COVID-19 vaccine effectiveness in the elderly population

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GVIRF, 28th March 2023

International Vaccine Institute

Agenda

- Introduction
- Experiences from studies in various countries
- Latest experience with bi-valent vaccines
- Challenges of vaccine development for older adults
- Strategies to overcome challenges

Introduction

- Globally, the ongoing pandemic of coronavirus disease 2019 (COVID-19) is still a severe public health issue.

- As of 16 March 2023, there have been approx. **760 million confirmed cases** of COVID-19, including approx. **6.8 million deaths** globally.

WHO Coronavirus COVID-19 Dashboard

- **Increasing age** is a leading risk factor of severe COVID-19 cases and mortality.

Infect. Chemother. 2020, 52, 154–164

- Aged **60 years and older** have been shown to be more likely than younger people to have severe COVID-19, require hospitalization, and die from COVID-19.

  - Participants aged ≥75 without additional risk factors were at 4-fold risk of COVID-19 mortality compared with all participants aged <65 years

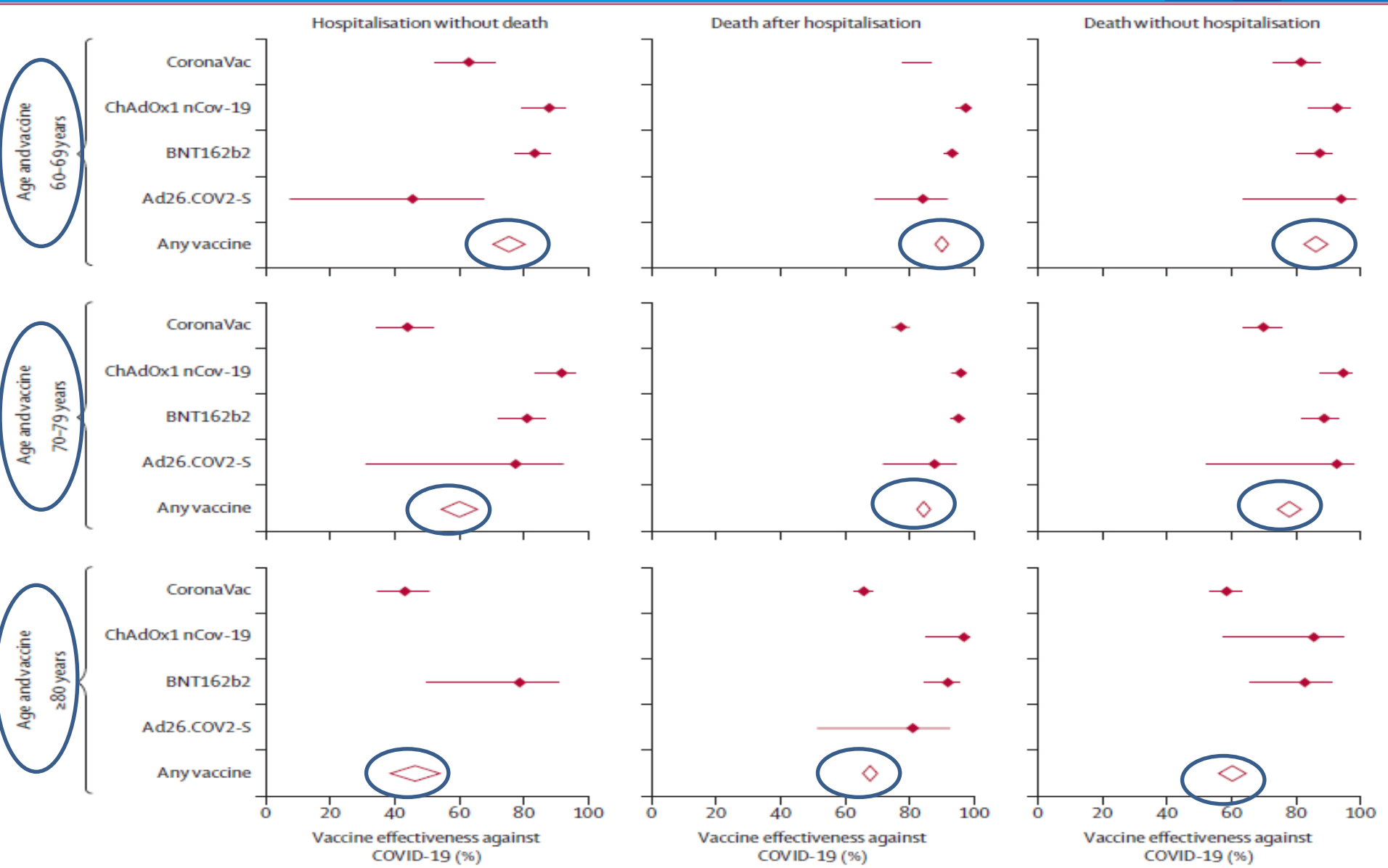
PLoS One. 2020 Nov 5;15(11):e0241824

- **Waning immunity** & evolving **highly contagious new variants** of SARSCoV-2 have led to the consensus recommendation of prioritizing high-risk groups, such as older adults

- COVID-19 vaccination is one of the **most cost-effective** measures in preventing deaths and other severe consequences caused by COVID-19 among older adults

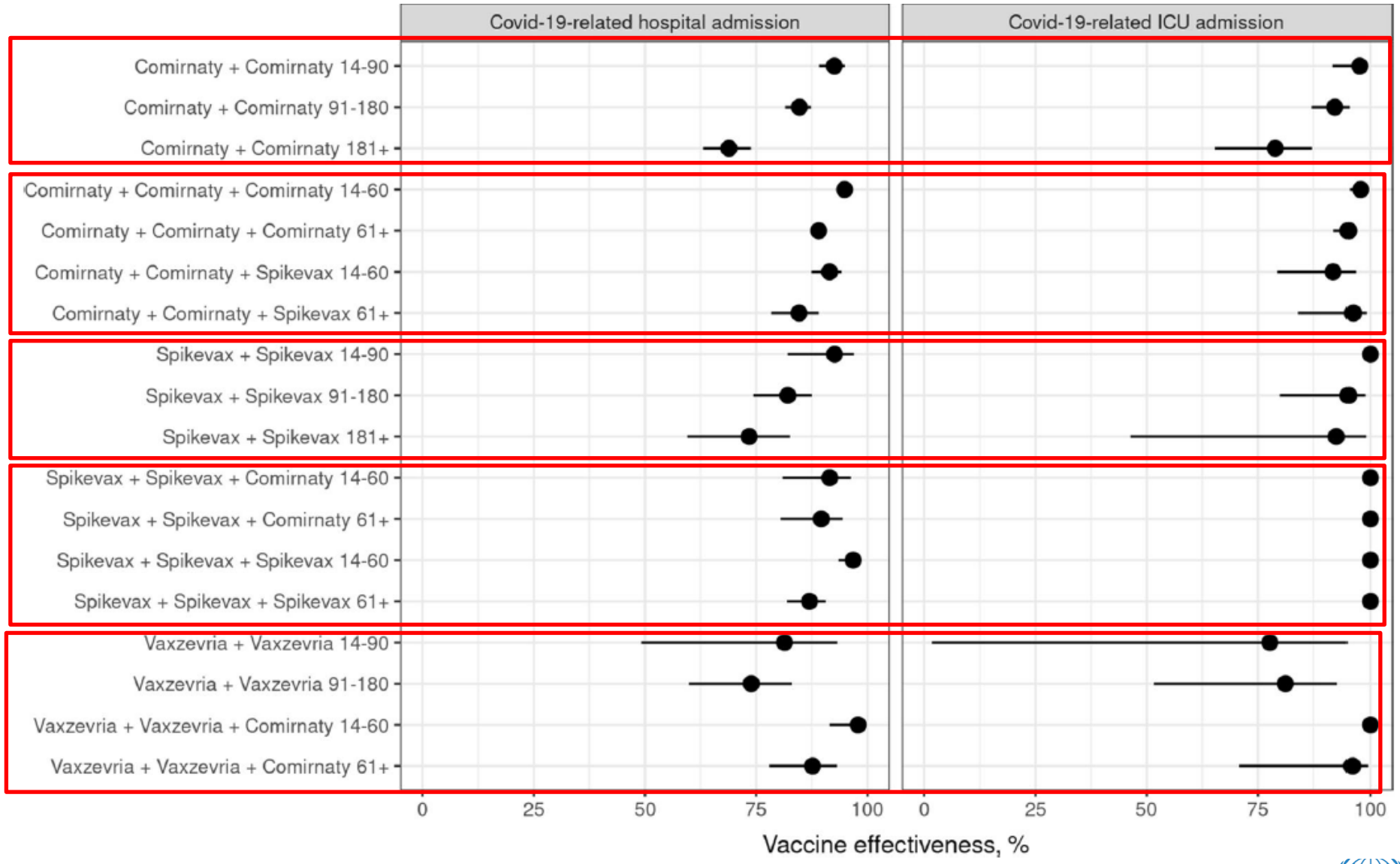
N. Engl. J. Med. 2021, 385, e84.

