Vaccine Effectiveness (VE) of 1st and 2nd booster dose

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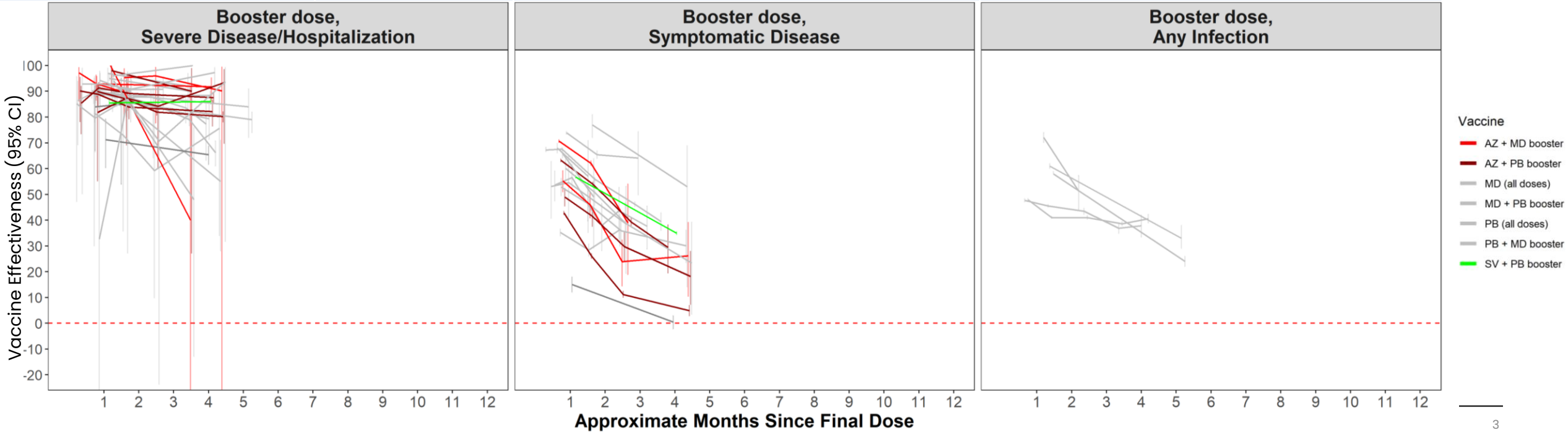
IVB

VE of 1st and 2nd mRNA booster dose

Duration of protection of 1st booster mRNA dose

- Meta-regression of Omicron-specific VE data from December 3, 2021-April 21, 2022
  - All 1st dose booster recipients received either Moderna or Pfizer vaccine

	Severe disease/ hospitalization	Symptomatic Disease	Infection
Percentage point decline from 1-4 months	4.9 (2.0-8.6)	25.1 (22.4-27.8)	15.8 (-0.3-38.2)
Projected percentage point decline from 1-6 months	7.7 (3.0-14.1)	31.5 (24.2-39.7)	23.1 (0.4-57.7)



