted vaccine			**Self-reported infections** • 18 to 59 years: 86.7 (68.7 (94.3) • 60 to 85 years: 85.3 (80.6-88.9)
			Received an mRNA booster dose and a dose of the Pfizer-BioNTech XBB.1.5 variant-adapted vaccine	Received an mRNA booster dose but did not receive an XBB.1.5 variant-adapted vaccine		**Self-reported infections** • 18 to 59 years: 44.6 (25.0-59.1) • 60 to 85 years: 51.4 (44.3-57.6)
Kirwan et al. (2024) - United Kingdom Peer-reviewed This study was not included in the figure above as it reported on positive PCR test regardless of the	Health care workers of the NHS, part of the SIREN study, who received their last COVID-19 booster more than 6 months ago, contributed at least 2 PCR tests to the study and did not receive more than 5 COVID-19 doses.	Omicron (primarily XBB, JN.1, EG.5.1 and BA)	Received the XBB.1.5 variant-adapted vaccine and at least one previous booster (maximum of 5 previous COVID-19 vaccine doses)	Received at least one booster (maximum of 5 COVID-19 vaccine doses) and did not receive the XBB.1.5 variant-adapted vaccine	61 to 122	**Positive PCR test:** 24.1 (-0.7-42.9) • Symptomatic: 36.8 (6.3-57.4) • Mild/asymptomatic: 12 (-26.4-38.8)
					123 to 183	**Positive PCR test:** 26.7 (-27.5-57.9) • Symptomatic: 64.8 (8.5-86.5)

presence of symptoms or the receival of medical attention.	(N=2,867)					• Mild/asymptomatic: -17.8 (-122.1-37.5)
Shresta et al. (2024) - USA (Ohio) Peer-reviewed This study was not included in the figure above as it reported on positive NAAT that were performed routinely as part of the study.	Cleveland Clinic Health System (CCHS) employees in employment at any Cleveland Clinic location in Ohio on 10 October 2023, the day the 2023–2024 formulation of the COVID-19 vaccine was available to employees at Cleveland Clinic, were included in the study. (N=48,210)	Omicron (before JN.1 lineages become pre-dominant)	Received an mRNA XBB.1.5 variant-adapted vaccine	Did not receive the XBB.1.5 variant-adapted vaccine (include unvaccinated individuals)	≥7	**Positive NAAT for SARS-CoV-2 any time after the study start date**: 42 (32-51)
		Omicron (after JN.1 lineages become pre-dominant)				**Positive NAAT for SARS-CoV-2 any time after the study start date:** 19 (-1-35)
Retrospective cohort						
*Chong et al. (2024) – Singapore Peer-reviewed This study was not included in the figure above as it reported on positive PCR or rapid antigen test regardless of the presence of symptoms or receival of medical attention.	Adult aged ≥18 years who did not receive non-mRNA COVID-19 vaccines, and who were boosted (received ≥3 mRNA COVID-19 vaccine doses) before study start date (N=3,086,562)	JN.1	Received an mRNA XBB.1.5 variant-adapted vaccine and at least one previous mRNA booster	Received at least one mRNA booster and did not receive the XBB.1.5 variant-adapted vaccine	8 to 120	**Positive PCR or rapid antigen test:** 41 (34-48) • Previous COVID-19 infection: 44 (33-53)
Ioannou et al. (2025) - United States Peer-reviewed	Emulated RCT including 1,098,498 adults aged 18+ years from the VHA integrated service network who received	Omicron (primarily XBB, EG.5.1 and JN.1)	Received an mRNA XBB.1.5 variant-adapted vaccine and at least one prior dose of earlier-	Received at least one prior dose of earlier-formulation COVID-19 vaccine but no	≥10	**Positive NAAT or antigen test** • 18 to 64 years: 8.56 (1.5-15.49) • 65 to 74 years: 0.22 (-6.49-7.32)

This study was not included in the figure above as it reported on positive test regardless of the presence of symptoms.	at least 1 earlier formulation COVID-19 vaccine		formulation COVID-19 vaccine	XBB.1.5 variant-adapted vaccine and		• ≥75 years: -12.93 (-18.32--7.26) • Prior infection 90 to 365 days earlier: -11.82 (-29.01-0.32) • Prior infection over a year ago: 8.32 (0.55-15.97) No prior infection: -5.97 (-10.36--1.26)
					60 days follow up	**Positive NAAT or antigen test** ≥18 years: 14.2 (10.17-17.74)
					90 days follow-up	**Positive NAAT or antigen test** ≥18 years: 7.3 (3.32-10.08)
					120 days follow-up	**Positive NAAT or antigen test** ≥18 years: 3.1 (-0.43-5.99)
					End of the study	**Positive NAAT or antigen test** ≥18 years: -3.3 (-6.78--0.22)
Kopel et al. (2024) – US Peer-reviewed This study was not included in the figure above as it included laboratory results in its	Adult aged ≥18 years from the Veradigm Network (EHR linked to healthcare claims sourced from Komodo Health). Individuals were required to have continuous enrollment in medical and pharmacy claims from	Omicron (primarily XBB, EG.5.1 and JN.1)	Received a dose of the Moderna mRNA XBB.1.5 variant adapted vaccine	Did not receive an XBB.1.5 variant adapted vaccine	Median (IQR): 63 (44-78)	Any COVID-19 infections • ≥18 years: 33.1 (30.2-35.9)
					Median (IQR): 64 (45-78)	Any COVID-19 infections • ≥18 years with medical conditions: 34.5 (31.2-37.6)

definition regardless of the presence of symptoms	September 12, 2022, through 7 days after the index date. (N=1,718,670)				Median (IQR): 64 (45-78)	Any COVID-19 infections • ≥50 years: 35.3 (32.2-38.2)
					Median (IQR): 65 (46-79)	Any COVID-19 infections • ≥65 years: 38.7 (35.4-41.9)
Lin et al. (2024) – United states (Nebraska) Peer-reviewed This study was not included in the figure above as it reported on positive PCR test regardless of the presence of symptoms (even though most were symptomatic)or the receival of medical attention.	Individuals of all ages whose information is available in the Nebraska Electronic Disease Surveillance System and the Nebraska State Immunization Information System (NESIIS) (N=1,830,088)	XBB.1.5 or JN.1	Received an XBB.1.5 variant-adapted vaccine	Did not receive an XBB.1.5 variant-adapted vaccine (include unvaccinated individuals)	**Positive PCR test. Individuals were generally symptomatic, but not all.**	
					7 to 13	16.8 (13.7-19.8)
					14 to 20	30.8 (25.6-35.7)
					21 to 27	42.5 (35.8-48.5)
					28 to 34	52.2 (44.6-58.7)
					35 to 41	45.0 (40.2-49.5)
					42 to 48	36.9 (30.2-42.9)
					49 to 55	35.8 (29.9-41.3)
					56 to 62	34.7 (29.5-39.6)
					63 to 69	33.7 (28.9-38.1)
					70 to 76	32.6 (28.1-36.8)
					77 to 83	31.4 (27.0-35.6)
					84 to 90	30.3 (25.5-34.8)
					91 to 97	29.1 (23.8-34.1)
					98 to 104	28.0 (21.8-33.7)
					105 to 111	26.8 (19.5-33.3)
					112 to 118	25.5 (17.1-33.1)
					119 to 125	24.3 (14.6-32.9)
					126 to 132	23.0 (11.9-32.7)
					133 to 139	21.8 (9.1-32.6)
					140 to 146	20.4 (6.2-32.5)
					147 to 153	19.1 (3.2-32.4)
					154 to 160	17.8 (0.1-32.4)

