Vaccines and Related Biological Products Advisory Committee Meeting

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State of Israel
Ministry of Health
משרד הבריאות

WEIZMANN INSTITUTE OF SCIENCE

TECHNION
Israel Institute of Technology

The Gertner Institute

THE HEBREW UNIVERSITY OF JERUSALEM

Booster protection against confirmed infections and severe disease - data from Israel

Israeli MOH, Weizmann Institute of Science,
Gertner Institute, Hebrew University & Technion

Sept. 17th, 2021

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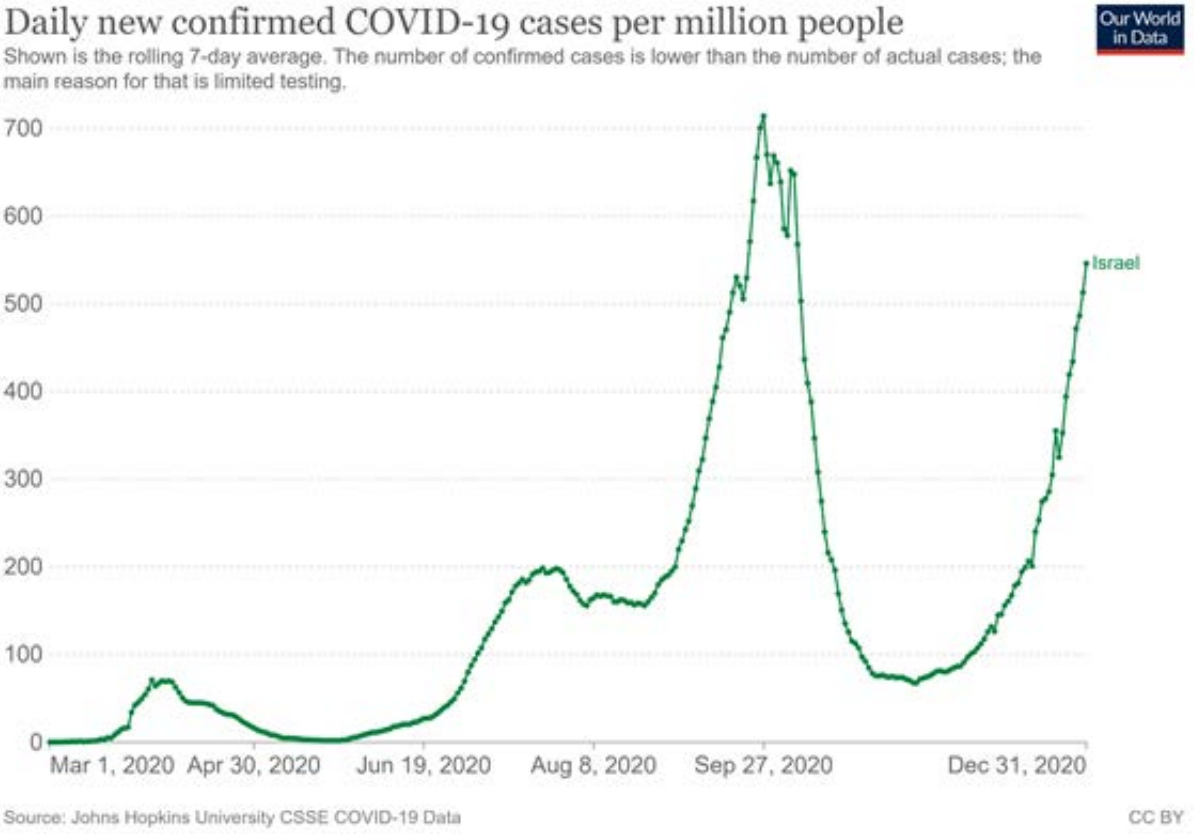
Sharon Alroy-Preis & Ron Milo have no competing financial interests to disclose.