1st Booster Dose Omicron VE in Pregnant Women and their infants

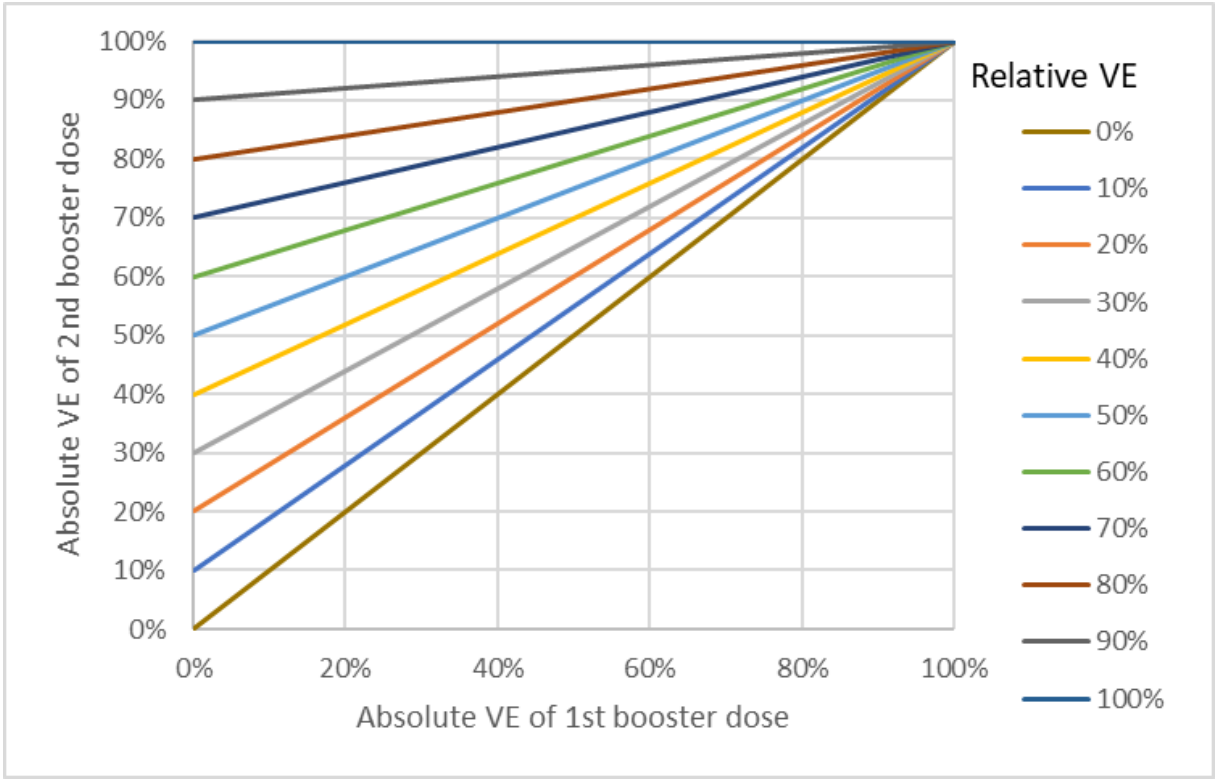
Study	Country	2nd Booster Dose Vaccine	Population	Comparison	Outcome	Absolute VE (95% CI)
Guedalia et al	Israel	Pfizer	Pregnant women	≥0 days after 1st booster dose versus ≥0 doses	Hospitalization	43 (31-53)
					Hospitalization with COVID-19 pneumonia or worse	97 (72-100)
					Hospitalization with serious COVID-19 or worse	94 (43-99)
Carlsen et al	Norway	mRNA	Infants aged 1-122 days	Pregnant women vaccinated ≥14 days prior to delivery vs 0 doses	Infection in infant	78 (57-88)

- No data on waning
- No data on 2nd booster dose in pregnant women

Absolute versus Relative VE

- Absolute VE: vaccinated versus unvaccinated
- Relative VE: X doses of vaccine versus Y doses of vaccine (2nd booster dose vs 1st booster dose)
  - Added protection
- Relationship between the two
  - Relative VE ≤ Absolute VE

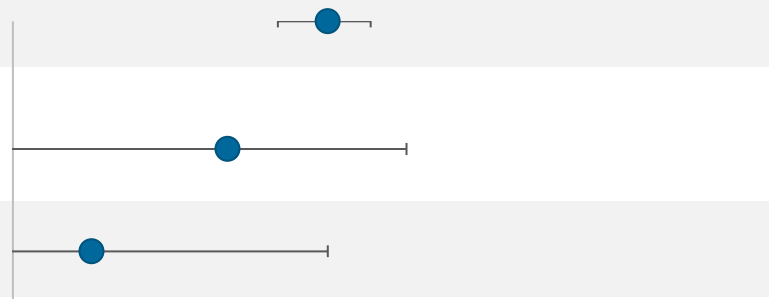
Absolute VE 1st booster dose	Relative VE 2nd booster dose	Absolute VE 2nd booster dose	Absolute gain in VE
90%	50%	95%	5%
0%	50%	50%	50%



- Relative VEs cannot be compared between studies as contingent upon residual immunity in comparator population