					161 to 167	16.4 (-3.2-32.3)
		XBB.1.5			**Positive PCR test. Individuals were generally symptomatic, but not all.**	
					7 to 13	22.7 (17.6-27.5)
					14 to 20	40.3 (32.2-47.5)
					21 to 27	53.9 (44.1-61.9)
					28 to 34	64.4 (54.0-72.4)
					35 to 41	57.1 (50.7-62.7)
					42 to 48	48.5 (40.7-55.2)
					49 to 55	46.7 (39.6-52.9)
					56 to 62	44.8 (38.5-50.5)
					63 to 69	42.9 (37.1-48.2)
					70 to 76	40.9 (35.6-45.8)
					77 to 83	38.9 (33.8-43.6)
					84 to 90	36.8 (31.6-41.6)
					91 to 97	34.6 (29.0-39.8)
					98 to 104	32.3 (25.9-38.2)
					105 to 111	30.0 (22.5-36.7)
					112 to 118	27.6 (18.7-35.4)
					119 to 125	25.0 (14.6-34.2)
					126 to 132	22.4 (10.2-33.1)
		JN.1			**Positive PCR test. Individuals were generally symptomatic, but not all.**	
					7 to 13	13.6 (9.7- 17.4)
					14 to 20	25.4 (18.4-31.7)
					21 to 27	35.5 (26.3-43.6)
					28 to 34	44.3 (33.5-53.4)
					35 to 41	34.8 (27.3-41.6)
					42 to 48	23.8 (11.4-34.4)
					49 to 55	22.2 (11.8-31.4)
					56 to 62	20.6 (11.6-28.7)

					63 to 69	19.0 (10.6-26.6)
					70 to 76	17.4 (8.5-25.4)
					77 to 83	15.7 (5.3-24.9)
					84 to 90	13.9 (1.3-25.0)

*The primary article presented outcomes in the form of hazard ratio (HR) data, subsequently translated into vaccine effects (VE)

Question 2: Impact of the XBB.1.5 COVID-19 vaccine on COVID-related ED or UC visits

Table 3: VE of the XBB.1.5 variant-adapted COVID-19 vaccine against COVID related ED or UC visits compared with those who have not received the XBB.1.5 variant-adapted COVID-19 vaccine (n = 6).

Author (date) - Country Type of publication	Population	Predominant variant	Intervention	Comparator group (reference)	Time since last dose (days)	VE (%) (95% CI)
Test-negative Case-control						
Caffrey et al. (2024) – United States Peer-reviewed	113,174 respiratory infection episodes in adults aged 18+ and diagnosed with an acute respiratory infection in hospital, emergency department, urgent care or outpatient setting from the US Veterans Affairs Healthcare system	Omicron (primarily XBB and JN.1 sublineages)	Received a Pfizer-BioNTech XBB1.5-adapted vaccine	Did not receive the XBB.1.5 variant-adapted vaccine but received at least one BA.4/5 bivalent dose	At least 14 days	≥18 years: 44 (37-51)
				Did not receive the XBB.1.5 variant-adapted vaccine but received 3 or more doses of original wild-type mRNA but no bivalent-adapted vaccines	At least 14 days	≥18 years: 41 (25-53)
				Did not receive the XBB.1.5 variant-adapted vaccine (includes unvaccinated individuals)	Median (IQR): 56 (36-76)	≥18 years: 39 (33-45)
					Median (IQR): 55 (35-74)	Immunocompromised: 34 (22-45)
					Median (IQR): 56 (36-77)	Immunocompetent: 42 (34-49)
					Median (IQR): 54 (35-74)	18 to 64 years: 48 (37-57)

					Median (IQR): 56 (36-77)	≥65 years: 35 (27-43)
		XBB sublineages and JN.1			Median (IQR): 53 (38-67)	≥18 years: 43 (33-52)
		XBB sublineages			Median (IQR): 31 (22-40)	≥18 years: 50 (35-61)
					14 to 60	≥18 years: 52 (37-63)
		JN.1			14 to 60	≥18 years: 41 (23-54)
					61 to 133 days	≥18 years: 30 (16-41)
					Median (IQR): 75 (55-90)	≥18 years: 33 (22-43)
DeCuir et al. (2024) – United States Report	128,825 immunocompetent adults aged ≥18 years from the Virtual SARS-CoV-2, Influenza, and Other respiratory viruses Network (VISION)	Omicron (primarily XBB, EG.5.1 and JN.1)	Received an XBB.1.5 variant-adapted vaccine	Did not receive the XBB.1.5 variant-adapted vaccine (includes unvaccinated individuals)	Median (IQR): 33 (20-46)	≥18 years: 51 (47-54)
					Median (IQR): 44 (26-64)	≥18 years: 47 (44-50)
					Median (IQR): 74 (66-83)	≥18 years: 39 (33-45)
					Median (IQR): 33 (21-46)	18 to 64 years: 52 (45-58)
					Median (IQR): 46 (27-66)	18 to 64 years: 50 (44-55)
					Median (IQR): 74 (66-83)	18 to 64 years: 45 (34-55)
					Median (IQR): 33 (21-46)	≥65 years: 49 (44-54)

					Median (IQR): 46 (27-66)	≥65 years: 45 (41-49)
					Median (IQR): 74 (66-83)	≥65 years: 37 (29-44)
*Tartof et al. (2024) – United States Peer-reviewed	≥18 years who have been at Kaiser Permanente Southern California (KPSC) for at least a year (N=52,036)	Omicron (primarily JN.1 and XBB sublineages)	Received a Pfizer-BioNTech XBB1.5-adapted vaccine	Did not receive the XBB.1.5 vaccine (including unvaccinated individuals)	Median of 59	≥18 years: 40 (34-45)
		JN.1 sublineages			Median of 59	≥18 years: 41 (32-49)
					14 to <60	≥18 years: 52 (39-61)
					60 to 156	≥18 years: 34 (22-44)
		XBB sublineages			Median of 52	≥18 years: 55 (45-64)
					14 to <60	≥18 years: 59 (48-68)
					60 to 128	≥18 years: 39 (10-59)
Retrospective cohort						
Andersen et al. (2025) - United States Peer-reviewed	Immunocompetent, non-pregnant adults ≥18 years of age residing in California or Louisiana, enrolled in health insurance plans reporting to HealthVerity. (N=6,344,448)	Omicron (primarily XBB, EG.5.1 and JN.1)	Received a Pfizer-BioNTech XBB1.5-adapted vaccine	Unvaccinated	≥14	≥18 years: 39 (27-49)
				Did not receive the XBB.1.5 vaccine (including unvaccinated individuals)		• ≥18 years: 45 (34-54) • ≥65 years: 48 (33-60)
				Did not receive the XBB.1.5 vaccine but received at least 1 BA.4/5 bivalent dose		≥18 years: 48 (38-57)
				Did not receive the XBB.1.5 vaccine but received at least 2 doses of wild-type vaccine only (no variant adapted vaccine of any kind)		≥18 years: 45 (35-54)
**Chong et al. (2024) – Singapore	Adult aged ≥18 years who did not receive	JN.1	Received an mRNA XBB.1.5	Received at least one mRNA booster and did	8 to 120	• Overall: 50 (27-66)

Peer-reviewed	non-mRNA COVID-19 vaccines, and who were boosted (received ≥3 mRNA COVID-19 vaccine doses) before study start date (N=3,086,562)		variant-adapted vaccine and at least one previous mRNA booster	not receive the XBB.1.5 variant-adapted vaccine		• Previous COVID-19 infection: 22 (-43-57)

* The primary article presented outcomes in the form of odds ratio (OR) data, subsequently translated into vaccine effectiveness (VE).

** The primary article presented outcomes in the form of hazard ratio (HR) data, subsequently translated into vaccine effects (VE).