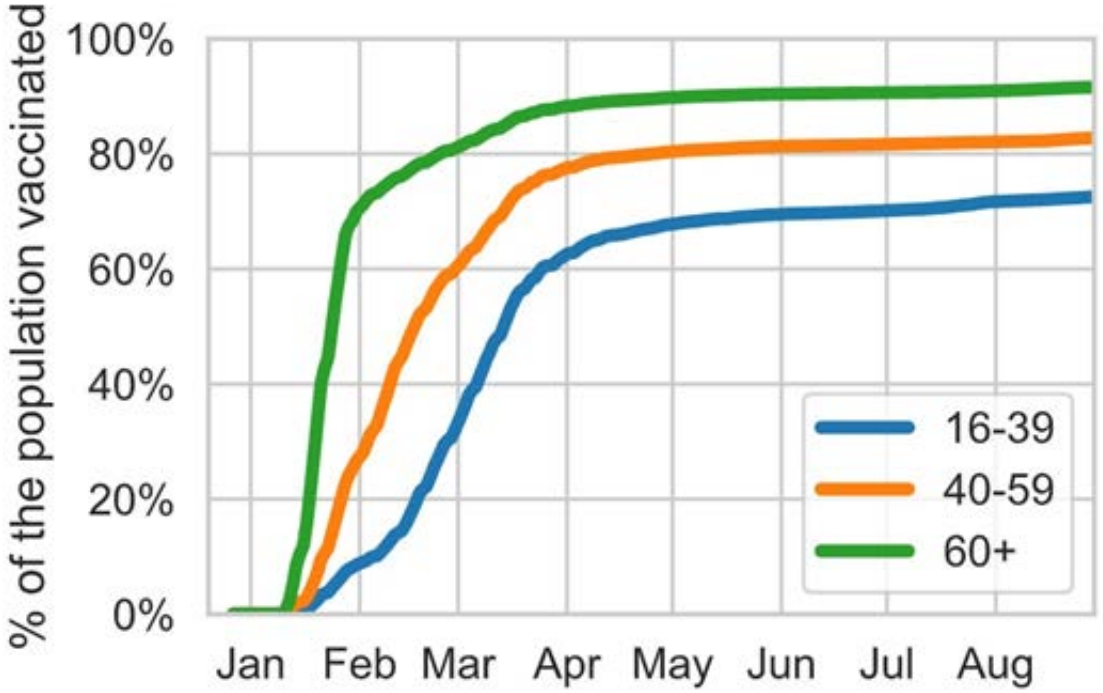
Israel MOH and Pfizer have a data sharing agreement. In relation to the immunity waning and booster effectiveness studies presented here only final results of the analysis were shared with Pfizer.