2nd Booster Dose Relative VE against infection: Israel

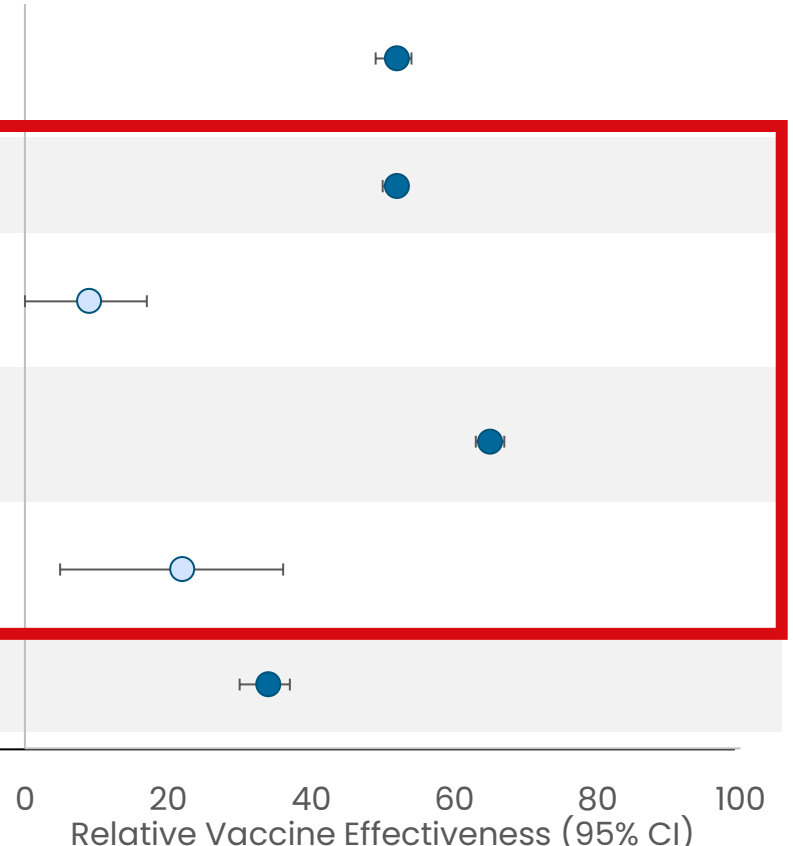
Study	2nd Booster Dose Vaccine	Population	Comparison	Relative VE against Infection (95% CI)
Cohen et al	Pfizer	HCWs	≥7 days after 2nd booster vs. ≥4 months after 1st booster	44% (37-50)
Regev-Yochay et al	Pfizer	HCWs	≥7 days after 2nd booster vs. ≥4 months after 1st booster	30% (-9-55)
	Moderna	HCWs	≥7 days after 2nd booster vs. ≥4 months after 1st booster	11% (-43-44)



HCW: Healthcare worker
LTCF: Long-term care facility

2nd Booster Dose Relative VE against infection: Israel

Study	2nd Booster Dose Vaccine	Population	Comparison	Relative VE against Infection (95% CI)
Magen et al	Pfizer	≥60 year olds	14-30 days after 2nd booster vs. ≥4 months after 1st booster	52% (49-54)
Bar-On et al	Pfizer	≥60 year olds	15-21 days after 2nd booster vs. ≥4 months after 1st booster	52% (50-52)
			50-56 days after 2nd booster vs. ≥4 months after 1st booster	9% (0-17)
Gazit et al	Pfizer	≥60 year olds	14-20 days after 2nd booster vs. ≥4 months after 1st booster	65% (63-67)
			63-69 days after 2nd booster vs. ≥4 months after 1st booster	22% (4.9-36.1)
Muhsen et al	Pfizer	LTCF residents	≥7 days after 2nd booster vs. ≥4 months after 1st booster	34% (30-37)