Effectiveness of COVID-19 vaccines in elderly (A study from Colombia)



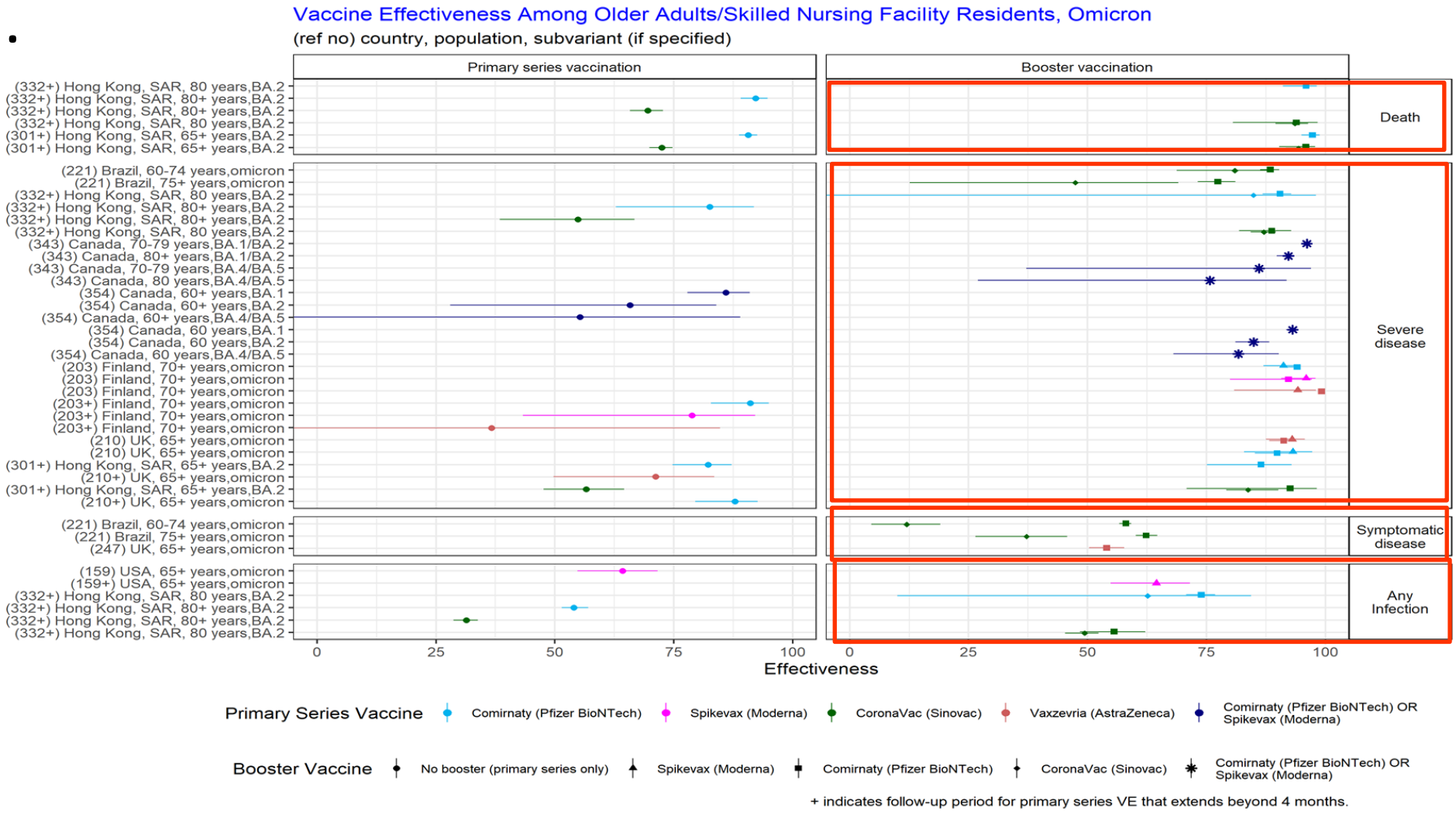
Leonardo Arregocés-Castillo, et al. Lancet Healthy Longev 2022; 3: e242–52