Israel began a vaccination campaign at the end of 2020 during a surge in cases



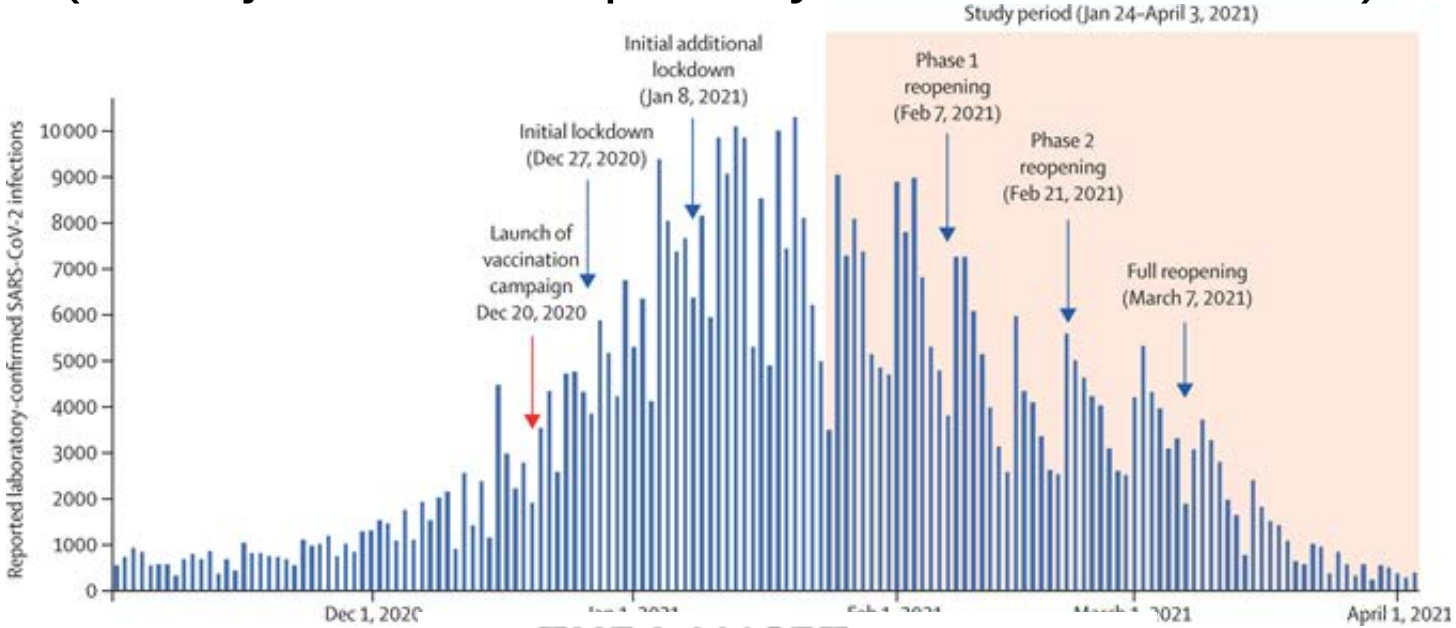
MINISTRY OF HEALTH

The vaccination campaign started early in Israel using the Pfizer BNT162b2 with 3 week regimen



MINISTRY OF HEALTH

Over 100-fold decrease in cases following vaccination campaign (in conjunction with partially effective lock-down)