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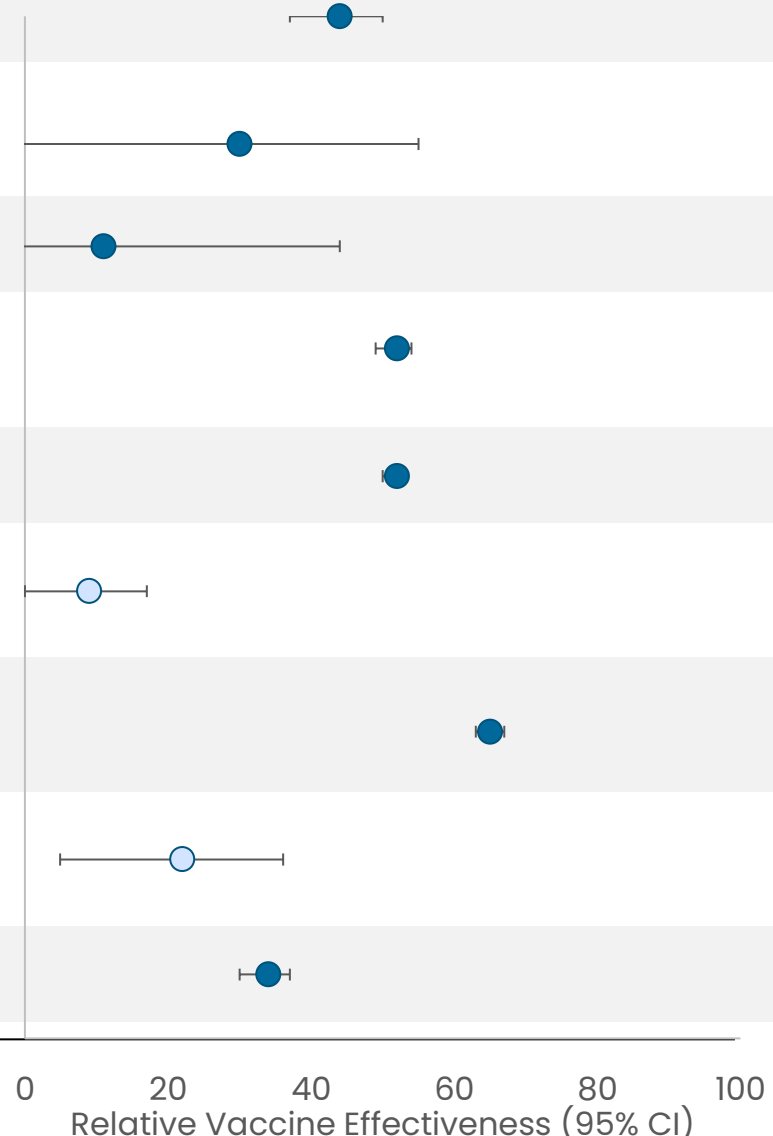

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2nd Booster Dose Relative VE against severe disease: Israel

Study	2nd Booster Dose Vaccine	Population	Comparison	Relative VE against severe disease (95% CI)
Amir et al	Pfizer	≥60 year olds	0-2 months after 2nd booster dose versus ≥4 months after *primary* series.	89% (87-91)
Arbel et al	Pfizer	≥60 year olds	≥7 days after 2nd booster dose versus ≥4 months after 1st booster dose	78% (72-83) against death
Magen et al	Pfizer	≥60 year olds	14-30 days after 2nd booster dose versus ≥4 months after 1st booster dose	64% (48-77) against severe hospitalization
				76% (48-91) against death
Bar-On et al	Pfizer	≥60 year olds	15-21 days after 2nd booster dose versus ≥4 months after 1st booster dose	58% (50-66)
			36-42 days after 2nd booster dose versus ≥4 months after 1st booster dose	77% (62-86)
Gazit et al	Pfizer	≥60 year olds	7-27 days after 2nd booster dose versus ≥4 months after 1st booster dose	77.5% (69.7-83.2)
			49-69 days after 2nd booster dose versus ≥4 months after 1st booster dose	86.5% (63.4-95)
Muhsen et al	Pfizer	LTCF residents	≥7 days after 2nd booster dose versus ≥4 months after 1st booster dose	67% (57-75) against severe hospitalization
				72% (57-83) against death

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2nd Booster Dose Relative VE against severe disease: Israel

Study	2nd Booster Dose Vaccine	Population	Comparison	Relative VE against severe disease (95% CI)	Absolute Reduction
Amir et al	Pfizer	≥60 year olds	0-2 months after 2nd booster dose versus ≥4 months after *primary* series.	89% (87-91)	10.3 cases / 100,000 person days at risk
Arbel et al	Pfizer	≥60 year olds	≥7 days after 2nd booster dose versus ≥4 months after 1st booster dose	78% (72-83) against death	71.2 / 100,000 persons (crude)
Magen et al	Pfizer	≥60 year olds	14-30 days after 2nd booster dose versus ≥4 months after 1st booster dose	64% (48-77) against severe hospitalization	54.8 (34.7-75.9) / 100,000 persons
				76% (48-91) against death	21.1 (10.4–32.8) / 100,000 persons
Bar-On et al	Pfizer	≥60 year olds	15-21 days after 2nd booster dose versus ≥4 months after 1st booster dose	58% (50-66)	3.6 (3.1–4.2) / 100,000 person-days at risk
			36-42 days after 2nd booster dose versus ≥4 months after 1st booster dose	77% (62-86)	4.2 (3.4-4.9) / 100,000 person-days at risk
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				72% (57-83) against death	

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Studies against Other Outcomes or in Other Countries