Question 3: Impact of the XBB.1.5 COVID-19 vaccine on hospitalisations related to COVID-19

Table 4: VE of the XBB.1.5 variant-adapted COVID-19 vaccine against hospitalisations related to COVID-19 compared with those who have not received the XBB.1.5 variant-adapted COVID-19 vaccine (n = 20).

Author (date) - Country Type of publication	Population	Predominant variant	Intervention	Comparator group (reference)	Time since last dose (days)	VE (%) (95% CI)
Retrospective cohort						
Andersen et al. (2025) - United States Peer-reviewed	Immunocompetent, non-pregnant adults ≥18 years of age residing in California or Louisiana, enrolled in health insurance plans reporting to HealthVerity. (N=6,344,448)	Omicron (primarily XBB, EG.5.1 and JN.1)	Received a Pfizer-BioNTech XBB1.5-adapted vaccine	Unvaccinated	≥14	≥18 years: 33 (13-48)
				Did not receive the XBB.1.5 vaccine (including unvaccinated individuals)		≥18 years: 36 (18-50) ≥65 years: 47 (28-61)
				Did not receive the XBB.1.5 vaccine but received at least 1 BA.4/5 bivalent dose		≥18 years: 40 (23-54)
				Did not receive the XBB.1.5 vaccine but received at least 2 doses of wild-type vaccine only (no variant adapted vaccine of any kind)		≥18 years: 34 (16-49)
Andersson et al. (2024) – Denmark, Sweden and Finland Peer-reviewed	≥65 years living in Denmark, Sweden or Finland (N=3,752,564)	Omicron (XBB, EG.5.1, HK.3 and JN.1)	Received the XBB.1.5 variant-adapted vaccine as their 5th dose	Received at least 4 prior doses of COVID-19 vaccine but not an XBB.1.5 variant-adapted vaccine	8 to 168	55.3 (43.2-67.4)
			Received the XBB.1.5 variant-			56.7 (51.4-6)

			adapted vaccine as their 6th dose			
			Received the XBB.1.5 variant-adapted vaccine as their 7th dose			56.5 (47.3- 65.8)
			Received at least 4 prior doses of COVID-19 vaccine and received an XBB.1.5 variant-adapted vaccine			• ≥65 years: 57.9 (49.9-65.8) • 65-74 years: 60.3 (51.9-68.7) • ≥75 years: 57.6 (47.8-67.5)
					8 to 27	64.5 (49.0-80.0)
					28 to 48	63.1 (54.9-71.3)
					49 to 69	55.4 (35.6-75.1)
					70 to 90	48.8 (33.1-64.4)
					91 to 111	60.1 (38.4-81.8)
					112 to 132	67.0 (41.3-92.8)
					133 to 153	52.3 (9.5-95.0)
					154 to 174	50.1 (-20.9-100.0)
		XBB sublineages			8 to 168	75.1 (69.6-80.5)
		BA.2.86 sublineages			8 to 168	56.3 (48.5-64.0)
*Chong et al. (2024) – Singapore Peer-reviewed This study was not included in the figure below as it reported for the VE after 8 to 120 days, which included both early and mid-times	Adult aged ≥18 years who did not receive non-mRNA COVID-19 vaccines, and who were boosted (received ≥3 mRNA COVID-19 vaccine doses) before study start date (N=3,086,562)	JN.1	Received an mRNA XBB.1.5 variant-adapted vaccine and at least one previous mRNA booster	Received at least one mRNA booster and did not receive the XBB.1.5 variant-adapted vaccine	8 to 120	• Overall: 42 (9-63) • Previous COVID-19 infection: 43 (3-67)

*Hansen et al. (2024) – Denmark Peer-reviewed	≥65 years living in Denmark (N=1,037,479)	Omicron EG.5.1, XBB sublineages	At least one Pfizer-BioNTech or Moderna bivalent BA.4/BA.5 or BA.1 booster dose plus an mRNA XBB.1.5-adapted vaccine	At least one Pfizer-BioNTech or Moderna bivalent BA.4/BA.5 or BA.1 booster dose but not the XBB.1.5 vaccine	≥7	76.1 (62.3 to 84.8)
Ioannou et al. (2025) - United States Peer-reviewed	Emulated RCT including 1,098,498 adults aged 18+ years from the VHA integrated service network who received at least 1 earlier formulation COVID-19 vaccine	Omicron (primarily XBB, EG.5.1 and JN.1)	Received an mRNA XBB.1.5 variant-adapted vaccine and at least one prior dose of earlier-formulation COVID-19 vaccine	Received at least one prior dose of earlier-formulation COVID-19 vaccine but no XBB.1.5 variant-adapted vaccine and	≥10	• 18 to 64 years: 29.7 (3.37-48.41) • 65 to 74 years: 15.65 (-5.44-34.15) • ≥75 years: 14.39 (0.71-26.52) • Prior infection 90 to 365 days earlier: 10.61 (-33.37-40.67) • Prior infection over a year ago: 9.26 (-15.13-30.24) No prior infection: 18.99 (7.68-29.56)
					60 days follow up	≥ 18 years: 37.6 (28.18-46.8)
					90 days follow-up	≥ 18 years: 30.8 (21.89-38.53)
					120 days follow-up	≥ 18 years: 25.2 (17.16-33.15)
					End of the study	≥ 18 years: 16.6 (6.47-25.77)
Kopel et al. (2024) – US Peer-reviewed	Adult aged ≥18 years from the Veradigm Network EHR linked to healthcare claims sourced from Komodo Health.	Omicron (primarily XBB, EG.5.1 and JN.1)	Received a dose of the Moderna mRNA XBB.1.5 variant adapted vaccine	Did not receive an XBB.1.5 variant adapted vaccine	Median (IQR): 63 (44-78)	≥18 years: 60.2 (53.4-66.0)
					Median (IQR): 64 (45-78)	≥18 years with medical conditions: 58.7 (51.3-65.0)

	Individuals were required to have continuous enrollment in medical and pharmacy claims from September 12, 2022, through 7 days after the index date. (N=1,718,670)				Median (IQR): 64 (45-78)	≥50 years: 61.1 (54.3-66.9)
					Median (IQR): 65 (46-79)	≥65 years: 60.5 (53.3-66.6)
Lin et al. (2024) – United states (Nebraska) Published	Individuals of all ages whose information is available in the Nebraska Electronic Disease Surveillance System and the Nebraska State Immunization Information System (NESIIS) (N=1,830,088)	XBB.1.5 or JN.1	Received an XBB.1.5 variant-adapted vaccine	Did not receive an XBB.1.5 variant-adapted vaccine (includes unvaccinated individuals)	7 to 13	24.1 (16.7-30.9)
					14 to 20	42.4 (30.5-52.2)
					21 to 27	56.3 (42.1-66.9)
					28 to 34	66.8 (51.7-77.1)
					35 to 41	65.3 (52.5-74.7)
					42 to 48	63.8 (52.6-72.4)
					49 to 55	62.3 (51.7-70.6)
					56 to 62	60.6 (49.4-69.4)
					63 to 69	58.9 (45.6-69.0)
					70 to 76	57.1 (40.4-69.2)
					77 to 83	55.3 (34.0-69.7)
					84 to 90	53.3 (26.3-70.5)
					91 to 97	51.3 (17.3-71.3)
					98 to 104	49.2 (7.0-72,2)
					105 to 111	47.0 (-4.8-73.2)
					112 to 118	44.7 (-18.3-74.1)
					119 to 125	42.3 (-33.6-75.1)
					126 to 132	39.8 (-51.0-76.0)
					133 to 139	37.1 (-70.8-76.9)
		XBB.1.5			7 to 13	28.4 (18.3-37.3)
					14 to 20	48.7 (33.2-60.7)
					21 to 27	63.3 (45.4-75.3)
					28 to 34	73.7 (55.4-84.5)
					35 to 41	71.7 (55.7-81.9)

