Results of COVID-19 Vaccine Effectiveness Studies: An Ongoing Systematic Review

Forest Plots: Vaccine Effectiveness of Bivalent Ancestral Strain/Omicron-based Vaccines

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METHODS FOR INCLUSION IN FOREST PLOTS

The plots included here summarize the evidence as of March 9, 2023 for the vaccine effectiveness (VE) of COVID-19 bivalent vaccines. At this time, limited evidence is available for only Moderna and Pfizer BioNTech bivalent vaccines: ancestral strain + Omicron BA.1 vaccines and ancestral strain + Omicron BA.4/BA.5 vaccines. VE estimates included in these plots are from an ongoing systematic review of COVID-19 vaccine effectiveness studies. Complete details on the methods of the systematic review as well as a summary table of results can also be found on the VIEW-hub Resources Page:

- "COVID-19 Vaccine Effectiveness and Impact Studies Review Methods"
- "COVID-19 Vaccine Effectiveness Results Summary Table"

There are some instances when more than one estimate from a study will be displayed in the same plot (e.g. a study includes VE estimates from two distinct populations or two different Omicron subvariant periods). Reference numbers are included for each VE estimate displayed so users can identify when a study is represented more than once within a plot. More information on each reference can be found in the weekly literature review summary table located on VIEW-HUB (https://view-hub.org/resources).

As the world is now in a later stage of the COVID-19 pandemic with an increasing smaller proportion of the population remaining unvaccinated, the majority of VE estimates presented here are *relative* VE estimates rather than *absolute* VE estimates. That is, the group being evaluated is compared to other vaccinated persons rather than unvaccinated persons (e.g. persons receiving a 2nd booster dose of bivalent vaccines are compared to persons receiving only a first booster of monovalent vaccines). It is important to note that interpretation of relative VE is not straightforward; it cannot be translated into absolute VE or cases prevented after a second booster dose, and declines in relative VE over time do not equate to declines in absolute VE over time. Moreover, relative VE cannot be compared across studies due to differences in the absolute VE (which is often not reported) and epidemiological context of the setting of each study.

Further complicating interpretation of relative VE, the comparator or reference group can vary between studies, with some studies comparing persons recently receiving a bivalent vaccine to persons who received one less dose of monovalent vaccines at any time in the past, or at a specific time point in the past (e.g. at least 4 months prior, at least 6 months prior, etc.). The choice of comparator is an important consideration in interpreting relative VE. For more information on interpreting relative VE, see the special focus on relative vaccine effectiveness from the June 29th Weekly Epidemiological Update.