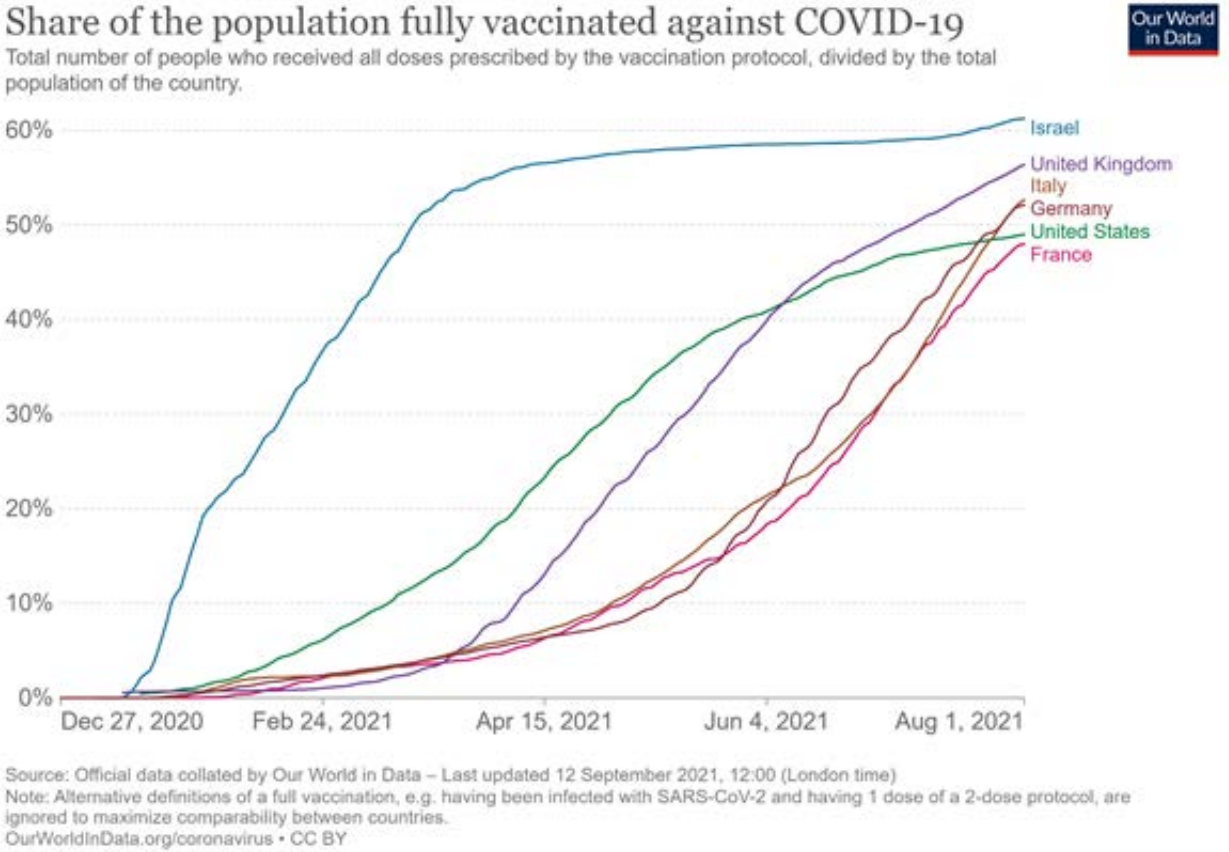
THE LANCET

Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data

Eric J Haas, Frederick J Angulo, John M McLaughlin, Emilia Anis, Shepherd R Singer, Farid Khan, Nati Brooks, Meir Smaja, Gabriel Mircus, Kaijie Pan, Jo Southern, David L Swerdlow, Lois Jodar, Yehenkel Levy, Sharon Alroy-Preis