					42 to 48	69.6 (55.5-79.2)
					49 to 55	67.2 (54.6-76.3)
					56 to 62	64.7 (52.4-73.8)
					63 to 69	62.0 (48.5-72.0)
					70 to 76	59.1 (42.4-71.0)
					77 to 83	56.0 (34.2-70.6)
					84 to 90	52.7 (23.7-70.6)
					91 to 97	49.0 (10.7-70.9)
					98 to 104	45.1 (-5.0-71.3)
					105 to 111	40.9 (-23.8-71.8)
		JN.1			7 to 13	20.5 (8.8-30.7)
					14 to 20	36.9 (16.9-52.0)
					21 to 27	49.8 (24.2-66.8)
					28 to 34	60.1 (30.9-77.0)
					35 to 41	56.8 (33.5-71.9)
					42 to 48	53.1 (28.6-69.2)
					49 to 55	49.2 (14.0-70.0)
					56 to 62	44.9 (-10.4-72.5)
					63 to 69	40.3 (-45.9-75.6)
Monge et al. (2024) - Belgium, Denmark, Italy, Spain (Navarra), Norway, Portugal and the Netherlands Peer-reviewed	Individuals aged 65 years or older, eligible to receive the autumnal booster vaccination at the beginning of the campaign and who received at least a complete primary vaccination and who, in the last 90 days, had no vaccine dose administered and no documented SARS-CoV-2 infection.	Omicron (primarily XBB, EG.5.1 and JN.1)	Received an mRNA XBB.1.5 variant adapted vaccine and at least a complete primary vaccination	Received at least a complete primary vaccination but no XBB.1.5 variant adapted vaccine and	≥14	• 65-79 years: 66.8 (58.1-73.7) • ≥80 years: 65.9 (56.9-73.1)

	(N=22,110,131)					
Nunes et al. (2024) - Belgium, Denmark, Italy, Navarre (Spain), Norway, Portugal and Sweden Peer-reviewed	≥65 years residing in one of the regions, included in and eligible to receive the autumnal 2023 vaccine dose at the start of the country-specific vaccination campaign and part of the VEBIS-HER study (N=20,183,622)	BA.2.86 and JN.1	Received the XBB.1.5 vaccine and at least 2 previous COVID-19 vaccine doses	Received at least 2 COVID-19 vaccine doses but have not received the XBB.1.5 vaccine	≥14	• 65-79 years: 50.2 (44.6-55.2) • ≥80 years: 40.7 (35.1-45.9)
					14 to 89	• 65-79 years: 50.9 (45.1-56.0) • ≥80 years: 42.1 (36.4-47.2)
					90 to 179	• 65-79 years: 47.3 (32.0-59.1) • ≥80 years: 38.6 (17.4-54.3)
Wilson et al. (2024) - United States Peer-reviewed	Observational matched cohort of adults aged ≥ 18 years who had continuous medical and pharmacy enrollment (with 45-day allowable gaps) from 365 days prior to index date through cohort entry date	Omicron (primarily XBB, EG.5.1 and JN.1)	Received a Moderna mRNA XBB.1.5 variant-adapted vaccine	Did not receive any XBB.1.5 variant adapted vaccine (including unvaccinated individuals)	Median (IQR): 84 (58-101)	• ≥18 years: 51 (48-54)
					≥8	• Immunocompromised: 46 (39-52) • 18-49 years: 51 (45-57) • 50 to 64 years: 47 (42-52) • ≥65 years: 56 (51-61)
Test-negative case-control						
Caffrey et al. (2024) – United States Peer-reviewed	113,174 respiratory infection episodes in adults aged 18+ and diagnosed with an acute respiratory infection in hospital, emergency department, urgent care or outpatient setting from the US Veterans Affairs Healthcare system	Omicron (primarily XBB and JN.1 sublineages)	Received a Pfizer-BioNTech XBB1.5-adapted vaccine	Did not receive the XBB.1.5 variant-adapted vaccine (includes unvaccinated individuals)	Median (IQR): 53 (34-74)	≥18 years: 43 (34-51)
					Median (IQR): 52 (33-73)	Immunocompromised: 33 (16-47)
					Median (IQR): 54 (34-74)	Immunocompetent: 49 (38-58)
					Median (IQR): 50 (34-67)	18 to <65 years: 58 (33-73)

					Median (IQR): 54 (33-74)	≥65 years: 41 (32-50)
		XBB sublineages and JN.1			Median (IQR): 50 (37-65)	≥18 years: 46 (32-58)
		XBB sublineages			Median (IQR): 30 (21-38)	≥18 years: 61 (44-73)
					14 to 60	≥18 years: 62 (44-74)
		JN.1			14 to 60	≥18 years: 32 (3-52)
					61 to 133 days	≥18 years: 37 (19-51)
					Median (IQR): 73 (53-89)	≥18 years: 35 (20-48)
				Did not receive the XBB.1.5 variant-adapted vaccine but received at least one BA.4/5 bivalent dose	At least 14 days	≥18 years: 45 (34-54)
				Did not receive the XBB.1.5 variant-adapted vaccine but received 3 or more doses of original wild-type mRNA but no bivalent-adapted vaccines	At least 14 days	≥18 years: 56 (36-69)
Carazo et al. (2024)- Canada Pre-print	114,005 NAAT from adults aged ≥60 years who presented with COVID-19	XBB	Received an mRNA XBB.1.5 variant-adapted vaccine	Did not receive the XBB.1.5 variant-adapted vaccine		≥60 years: 53.8 (37.3-66.0)

	symptoms, in Québec, Canada.			Did not receive the XBB.1.5 variant-adapted vaccine but received an ancestral mRNA monovalent or bivalent vaccine dose during Quebec's prior vaccination campaign from July to December 2022		• ≥60 years: 54.4 (45.9-61.6) • 60-69 years: 47.5 (10.5-69.2) • 70-79 years: 56.1 (40.6-67.6) • ≥ 80 years: 54.9 (43.3-64.1)
					7 to 60	• 60-69 years: 47.5 (10.5-68.2) • 70-79 years: 56.1 (40.6-67.6) • ≥ 80 years: 54.9 (43.3-64.1)
					7 to 30	≥60 years: 53.2 (43.5-61.3)
					31 to 60	≥60 years: 60.44 (46.0-70.9)
			Received an mRNA XBB.1.5 variant-adapted vaccine and **had a prior COVID-19 infection**		At least 7 days	≥60 years: 73.6 (61.1-82.1)
				Did not receive the XBB.1.5 variant-adapted vaccine but received an ancestral mRNA monovalent or bivalent vaccine dose during Quebec's prior vaccination campaign from July to December 2022 and **had a prior COVID-19 infection**		≥60 years: 65.5 (46.8-77.6)