In addition, it is important to note that observed differences in vaccine effectiveness between bivalent and monovalent vaccines could also be explained in part by methodological issues (e.g. biases resulting from differences in the timing of vaccine rollout and omicron subvariant circulation, differences in time since last dose was received, different risk groups receiving monovalent vs. bivalent vaccines, etc.). More studies are needed to assess the effectiveness of bivalent vaccines against currently circulating Omicron subvariants.
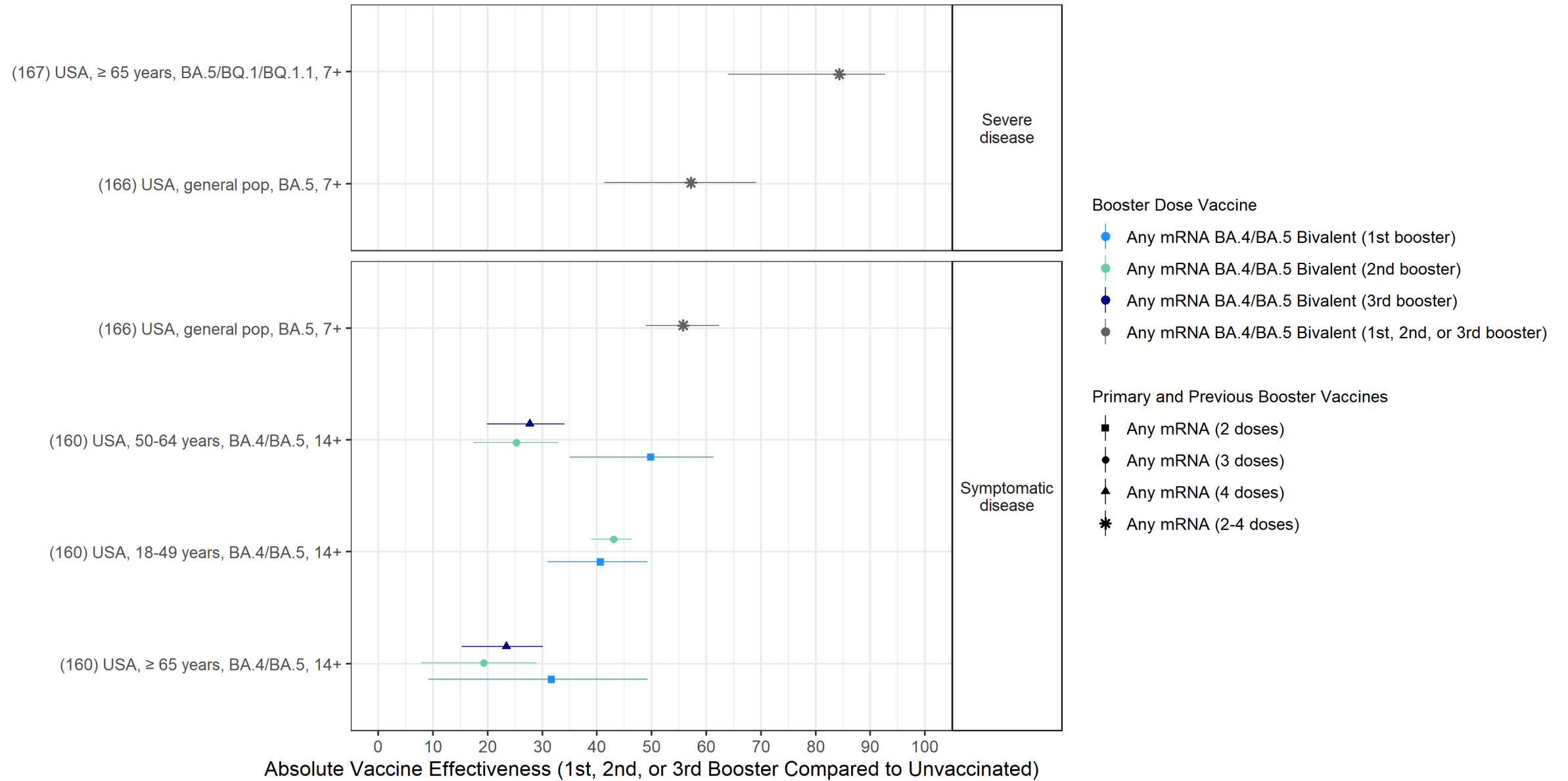
ABBREVIATIONS

pop = population

Vaccine Effectiveness of Bivalent Vaccines

Absolute Vaccine Effectiveness Bivalent mRNA Vaccines: 1st, 2nd, and 3rd Booster dose

(ref no) country, population, omicron subvariant, time since last booster dose (days)