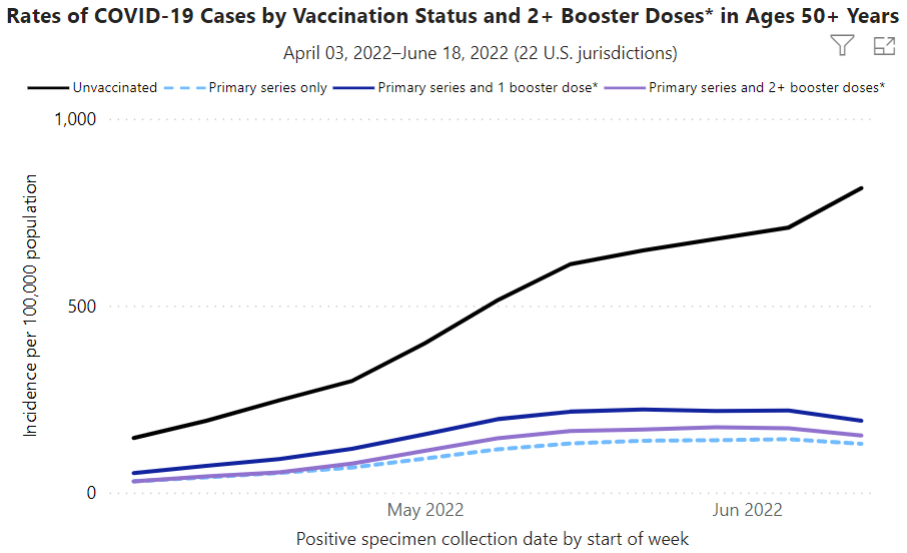
Study	Country	2nd Booster Dose Vaccine	Population	Comparison	Outcome	Relative VE (95% CI)	Absolute VE (95% CI)	Absolute VE point estimate difference (2nd–1st booster dose)
Grewal et al	Canada	mRNA	≥60 year olds living in LTCF	≥7 days after 2nd booster dose versus ≥84 days after 1st booster dose /0 doses	Infection	19% (12-26)	49% (43-54)	12% (≥84 days after 1st booster)
					Severe disease	40% (24-52)	86% (81-90)	9% (≥84 days after 1st booster)
Link-Gelles et al	USA	mRNA	≥50 year olds	≥7 days after 2nd booster dose vs 0 doses	Emergency department/ urgent care visits		66% (60–71)	34% (≥120 days after 1st booster)
					Hospitalization		80% (71-85)	25% (≥120 days after 1st booster)
Chariyalertsak et al	Thailand	Pfizer	≥18 year olds	≥7 days after 2nd booster dose vs 0 doses	Symptomatic disease		71% (60-79%)	40% (≥7 days after 1st booster
		Moderna					71% (59-79%)	40% (≥7 days after 1st booster)

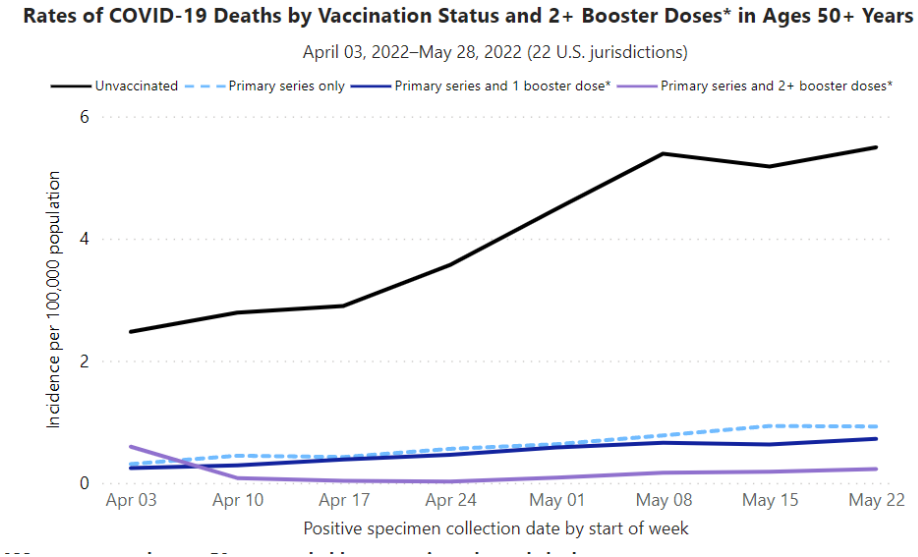
US Surveillance Data

- March 29: US recommends a 2nd booster dose among 50+ and moderate/severely immunocompromised populations/JNJ booster
- Surveillance data from 22 jurisdictions linked to vaccination data allowing calculation of CRUDE rates by vaccination status