			Received an mRNA XBB.1.5 variant-adapted vaccine	Unvaccinated		≥60 years: 54.0 (46.1-60.7)
		JN.1		Did not receive the XBB.1.5 variant-adapted vaccine		• ≥60 years: 30.8 (12.7-45.1)
				Did not receive the XBB.1.5 variant-adapted vaccine but received an ancestral mRNA monovalent or bivalent vaccine dose during Quebec's prior vaccination campaign from July to December 2022		• ≥60 years: 22.7 (12.1-32.0) • 60-69 years: -6.7 (-47.5-22.8) • 70-79 years: 25.5 (7.5-40.1) • ≥ 80 years: 28.8 (14.5-40.7)
					7 to 60	• 60-69 years: -23.7 (-91.7-20.2) • 70-79 years: 34.7 (11.1-52.0) • ≥ 80 years: 27.2 (6.2-43.6)
					7 to 30	≥60 years: 27.8 (3.4-46.0)
					31 to 60	≥60 years: 22.5 (6.2-36.0
					61 to 91	≥60 years: 27.6 (14.5-38.8)
					92 to 121	≥60 years: 19.8 (0.2-35.5)
					122 to 152	≥60 years: 23.1 (-3.1-42.6)
					153 to 182	≥60 years: 6.5 (-44.1-39.3)
					183 to 213	≥60 years: -5.2 (-159.5-57.4)
			Received an mRNA XBB.1.5 variant-adapted vaccine and **had a**		At least 7 days	≥60 years: 41.1 (27.5-52.1)
				Did not receive the XBB.1.5		≥60 years: 14.1 (-18.8,-37.9)

			prior COVID-19 infection	variant-adapted vaccine but received an ancestral mRNA monovalent or bivalent vaccine dose during Quebec's prior vaccination campaign from July to December 2022 and **had a prior COVID-19 infection**		
			Received an mRNA XBB.1.5 variant-adapted vaccine	Unvaccinated		≥60 years: 25.2 (17.5-32.1)
		KP.2/KP.3		Did not receive the XBB.1.5 variant-adapted vaccine		≥60 years: 7.4 (-24.2-30.9)
			Received **one dose** of an mRNA XBB.1.5 variant-adapted vaccine	Did not receive the XBB.1.5 variant-adapted vaccine but received an ancestral mRNA monovalent or bivalent vaccine dose during Quebec's prior vaccination campaign from July to December 2022		≥60 years: -3.5 (-21.5-11.8)
					7 to 60	≥60 years: 70.1 (31.4-86.9)
					61 to 121	≥60 years: 37.8 (-9.6-64.6)
					122 to 182	≥60 years: 12.3 (-24.2-38.0)
					183 to 243	≥60 years: 3.2 (-18.0-20.5)
					244 to 304	≥60 years: -20.0 (-45.6-1.0)
			Received **two doses** of an mRNA XBB.1.5 variant-adapted vaccine		At least 7 days	≥60 years: 38.6 (13.6-56.4)
					7 to 60	≥60 years: 57.1 (31.0-73.4)
					61 to 121	≥60 years: 32 (-5.1-56.0)

			Received an mRNA XBB.1.5 variant-adapted vaccine		At least 7 days	• ≥60 years: 0 (-16.7-15.2) • 60-69 years: -47.2 (-130.3-5.9) • 70-79 years: 10.3 (-18.5-32.0) • ≥ 80 years: 6.6 (-16.3-25.0)
					7 to 60	• ≥60 years: 60.2 (38.9-74.0) • 60-69 years: 53.2 (-136.2-90.7) • 70-79 years: 55.9 (-7.8-82.0) • ≥ 80 years: 63.0 (28.3-77.9)
					61 to 121	≥60 years: 33.2 (3.6-53.7)
					122 to 182	≥60 years: 13.6 (-22.1-38.9)
					183 to 243	≥60 years: 3.2 (-18.0-20.5)
					244 to 304	≥60 years: -20.0 (-45.6-1.0)
			Received an mRNA XBB.1.5 variant-adapted vaccine and **had a prior COVID-19 infection**		At least 7 days	≥60 years: 5.9 (-19.3-25.8)
				Did not receive the XBB.1.5 variant-adapted vaccine but received an ancestral mRNA monovalent or bivalent vaccine dose during Quebec's prior vaccination campaign from		≥60 years: -24.9 (-97.3-21.0)

				July to December 2022 and **had a prior COVID-19 infection**		
			Received an mRNA XBB.1.5 variant-adapted vaccine	Unvaccinated		≥60 years: -0.7 (-12.8-10.1)
		Omicron (XBB, JN.1 or KP.2/3)	Received an mRNA XBB.1.5 variant-adapted vaccine	Did not receive the XBB.1.5 variant-adapted vaccine	At least 7 days	≥60 years: 35.8 (26.3-44.1)
				Did not receive the XBB.1.5 variant-adapted vaccine but received an ancestral mRNA monovalent or bivalent vaccine dose during Quebec's prior vaccination campaign from July to December 2022		• ≥60 years: 29.9 (24.4-35.0) • 60-69 years: 3.9 (-17.7-21.5) • 70-79 years: 33.4 (24.1-41.5) • ≥ 80 years: 33.5 (26.2-40.0)
			Received an mRNA XBB.1.5 variant-adapted vaccine and **had a prior COVID-19 infection**			≥60 years: 43.4 (35.9-50.1)
				Did not receive the XBB.1.5 variant-adapted vaccine but received an ancestral mRNA monovalent or bivalent vaccine dose during Quebec's prior vaccination campaign from July to December		≥60 years: 28.2 (13.6-40.3)

				2022 and **had a prior COVID-19 infection**		
			Received an mRNA XBB.1.5 variant-adapted vaccine	Unvaccinated		≥60 years: 29.6 (25.3-33.6)
DeCuir et al. (2024) – United States Report	37,503 immunocompetent adults aged ≥18 years from the Virtual SARS-CoV-2, Influenza, and Other respiratory viruses Network (VISION)	Omicron (primarily XBB, EG.5.1 and JN.1)	Received an XBB.1.5 variant-adapted vaccine	Did not receive the XBB.1.5 variant-adapted vaccine (includes unvaccinated individuals)	Median (IQR): 32 (19-45)	≥18 years: 53 (46-59)
					Median (IQR): 42 (24-62)	≥18 years: 52 (47-57)
					Median (IQR): 73 (66-81)	≥18 years: 50 (40-59)
					Median (IQR): 30 (19-44)	18 to <65 years: 42 (14-61)
					Median (IQR): 38 (22-58)	18 to <65 years: 43 (20-59)
					Median (IQR): 74 (67-81)	18 to <65 years: 45 (-6-71)
					Median (IQR): 32 (19-46)	≥65 years: 54 (47-60)
					Median (IQR): 43 (25-62)	≥65 years: 53 (47-58)
					Median (IQR): 73 (66-81)	≥65 years: 50 (39-59)
Lee et al. (2024) - Canada	Community-dwelling adults aged ≥50 years	Omicron (primarily JN.1 and KP)	Received an mRNA XBB.1.5	Received at least 2 doses of a non	91 to 182	≥50 years: 44 (32-54)
					183 to 274	≥50 years: 21 (-15-46)

Preprint	who underwent ≥1 polymerase chain reaction (PCR) test (N=24,498)		variant-adapted vaccine and at least 2 doses of a non XBB.1.5 mRNA vaccine	XBB.1.5 mRNA vaccine		
				Received the original monovalent mRNA vaccine	91 to 182	≥50 years: 53 (42-62)
				Received a bivalent mRNA vaccine	91 to 182	≥50 years: 43 (28-55)
Lee et al. (2024) – South Korea Peer-reviewed	Adults aged ≥18 year who underwent PCR testing or rapid antigen testing in the emergency department, outpatient clinics, general wards, or intensive care units of each hospital were included in the study. (N=5,516)	Omicron (primarily XBB, EG.5.1, HK.3 and JN.1 sub variants)	Received an mRNA XBB.1.5 variant-adapted vaccine	Unvaccinated individuals	7 to 59	• ≥18 years: 77.3 (51.1-89.5) • ≥ 65 years: 72.8 (37.3-88.2)
				Did not receive the XBB.1.5 vaccine (includes unvaccinated individuals)	7 to 59	• ≥18 years: 64.3 (35.9-80.2) • ≥ 65 years: 66.5 (38.1-81.8)
				Did not receive the XBB.1.5 vaccine but have received at least one dose of COVID-19 vaccine	7 to 59	• ≥18 years: 61.2 (29.7-78.6) • Immunocompromised: 79.4 (7.4-95.4) • Immunocompetent: 56.4 (16.2-77.3) • ≥ 65 years: 64.1 (33.2-80.7)
Link-Gelles et al. (2024) – United States Report This study was not included in the figure below as it reported on immunocompromised individuals	Immunocompromised adults aged ≥18 years from the VISION Network (N=14,586)	Omicron XBB sublineages and JN.1	Received an XBB.1.5 variant-adapted vaccine	Did not receive an XBB.1.5 variant-adapted vaccine (includes unvaccinated individuals)	≥7	36 (25-46)
					7 to 59	38 (23-50)
					60 to 119	34 (16-47)