RELATIVE* VACCINE EFFECTIVENESS BIVALENT mRNA VACCINES: 1ST, 2ND, AND 3RD BOOSTER DOSE

(ref no) country, population, subvariant (if specified), time since last booster dose (days)
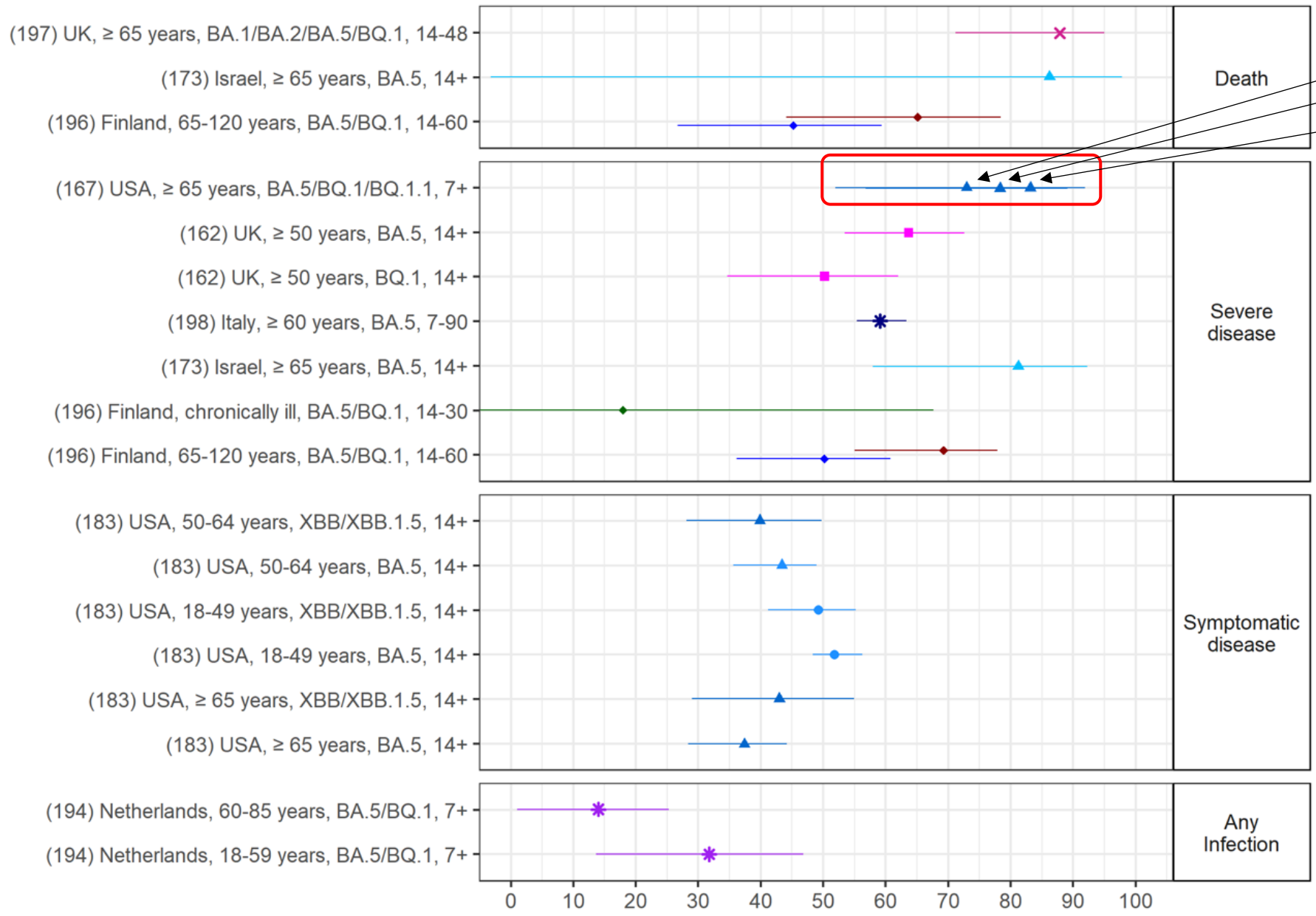
Comparator Group
One less dose received 2 or more months prior
One less dose received 6-11 months prior
One less dose received 12 or more months prior

Death
- (197) UK, ≥ 65 years, BA.1/BA.2/BA.5/BQ.1, 14-48
- (173) Israel, ≥ 65 years, BA.5, 14+
- (196) Finland, 65-120 years, BA.5/BQ.1, 14-60

Severe disease
- (167) USA, ≥ 65 years, BA.5/BQ.1/BQ.1.1, 7+
- (162) UK, ≥ 50 years, BA.5, 14+
- (162) UK, ≥ 50 years, BQ.1, 14+
- (198) Italy, ≥ 60 years, BA.5, 7-90
- (173) Israel, ≥ 65 years, BA.5, 14+
- (196) Finland, chronically ill, BA.5/BQ.1, 14-30
- (196) Finland, 65-120 years, BA.5/BQ.1, 14-60

Symptomatic disease
- (183) USA, 50-64 years, XBB/XBB.1.5, 14+
- (183) USA, 50-64 years, BA.5, 14+
- (183) USA, 18-49 years, XBB/XBB.1.5, 14+
- (183) USA, 18-49 years, BA.5, 14+
- (183) USA, ≥ 65 years, XBB/XBB.1.5, 14+
- (183) USA, ≥ 65 years, BA.5, 14+

Any Infection
- (194) Netherlands, 60-85 years, BA.5/BQ.1, 7+
- (194) Netherlands, 18-59 years, BA.5/BQ.1, 7+

Relative Vaccine Effectiveness (1st, 2nd, 3rd, or 4th Booster Compared to 1 less dose)

*All values shown estimate VE of an additional booster dose relative one less dose.