Vaccination status	Incidence of Infection /100,000	Incidence of Death /100,000
Unvaccinated	814.41	5.49
Primary series	130.49	0.92
1 booster dose	192.13	0.72
2+ booster doses	152.79	0.23

- Overall 4x risk of dying if 1 booster vs 2 booster
- Limitations:
  - Interpretation of recent trends challenging due to
    - Higher prevalence of prior infection among the unvaccinated and un-boosted groups;
    - Difficulty in accounting for time since vaccination and waning protection
    - Confounding due to differences in testing practices (such as at home testing), prevention behaviors by age and vaccination status.





https://covid.cdc.gov/covid-data-tracker/#rates-by-vaccine-status

VE of 1st and 2nd non-mRNA booster dose

Duration of Protection of non-mRNA 1st booster dose

- Not enough studies to run metaregression

Study	Country	Population	1st booster dose Vaccine	Timing of booster dose	Absolute VE (95% CI) against symptomatic disease	Absolute VE (95% CI) against severe outcomes
Cerqueria-Silva	Brazil	≥18 years old with previous infection	Janssen (2 doses)	0-1 week	34.1 (26.2-41.1)	55.2 (-82.7-89)
				2-9 weeks	22.8 (18.8-26.6)	84 (56.6-94.1)
Natarajan*	USA	≥18 years old	Janssen (2 dose)	7-120 days	54 (43–63)	67 (52–77)
Ranzani	Brazil	≥18 years old	Coronavac	8-59 days	15 (12-18)	71.3 (60.3-79.2)
				≥60 days	0.4 (-2.2-2.9)	65.4 (61.5-68.8)
Cerqueria-Silva	Brazil	≥18 years old with previous infection	Coronavac	0-1 week	54.7 (51.4-57.8)	67.9 (32.6-84.7)
				≥10 weeks	37.9 (35.8-40)	75.7 (69.6-80.7)
Cerqueria-Silva	Brazil	≥18 years old with previous infection	AZ	0-1 week	56 (53.8-58)	79.4 (66.8-87.3)
				≥10 weeks	32.6 (29.4-35.7)	81.2 (72.5-87.1)
Kirsebom	UK	≥40 years old	AZ	7-13 days	61.2 (40.9 to 74.6)	
				70-104 days	40.8 (18.6 to 56.9)	
		≥65 years old		7-13 days	66.1 (16.6 to 86.3)	
				35-69 days	44.5 (22.4 to 60.2)	

*against emergency department/ urgent care visits

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Thailand: Absolute VE of AZ booster dose against symptomatic disease

- TND study among ≥18 year olds by linking administrative databases between February 1-April 10, 2022
- Calculated absolute VE by booster dose received
  - Most 18-59 year olds vaccinated with Coronavac, ≥60 vaccinated with AZ as primary series
- Results
  - Absolute 1st booster dose AZ 26% (8-40)→2nd booster dose VE 73% (48-89)
    - Median days ~40 since 4th dose
    - No difference between Pfizer, Moderna, AZ 4th dose
- Does not account for waning and significant confounders

Chariyalertsak, S., Chalom Chiang Mai Provincial Health Oce Thanachol Wonghirundecha Chiang Mai Provincial Health Oce Woravut Kowatcharakul Sansai Hospital, K., Mai, C., Teacharak Nakornping Hospital, W., Mai Pimpinan khammawan Nakornping Hospital, C., & Mai Jarurin Waneesorn, C. (2022). *Effectiveness of heterologous 3 rd and 4 th dose COVID-19 vaccine schedules for SARS-CoV-2 infection during delta and omicron predominance in Thailand*. https://doi.org/10.21203/rs.3.rs-1792139/v1

Conclusions

- 1st booster dose VE
  - Declines dramatically against infection and symptomatic disease in the first 4 months
  - Declines minimally against severe disease/hospitalization
  - Data only for BA1/BA2
- 2nd booster dose VE
  - Increases VE against infection, symptomatic disease and severe disease
  - Hard to quantify absolute gain against severe disease
  - Limited follow-up time
  - Only 1 study from a non-high income country
  - Only 1 study for non-mRNA 2nd booster dose

} More data needed