Effectiveness of COVID-19 vaccines in elderly (A study from Finland)



Baum et al. BMC Infectious Diseases (2022) 22:816

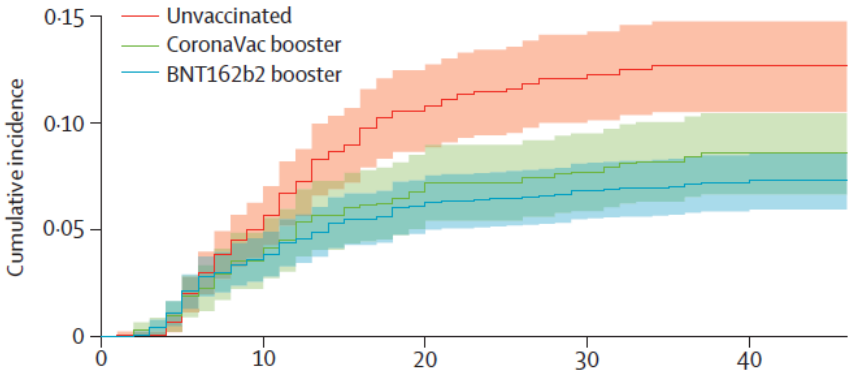
Forest plot of VE among older adults against Omicron



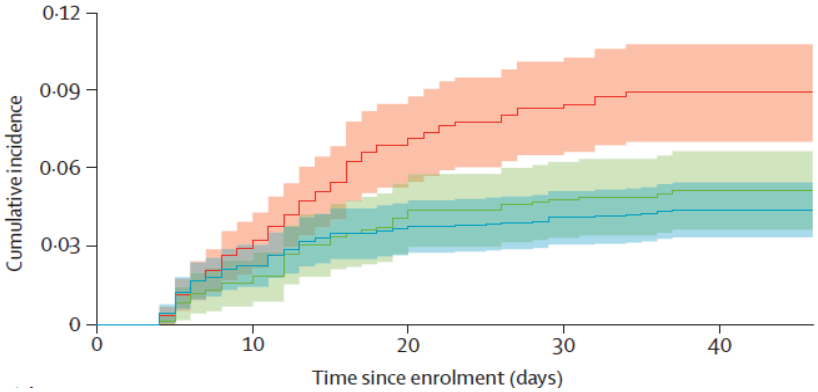
(Courtesy: Daniel Feikin)

Effectiveness of the BNT162b2 and CoronaVac vaccines against COVID-19 omicron BA.2 infection (A study from Hong Kong)

Asymptomatic +Symptomatic



Symptomatic



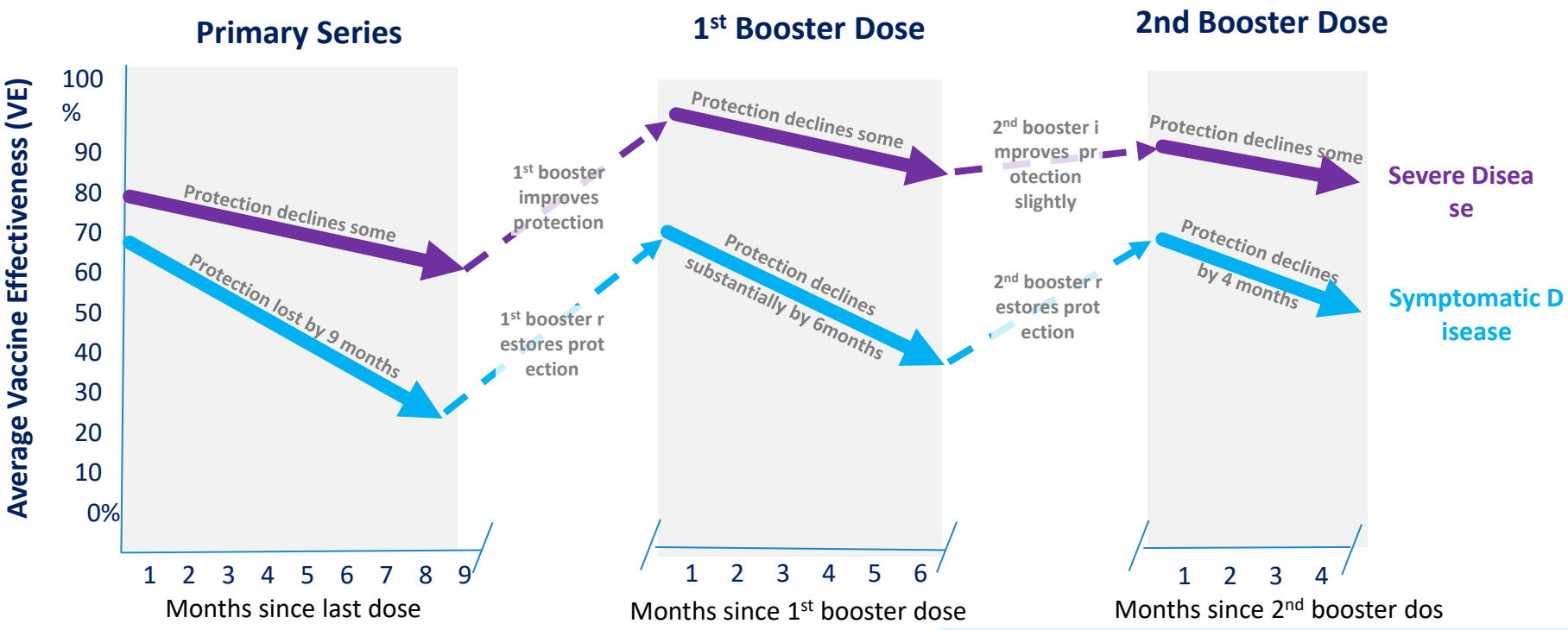
Nicole Ngai Yung Tsang, et a.l.Lancet Infect Dis 2023; 23: 421–34