Booster Dose Vaccine
- Any mRNA BA.4/BA.5 Bivalent (1st or 2nd booster)
- Any mRNA BA.4/BA.5 Bivalent (1st, 2nd, or 3rd booster)
- Any mRNA BA.4/BA.5 Bivalent (2nd booster)
- Any mRNA BA.4/BA.5 Bivalent (1st - 4th booster)
- Pfizer BA.4/BA.5 Bivalent (1st, 2nd, or 3rd booster)
- Any mRNA BA.1 Bivalent (1st, 2nd, or 3rd booster)
- Any mRNA BA.1 Bivalent (2nd booster)
- Any mRNA BA.1 Bivalent (3rd booster)
- Any mRNA BA.1 Bivalent (1st - 4th booster)
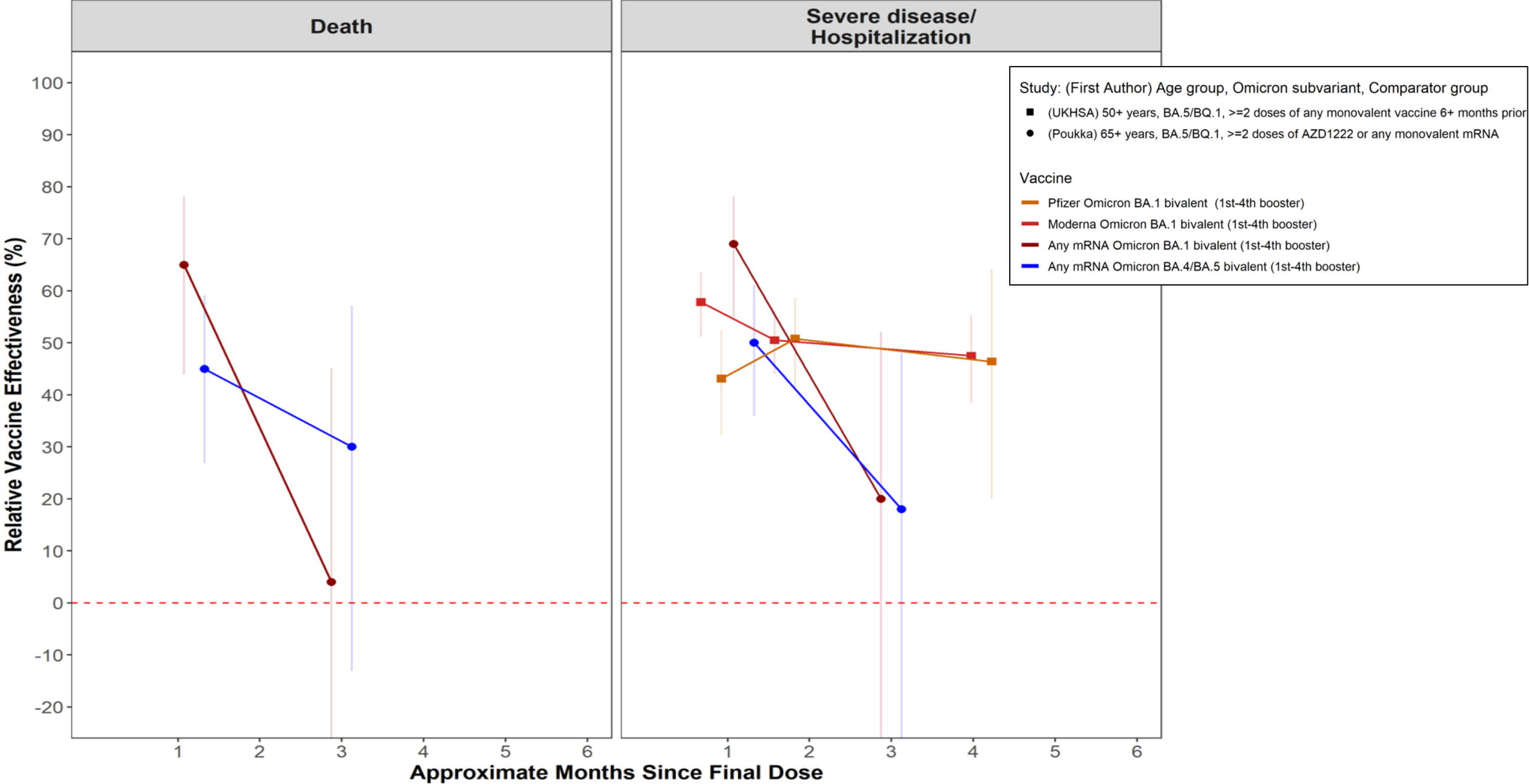- Any mRNA BA.1 or BA.4/BA.5 Bivalent (1st - 4th booster)

Primary and Previous Booster Vaccines
- AstraZeneca or any mRNA (2-3 doses)
- AstraZeneca or any mRNA (2-5 doses)
- Any primary series + any mRNA (3rd dose)
- Any primary series + any mRNA (3rd and 4th dose)
- Any mRNA (2-3 doses)
- Any mRNA (2-4 doses)