Kirsebom et al. (2024) – England Peer-review	≥65 years (N=28,916)	Omicron (primarily XBB, JN.1, EG.5.1 and BA)	Received an XBB.1.5 variant-adapted vaccine	Did not receive an XBB.1.5 variant-adapted vaccine (includes unvaccinated individuals)	9 to 13	37.4 (17.8-52.3)
					14 to 28	54.8 (46.8-61.6)
					29 to 63	48.3 (41.0-54.7)
					64 to 98	42.2 (32.3-50.6)
Nguyen et al. (2025) - Belgium, Germany, Italy, Spain Peer-reviewed	≥18 years individuals eligible for COVID-19 vaccination and admitted at one of the study centers (hospitals) of the id.Drive study for at least one overnight stay with a severe acute respiratory infection (SARI). Symptom onset must have occurred within 1 days prior to admission. Patients who were infected with the JN.1 variant or experienced symptom onset during the JN.1 predominance period were included. (N=1,425)	JN.1	Received a Pfizer-BioNTech XBB1.5-adapted vaccine	Did not receive an XBB.1.5 variant-adapted vaccine (includes unvaccinated individuals)	Median (IQR): 63 (48-79)	≥18 years: 53.8 (38.4-65.4)
					Median (IQR): 24 (22-26)	≥18 years: 52.2 (41.3-61.1)
					Median (IQR): 45 (37-50)	≥18 years: 48.9 (17.9-68.2)
					Median (IQR): 68 (62-76)	≥18 years: 56.9 (39.5-69.2)
					Median (IQR): 91 (87-98)	≥18 years: 54.6 (50.2-58.5)
					Median (IQR): 126 (120-140)	≥18 years: 59.5 (21.4-79.1)
					Median (IQR): 58 (41-72)	Immunocompromised or cancer: 56.0 (22.4-75.0)
					At least 14 days	Prior infection: 58.2 (34.0-73.5)
					At least 14 days	No prior infection: 53.9 (27.5-70.7)
					Median (IQR): 56 (38-78)	18 to <65 years: 56.5 (18.6-76.8)

					Median (IQR): 64 (49-79)	≥65 years: 53.9 (40.4-64.3)
					Median (IQR): 23 (22-26)	≥65 years: 61.6 (34.2-77.6)
					Median (IQR): 46 (38-50)	≥65 years: 44.4 (11.7-65.0)
					Median (IQR): 68 (62-75)	≥65 years: 57.4 (43.7-67.7)
					Median (IQR): 91 (86-98)	≥65 years: 60.5 (57.7-63.3)
					Median (IQR): 125 (119-135)	≥65 years: 51.2 (16.1-71.6)
					Median (IQR): 59 (44-73) days	65 to 79 years: 62.5 (40.0-76.6)
					Median (IQR): 67 (52-81) days	≥80 years: 48.8 (36.9-58.5)
				Did not receive an XBB.1.5 variant-adapted vaccine and received at least 1 BA.4/5 bivalent dose	Median (IQR): 63 (48-78)	≥18 years: 61.0 (35.1-76.6)
				Only received 2 mRNA wild type doses	Median (IQR): 65 (49-80)	≥18 years: 48.8 (44.2-53.0)

				Unvaccinated	Median (IQR): 65 (49-80)	≥18 years: 52.1 (9.8-74.5)
UK Health Security Agency (2024) – England Report	≥65 years (N=16,549)	Omicron BA.5, BA.2.75, BQ.1, EG.5.1, XBB sublineages	Received a Pfizer-BioNTech or Moderna bivalent BA.1 booster vaccine as part of the autumn 2022 booster programme plus a Pfizer-BioNTech XBB1.5-adapted vaccine	Received a Pfizer-BioNTech or Moderna bivalent BA.1 booster vaccine as part of the autumn 2022 booster programme	9 to 13	42.3 (20.5 to 58.2)
					14 to 28	55.4 (45 to 63.8)
					29 to 63	50.9 (37.5 to 61.5)
**Tartof et al. (2024) – United States Peer-reviewed	≥18 years who have been at Kaiser Permanente Southern California (KPSC) for at least a year (N=52,036)	Omicron (primarily JN.1 and XBB sublineages)	Received a Pfizer-BioNTech XBB1.5-adapted vaccine	Did not receive the XBB.1.5 vaccine (including unvaccinated individuals)	Median of 57	≥18 years: 57 (45-66)
		JN.1			Median of 57	≥18 years: 54 (33-69)
					14 to <60	≥18 years: 50 (15-71)
					60 to 156	≥18 years: 57 (30-73)
		XBB sublineages			Median of 52	≥18 years: 65 (41-79)
					14 to <60	≥18 years: 74 (49-87)

*The primary article presented outcomes in the form of hazard ratio (HR) data, subsequently translated into vaccine effectiveness (VE);

**The primary article presented outcomes in the form of odds ratio (OR) data, subsequently translated into vaccine effectiveness (VE).

Question 4: Impact of the XBB.1.5 COVID-19 vaccine on COVID-related ED or UC visits or hospitalisation

Table 5: VE of the XBB.1.5 variant-adapted COVID-19 vaccine against COVID related ED or UC visits or hospitalisation compared with those who have not received the XBB.1.5 variant-adapted COVID-19 vaccine (n = 1).

Author (date) - Country Type of publication	Population	Predominant variant	Intervention	Comparator group (reference)	Time since last dose (days)	VE (%) (95% CI)
Test-negative case control						
Tartof et al. (2024) – United States Peer-reviewed	Children aged 5 to 17 years in a large integrated US health system (Kaiser Permanente Southern California) who visited the ED/UC or were admitted to the hospital for an acute respiratory infection. (N=15,233)	Omicron (primarily XBB, EG.5.1, JN.1 and KP.3)	Received a Pfizer-BioNTech XBB1.5-adapted vaccine	Did not receive the XBB.1.5 vaccine (including unvaccinated individuals)	≥14	**ED/UC visits or hospitalisation:** 5-17 years: 65 (36-81)
					median (range): 65 (15-199)	**ED/UC visits or hospitalisation:** 5-11 years: 68 (11-88)
					median (range): 64.5 (16-197)	**ED/UC visits or hospitalisation:** 12-17 years: 63 (20-83)

Question 5: Impact of the XBB.1.5 COVID-19 vaccine on COVID-related intensive care unit (ICU) admissions

No data to report

Question 6: Impact of the XBB.1.5 COVID-19 vaccine on COVID-related deaths

Table 6: VE of the XBB.1.5 variant-adapted COVID-19 vaccine against death related to COVID-19 compared with those who did not receive the XBB.1.5 variant-adapted COVID-19 vaccine (n = 6).