	Median length of follow-up (person-days)	Total length of follow-up (person-days)	Number of events	Adjusted hazard ratio (95% CI)	Vaccine effectiveness (95% CI)	p value
Asymptomatic and symptomatic infection						
Unvaccinated	31	31 166	123	1 (ref)	1 (ref)	..
BNT162b2						
One dose	22	13 143	40	0·84 (0·58 to 1·19)	16·5% (–19·5 to 41·6)	0·32
Two doses (≥3 months)	32	85 088	323	0·99 (0·80 to 1·22)	1·1% (–22·4 to 20·1)	0·92
Two doses (<3 months)	27	14 524	34	0·72 (0·49 to 1·06)	27·6% (–6·3 to 50·7)	0·10
Three doses	32	66 787	110	0·59 (0·45 to 0·77)	41·4% (23·2 to 55·2)	0·0001
CoronaVac						
One dose	24	13 892	54	1·02 (0·74 to 1·40)	–1·6% (–39·8 to 26·2)	0·92
Two doses (≥3 months)	21	19 891	81	0·95 (0·71 to 1·26)	5·4% (–25·6 to 28·8)	0·70
Two doses (<3 months)	21	11 367	29	0·77 (0·52 to 1·15)	22·7% (–15·2 to 48·2)	0·21
Three doses	36	32 882	72	0·68 (0·50 to 0·91)	32·4% (9·0 to 49·8)	0·0098
CoronaVac plus BNT162b2						
Two-dose CoronaVac plus BNT162b2	36	14 809	34	0·69 (0·47 to 1·01)	31·3% (–1·0 to 53·3)	0·056
Two-dose BNT162b2 plus CoronaVac	36	824	0	..	..	..
Other vaccine combination						
One dose	0	0	0	..	..	..
Two doses (≥3 months)	21	377	2	1·17 (0·27 to 5·12)	–16·8% (–412·1 to 73·4)	0·84
Two doses (<3 months)	27	129	0	..	..	..
Three doses	29	537	1	0·77 (0·12 to 4·78)	23·3% (–377·9 to 87·7)	0·78
Symptomatic infection only						
Unvaccinated	31	31 166	82	1 (ref)	1 (ref)	..
BNT162b2						
One dose	22	13 143	25	0·77 (0·49 to 1·21)	22·9% (–21·4 to 51·0)	0·26
Two doses (≥3 months)	32	85 088	219	0·95 (0·73 to 1·24)	4·7% (–23·5 to 26·6)	0·71
Two doses (<3 months)	27	14 524	23	0·68 (0·43 to 1·09)	31·6% (–9·3 to 57·2)	0·11
Three doses	32	66 787	66	0·49 (0·35 to 0·69)	50·9% (31·0 to 65·0)	<0·0001
CoronaVac						
One dose	24	13 892	38	1·09 (0·74 to 1·61)	–9·3% (–60·5 to 25·6)	0·65
Two doses (≥3 months)	21	19 891	55	0·94 (0·66 to 1·32)	6·4% (–32·1 to 33·7)	0·71
Two doses (<3 months)	21	11 367	22	0·88 (0·55 to 1·40)	12·2% (–40·0 to 44·9)	0·59
Three doses	36	32 882	43	0·58 (0·40 to 0·85)	41·6% (15·0 to 59·8)	0·0049
CoronaVac plus BNT162b2						
Two-dose CoronaVac plus BNT162b2	36	14 809	15	0·44 (0·25 to 0·77)	55·8% (22·9 to 74·6)	0·0040
Two-dose BNT162b2 plus CoronaVac	36	824	0	..	..	..
Other vaccine combination						
One dose	0	0	0	..	..	..
Two doses (≥3 months)	21	377	1	0·92 (0·12 to 7·08)	7·6% (–608·2 to 88·0)	0·94
Two doses (<3 months)	27	129	0	..	..	..
Three doses	29	537	0	..	..	..