RELATIVE VACCINE EFFECTIVENESS OF BIVALENT mRNA VACCINES OVER TIME

Vertical bars represent 95% confidence intervals

RELATIVE VACCINE EFFECTIVENESS OF A 1ST BOOSTER DOSE OF MONOVALENT VS. BIVALENT VACCINES

*All values shown estimate VE of a 1st booster dose relative to primary series

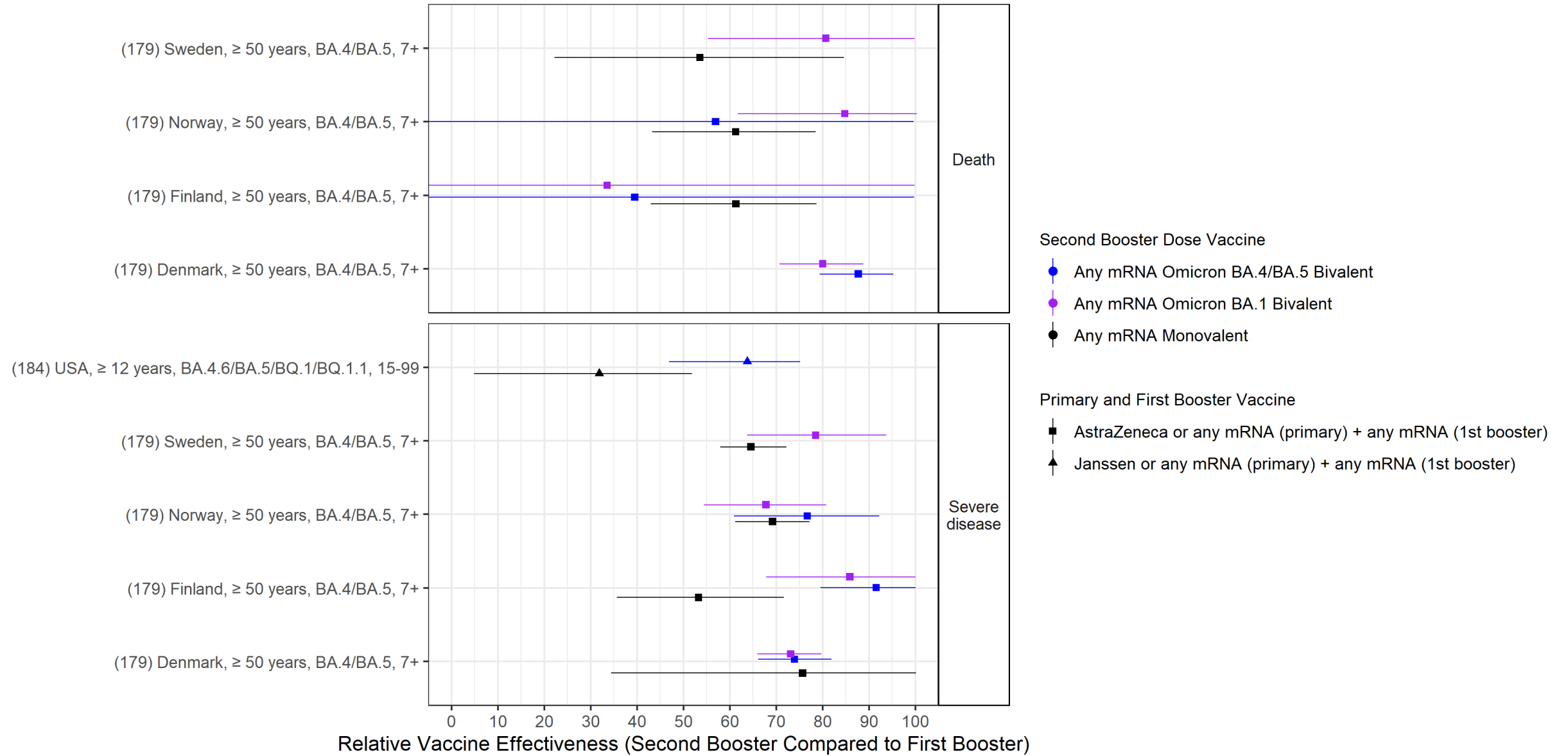# RELATIVE VACCINE EFFECTIVENESS OF A 2ND BOOSTER DOSE OF MONOVALENT VS. BIVALENT VACCINES

(ref no) country, population, subvariant (if specified), time since 2nd booster (days)

*All values shown estimate VE of a 2nd booster dose relative to a first booster dose.