Author (date) - Country Type of publication	Population	Predominant variant	Intervention	Comparator group (reference)	Time since last dose (days)	VE (%) (95% CI)
Retrospective cohort						
Andersson et al. (2024) – Denmark, Sweden and Finland Peer-reviewed	≥65 years living in Denmark, Sweden or Finland (N=3,752,564)	Omicron (XBB, EG.5.1, HK.3 and JN.1)	Received the XBB.1.5 variant-adapted vaccine as their 5th dose	Received at least 4 prior doses of COVID-19 vaccine but not an XBB.1.5 variant-adapted vaccine	8 to 168	74.9 (67.4-82.3)
			Received the XBB.1.5 variant-adapted vaccine as their 6th dose			75.6 (71.0-80.3)
			Received the XBB.1.5 variant-adapted vaccine as their 7th dose			66.0 (54.4-77.5)
			Received at least 4 prior doses of COVID-19 vaccine and received an XBB.1.5 variant-adapted vaccine			• ≥65 years: 75.2 (70.6-79.9) • 65-74 years: 71.7 (62.4-81.0) • ≥75 years: 76.0 (70.4-81.5)
					8 to 27	82 (78.5-85.5)
					28 to 48	79.3 (72.4-86.1)
					49 to 69	74.6 (63.3-86.0)
					70 to 90	70.3 (53.6-87.0)
					91 to 111	66.9 (35.3-98.4)
					112 to 132	33.1 (-17.3-83.6)
					133 to 153	33.1 (-17.3-83.6)
					154 to 174	73.4 (6.7-100.0)

		XBB sublineages			8 to 168	85.7 (80.6-90.8)
		BA.2.86 sublineages			8 to 168	78.0 (74.3-81.6)
Ioannou et al. (2025) - United States Peer-reviewed	Emulated RCT including 1,098,498 adults aged 18+ years from the VHA integrated service network who received at least 1 earlier formulation COVID-19 vaccine	Omicron (primarily XBB, EG.5.1 and JN.1)	Received an mRNA XBB.1.5 variant-adapted vaccine and at least one prior dose of earlier-formulation COVID-19 vaccine	Received at least one prior dose of earlier-formulation COVID-19 vaccine but no XBB.1.5 variant-adapted vaccine and	≥10	• 18 to 64 years: 83.62 (20.84-100) • 65 to 74 years: 27.2 (-21.05-58.62) • ≥75 years: 23.27 (-1.06-44.95) • Prior infection 90 to 365 days earlier: 8.27 (-153.94-65.64) • Prior infection over a year ago: 11.62 (-104.1-57.82) No prior infection: 29.92 (6.27-48.53)
					60 days follow up	≥ 18 years: 54.2 (28.26-72.57)
					90 days follow-up	≥ 18 years: 44.3 (22.03-60.98)
					120 days follow-up	≥ 18 years: 30.2 (6.96-47.7)
					End of the study	≥ 18 years: 26.6 (5.53-42.32)
Lin et al. (2024) – United states (Nebraska) Published	Individuals of all ages whose information is available in the Nebraska Electronic Disease Surveillance System and the Nebraska State Immunization	XBB.1.5 or JN.1	Received an XBB.1.5 variant-adapted vaccine	Did not receive an XBB.1.5 variant-adapted vaccine (include unvaccinated individuals)	7 to 13	27.2 (9.9-41.3)
					14 to 20	47.1 (18.8-65.5)
					21 to 27	61.5 (26.8-79.7)
					28 to 34	72.0 (34.0-88.1)
					35 to 41	70.5 (36.2-86.3)
					42 to 48	68.8 (37.9-84.4)
					49 to 55	67.1 (39.0-82.3)
					56 to 62	65.3 (39.5-80.1)

	Information System (NESIIS) (N=1,830,088)				63 to 69	63.4 (38.9-78.1)
					70 to 76	61.4 (37.1-76.4)
					77 to 83	59.3 (33.7-75.1)
					84 to 90	57.1 (28.5-74.3)
					91 to 97	54.8 (21.2-74.0)
					98 to 104	52.3 (11.8-74.2)
					105 to 111	49.7 (0.1-74.7)
					112 to 118	46.9 (-14.2-75.3)
					119 to 125	44.0 (-31.3-76.1)
					126 to 132	41.0 (-51.6-77.0)
					133 to 139	37.7 (-75.7-77.9)
		XBB.1.5			7 to 13	39.0 (11.6-57.9)
					14 to 20	62.8 (21.9-82.3)
					21 to 27	77.3 (31.0-92.6)
					28 to 34	86.2 (39.0-96.9)
					35 to 41	84.6 (40.4-96.0)
					42 to 48	82.7 (41.6-94.9)
					49 to 55	80.7 (42.4-93.5)
					56 to 62	78.4 (42.7-91.8)
					63 to 69	75.8 (42.5-89.8)
					70 to 76	72.9 (41.3-87.5)
					77 to 83	69.7 (38.8-85.0)
					84 to 90	66.1 (34.4-82.5)
					91 to 97	62.1 (27.2-80.3)
					98 to 104	57.6 (16.4-78.5)
					105 to 111	52.6 (0.9-77.3)
					112 to 118	46.9 (-20.4-76.6)
					119 to 125	40.6 (-49.0-76.3)
					126 to 132	33.6 (-86.7-76.4)
		JN.1			7 to 13	20.4 (-4.6-39.4)
					14 to 20	36.6 (-9.5-63.3)

					21 to 27	49.6 (-14.5-77.8)
					28 to 34	59.8 (-19.8-86.5)
					35 to 41	58.0 (-7.7-83.6)
					42 to 48	56.0 (0.8-80.5)
					49 to 55	54.0 (5.0-77.7)
					56 to 62	51.9 (4.1-75.9)
					63 to 69	49.7 (-2.9-75.4)
					70 to 76	47.3 (-16.8-76.2)
					77 to 83	44.9 (-37.9-78.0)
					84 to 90	42.3 (-67.4-80.1)
Liu et al. (2024) – Australia Preprint	≥65 years individuals recorded in the Census who had not migrated or died by study commencement on the 1 August 2023 (N=4,119,000)	Omicron (primarily EG.5, BA.2.86 and JN.1)	Received an mRNA XBB.1.5 variant-adapted vaccine and at least one booster	Received at least one COVID-19 booster at least one year earlier	8 to 90	• ≥65 years: 74.7 (59.9-84.1) • ≥75 years: 76.7 (61.4-85.9)
		JN.1 (1 Dec 2023 to 29 Feb 2024)			8 to 90	• ≥65 years:74.6 (59.4-84.0)
Monge et al. (2024) - Belgium, Denmark, Italy, Spain (Navarra), Norway, Portugal and the Netherlands Peer-reviewed	Individuals aged 65 years or older, eligible to receive the autumnal booster vaccination at the beginning of the campaign and who received at least a complete primary vaccination and who, in the last 90 days, had no vaccine dose administered and no documented	Omicron (primarily XBB, EG.5.1 and JN.1)	Received an mRNA XBB.1.5 variant adapted vaccine and at least a complete primary vaccination	Received at least a complete primary vaccination but no XBB.1.5 variant adapted vaccine and	≥14	• 65-79 years: 66.9 (42.2-81.0) • ≥80 years: 72.3 (50.5-84.5)

	SARS-CoV-2 infection. (N=22,110,131)					
Nunes et al. (2024) - Belgium, Denmark, Italy, Navarre (Spain), Norway, Portugal and Sweden Peer-reviewed	≥65 years residing in one of the regions, included in and eligible to receive the autumnal 2023 vaccine dose at the start of the country-specific vaccination campaign and part of the VEBIS-HER study (N=20,183,622)	BA.2.86 and JN.1	Received the XBB.1.5 vaccine and at least 2 previous COVID-19 vaccine doses	Received at least 2 COVID-19 vaccine doses but have not received the XBB.1.5 vaccine	≥14	• 65-79 years: 57.5 (41.5-69.1) • ≥80 years: 48.4 (38.2-56.9)
					14 to 89	• 65-79 years: 59.2 (41.3-71.7) • ≥80 years: 51.2 (41.9-59.0)
					90 to 179	• 65-79 years: 54.0 (-16.3-81.8) • ≥80 years: 9.4 (-85.5-55.8)

Question 7: Impact of the XBB.1.5 COVID-19 vaccine on multisystem inflammatory syndrome in children (MIS-C)

No data to report

Question 8: Impact of the XBB.1.5 COVID-19 vaccine on post-COVID conditions

No data to report

Question 9: Impact of the 2024/2025 variant-adapted COVID-19 vaccine on symptomatic and medically attended COVID-19 infections

Table 7: VE of the 2024/2025 variant-adapted COVID-19 vaccine against symptomatic and medically attended COVID-19 infections compared with those who have not received the 2024/2025 variant-adapted COVID-19 vaccine (n=2).