Data are n, unless otherwise indicated. Data were adjusted for age group, gender, chronic illness, household size, district, housing type, Hong Kong tertiary planning unit level, and monthly household rent. Symptomatic infections were defined as those with a positive rapid antigen test result after an individuals reported at least one of 19 surveyed symptoms.

Nicole Ngai Yung Tsang, et al.Lancet Infect Dis 2023; 23: 421–34

Summary of COVID-19 VE against Omicron over time (ancestral strain vaccines)

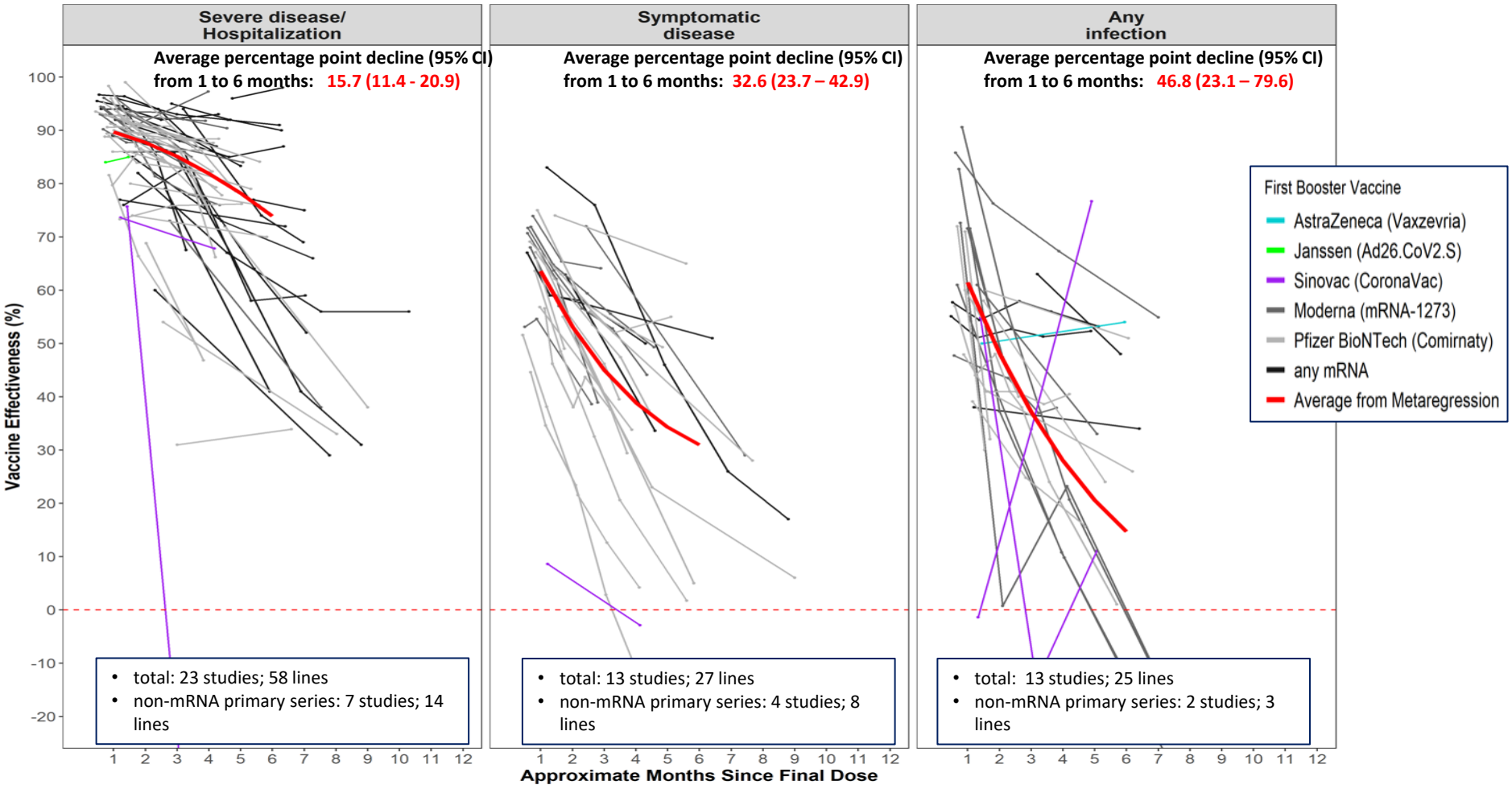


Limitations

- Few studies evaluated 2nd booster (imprecision around average VE)
- Different studies evaluated 1st and 2nd booster
- Possible differences in subvariant circulation for 1st and 2nd booster

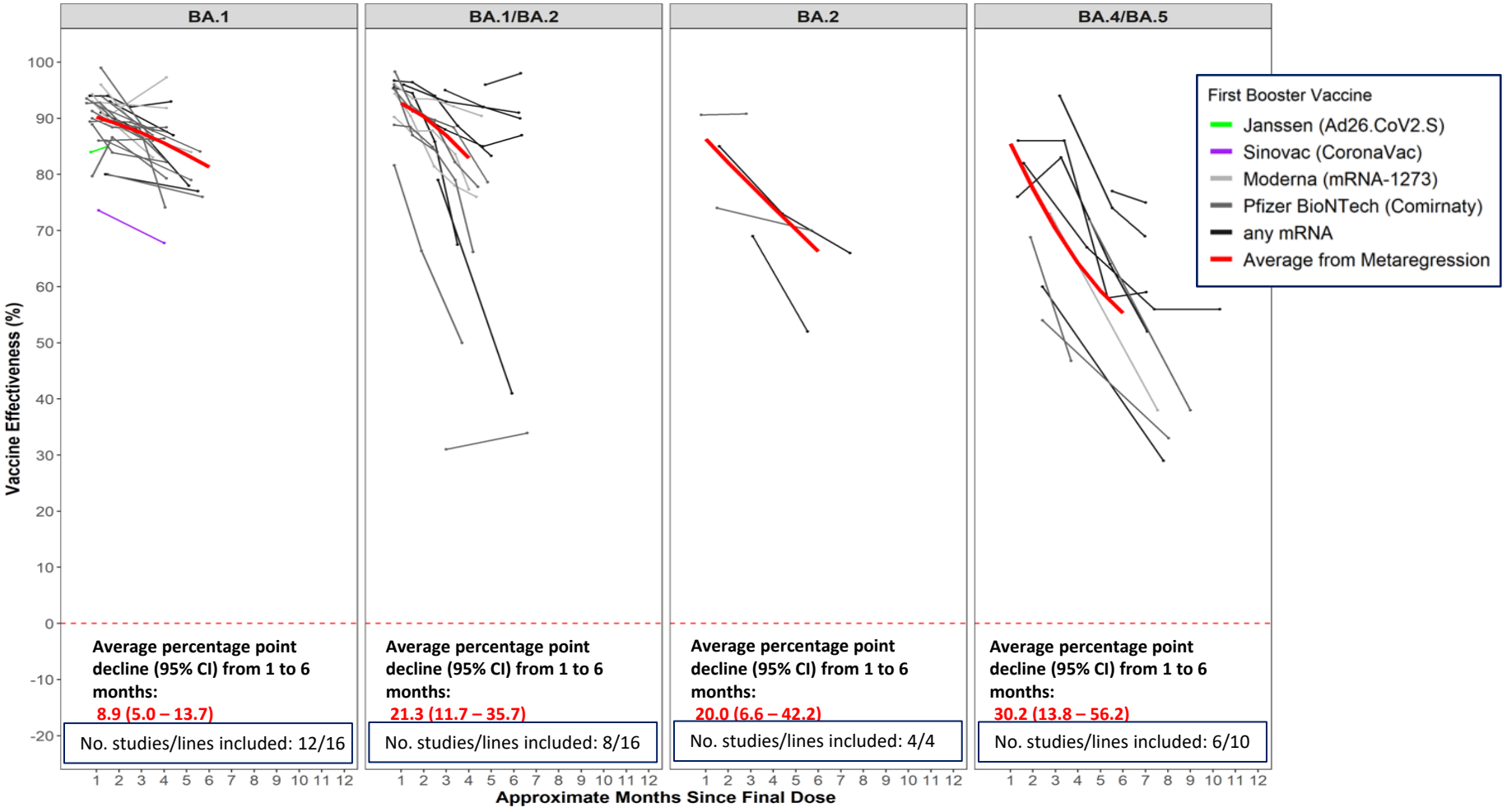
From meta-regression by JHU/IVAC,
Methods in Feikin D, et al, Lancet 2022, doi: 10.1016/S0140-6736(22)00152-0