Author (date) - Country Type of publication	Population	Predominant variant	Intervention	Comparator group (reference)	Time since last dose (days)	VE (%) (95% CI)
Test-negative case control						
Appaneal et al. (2024) - United States Pre-print	44,598 respiratory infection episodes in adults aged 18+ and diagnosed with an acute respiratory infection in hospital, emergency department, urgent care or outpatient setting from the US Veterans Affairs Healthcare system	Omicron (primarily KP.2, KP.3, JN.1, and XEC)	Received a Pfizer-BioNTech KP.2-adapted vaccine	Did not receive any KP.2 variant adapted vaccine (includes unvaccinated individuals)	Median (IQR): 31 (20-45)	**Medically attended infections:** ≥18 years: 56 (36-69)
					Median (IQR): 31 (20-46)	**Medically attended infections:** ≥65 years: 58 (36-73)
Rudolph et al. (2024)* - United States Pre-print	CVS MinuteClinic patients aged ≥18 years who had at least one symptom and who tested for SARS-CoV-2 (N=23,884)	Omicron (primarily KP.2, KP.3, JN.1, and XEC)	Received a Pfizer-BioNTech mRNA KP.2 variant-adapted vaccine	Did not receive the KP.2 variant adapted vaccine (includes unvaccinated individuals)	≥14	**Medically attended infections:** • ≥18 years: 48 (35-59) • 18-64 years: 57 (41-68) • 18-49 years: 59 (41-72) • 50-64 years: 55 (20-75) • ≥50 years: 39 (20-53) • ≥65 years: 24 (2-42)

Question 10: Impact of the 2024/2025 variant-adapted COVID-19 vaccine on COVID-related ED or UC visits

Table 8: VE of the 2024/2025 variant-adapted COVID-19 vaccine against COVID related ED or UC visits compared with those who have not received the 2024/2025 variant-adapted COVID-19 vaccine (n = 2).

Author (date) - Country Type of publication	Population	Predominant variant	Intervention	Comparator group (reference)	Time since last dose (days)	VE (%) (95% CI)
Test-negative Case-control						
Appaneal et al. (2024) - United States Pre-print	44,598 respiratory infection episodes in adults aged 18+ and diagnosed with an acute respiratory infection in hospital, emergency department, urgent care or outpatient setting from the US Veterans Affairs Healthcare system	Omicron (primarily KP.2, KP.3, JN.1, and XEC)	Received a Pfizer-BioNTech KP.2-adapted vaccine	Did not receive any KP.2 variant adapted vaccine (includes unvaccinated individuals)	Median (IQR): 35 (25-43)	≥18 years: 57 (46-65)
Retrospective cohort						
Link-Gelles et al. (2025) - United States Report	Adults aged ≥18 years with COVID-19-like illness who visited emergency departments (EDs), urgent care (UC) facilities. (N=173,883)	JN.1 or KP.2/3	Received a 2024-2025 variant adapted vaccine	Did not receive a 2024/2025 variant adapted vaccine	Median (IQR): 55 (32–80)	≥18 years: 33 (28-38)
					Median (IQR): 33 (20–46)	≥18 years: 36 (29-42)
					Median (IQR): 82 (71–97)	≥18 years: 30 (22-37)
					Median (IQR): 53 (29–77)	18 to 64 years: 30 (20-39)
					Median (IQR): 32 (20–45)	18 to 64 years: 36 (23-46)

					Median (IQR): 81 (70–95)	18 to 64 years: 21 (5-35)
					Median (IQR): 57 (33–82)	≥65 years: 35 (29-41)
					Median (IQR): 34 (21–47)	≥65 years: 36 (28-44)
					Median (IQR): 83 (71–97)	≥65 years: 34 (25-42)

Question 11: Impact of the 2024/2025 variant-adapted COVID-19 vaccine on hospitalisations related to COVID-19

Table 9: VE of the 2024/2025 variant-adapted COVID-19 vaccine against hospitalisations related to COVID-19 compared with those who have not received the 2024/2025 variant-adapted COVID-19 vaccine (n = 1).

Author (date) - Country Type of publication	Population	Predominant variant	Intervention	Comparator group (reference)	Time since last dose (days)	VE (%) (95% CI)
Test-negative Case-control						
Appaneal et al. (2024) - United States Pre-print	44,598 respiratory infection episodes in adults aged 18+ and diagnosed with an acute respiratory infection in hospital, emergency department, urgent care or outpatient setting from the US Veterans Affairs Healthcare system	Omicron (primarily KP.2, KP.3, JN.1, and XEC)	Received a Pfizer-BioNTech KP.2-adapted vaccine	Did not receive any KP.2 variant adapted vaccine (includes unvaccinated individuals)	Median (IQR): 30 (21-43)	≥18 years: 57 (46-65)
					Median (IQR): 30 (22-43)	≥65 years: 56 (44-66)

Definitions for vaccine effectiveness (VE)

- The WHO defines preferred levels of initial VE as:
  - VE against symptomatic disease ≥70%, with the lower 95% CI ≥50%; or
  - VE against severe disease ≥90%, with the lower 95% CI ≥70%
- The CDC defines the different terms for VE as follows:
  - Absolute VE (aVE) refers to vaccine protection that is estimated by comparing vaccinated individuals with unvaccinated individuals.
  - Relative VE (rVE) refers to vaccine protection that is estimated by comparing individuals who received the vaccine or regimen of interest with those who received a different vaccine or a different vaccine schedule.
  - Incremental VE (iVE) refers to vaccine protection that is estimated by comparing individuals who received more doses with those who received fewer doses.

Risk of bias (RoB) assessment

The risk of bias data for each individual study is provided in the Supplementary File (les21.5_vaccine_effectiveness_3_RoB_2025-03-01.xlsx).

Strengths and Limitations

Key strengths of the present review include the broad search terms that were included during the initial screening phase, the rigorous methodologies that were employed throughout the review, and validation processes that were included to ensure consistency. In spite of these strengths, there were several limitations that need to be noted. As with any rapid review process, there is a slightly increased possibility that studies might be missed when compared to a full systematic review. However, this was potentially mitigated as we validated our study inclusions against another evidence synthesis team. Due to the turnaround time for the review, we weren't able to contact authors for studies that could have potentially provided data, which means that some studies which had the potential to be included, were excluded (e.g., those that graphed data but did not provide explicit data within the manuscript).

Land Acknowledgements

The Montreal Behavioural Medicine Centre, Concordia University, UQAM, and the CIUSSS-NIM are located on unceded Indigenous lands. The Kanien'kehá:ka Nation is recognized as the custodians of the lands and waters on which these institutions stand today. Tiohtiá:ke commonly known as Montreal is historically known as a gathering place for many First Nations. Today, it is home to a diverse population of Indigenous and other peoples. We respect the continued connections with the past, present, and future in our ongoing relationships with Indigenous and other peoples within the Montreal community.

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