First Booster Dose VE over time against Omicron



Meta-regression by JHU/IVAC, Methods in Feikin D, et al, Lancet 2022

First Booster Dose VE over time: Severe Disease, by Subvariant



Meta-regression by JHU/IVAC, Methods in Feikin D, et al, Lancet 2022

Experience with Bivalent COVID-19 vaccine booster dose

- The bivalent booster dose provided (during Omicron BA.5 or BQ.1/BQ.1.1 predominance) **73% additional protection against Covid-19 hospitalization among immunocompetent adults ages 65 and over** who had received past monovalent mRNA vaccination only.

Diya Surie et al. Weekly / December 30, 2022 / 71(5152);1625–1630

- A **real-world study from Israel** found that patients 65 and older who received the bivalent booster were **81% less likely to be hospitalized** with Covid-19 and **86% less likely to die** from the virus than those who did not.

Ronen Arbel et al, pre-print The Lancet, Jan 2023

- In the **United Kingdom, among adults aged ≥50 years, a BA.1 bivalent booster** dose was found to have a **relative VE of 57%** compared with ≥2 COVID-19 vaccine doses received ≥6 months earlier

UK Health Security Agency. COVID-19 vaccine surveillance report: week 48.

- A report among adults aged ≥18 years from the VISION Network in the United States using **BA.4/BA.5 bivalent booster doses showed a relative VE of 42% against COVID-19–associated hospitalization compared with ≥2 monovalent** COVID-19 vaccine doses received 8–10 months earlier

Tenforde MW, et al.. MMWR Morb Mortal Wkly Rep 2022;71.

Challenges of vaccine development for older adults

- Age-dependent decline of immunogenicity and clinical effectiveness
- Potentially more rapid waning of immune responses and protection with age
- Lack of vaccines for relevant strains/antigens
- Unsatisfactory vaccination coverage
  - Limited access
  - Vaccine Hesitancy
  - Vaccine Fatigue

Strategies to overcome challenges/ limitations(1/2)

- Higher antigen dose
  - **HD-TIV** induces higher anti-hemagglutinin antibody concentrations and sero-protection rates, increased numbers of influenza specific T cells in older adults compared to TIV

Lee JKH,et al. Expert Rev Vaccines. 2018;17:435–43

- Use of adjuvants
  - Greater efficacy of **aTIV** in preventing laboratory-confirmed influenza (adjusted odds ratio 0.37; and hospitalizations due to pneumonia/influenza (adjusted risk ratio 0.75 compared to standard TIV.

Domnich A,et al. Vaccine. 2017;35:513–20.

  - New adjuvants: **MF59, AS03, AF03** (squalene-based emulsion), Advax-**CpG**55.2 (inulin + TLR9-agonist), **GLA-SE** (emulsion of TLR4-agonist)

- Improved & better vaccines platforms
  - "traditional" influenza vaccine manufacturing **in eggs** or **cell culture**, **mRNA** vaccines
  - Shingrix, a recombinant**, adjuvanted protein** vs Zostavax, live attenuated **vector** zoster vaccine (97.2% vs. 51%)

Strategies to overcome challenges/ limitations(2/2)

- New Delivery system
  - Needle free vaccines(Nasal spray)
- Optimal timing for additional vaccines
  - Longer vaccine intervals, Heterologous prime-boost schedules
- Universal vaccines
  - Universal influenza or pneumococcal vaccines
  - Sarbecovirus (lineage B) betacoronaviruses vaccines
  - Pan Coronavirus vaccines
- Novel vaccines against pathogens
- Education/Awareness
- Continued monitoring

Thank You