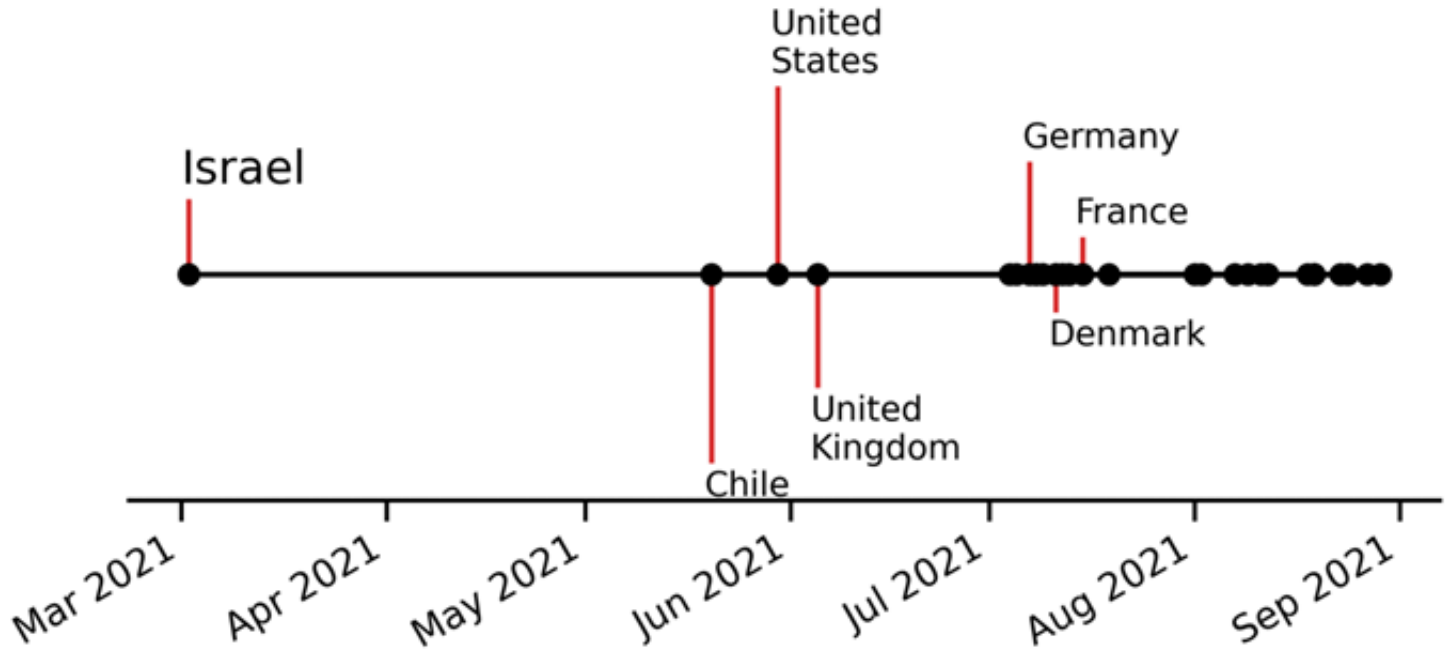
MINISTRY OF HEALTH

Israel reached high levels of population-wide immunity early on



MINISTRY OF HEALTH

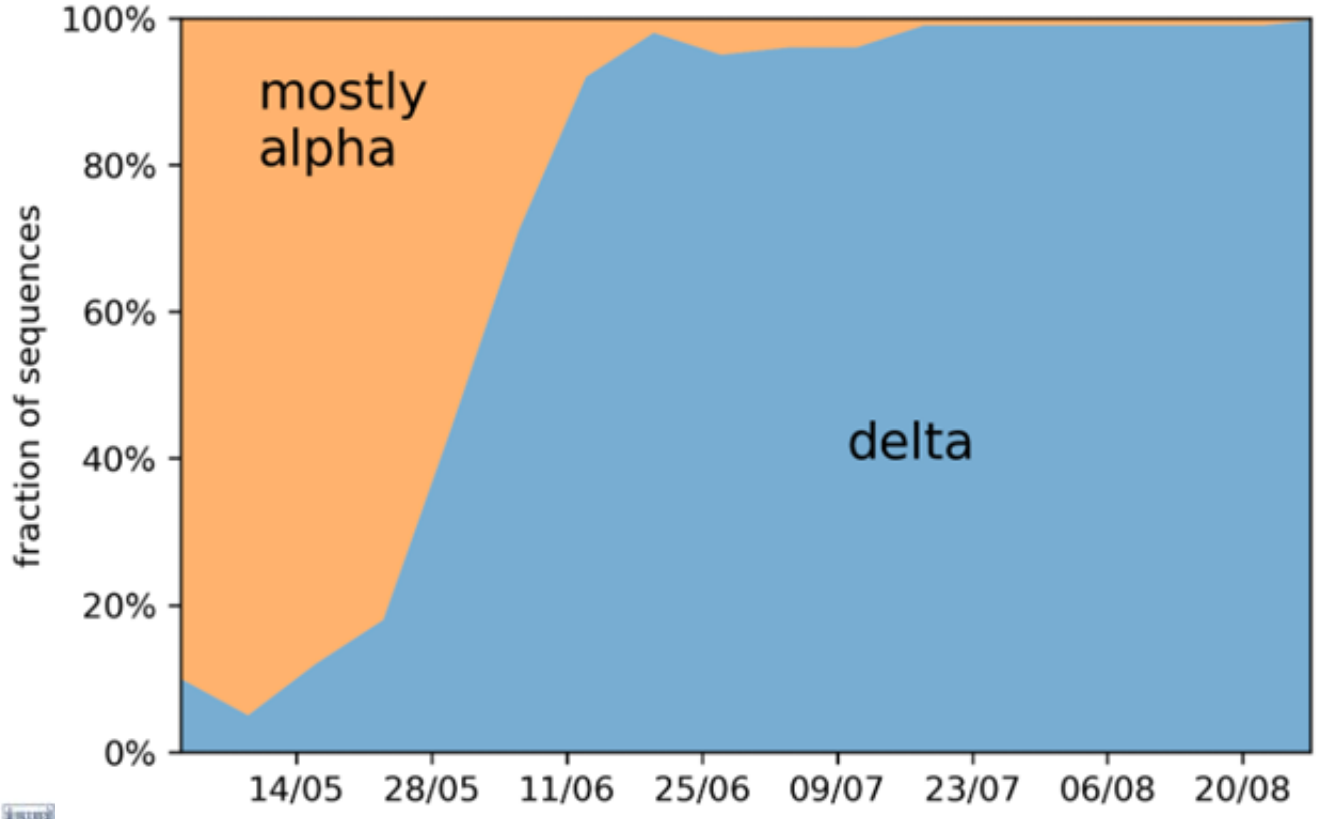
Israel reached high levels of population-wide immunity ≈3 months before most countries



Israel has large testing capacity (16,000 daily tests per million) & comprehensive electronic COVID19 records for the entire population

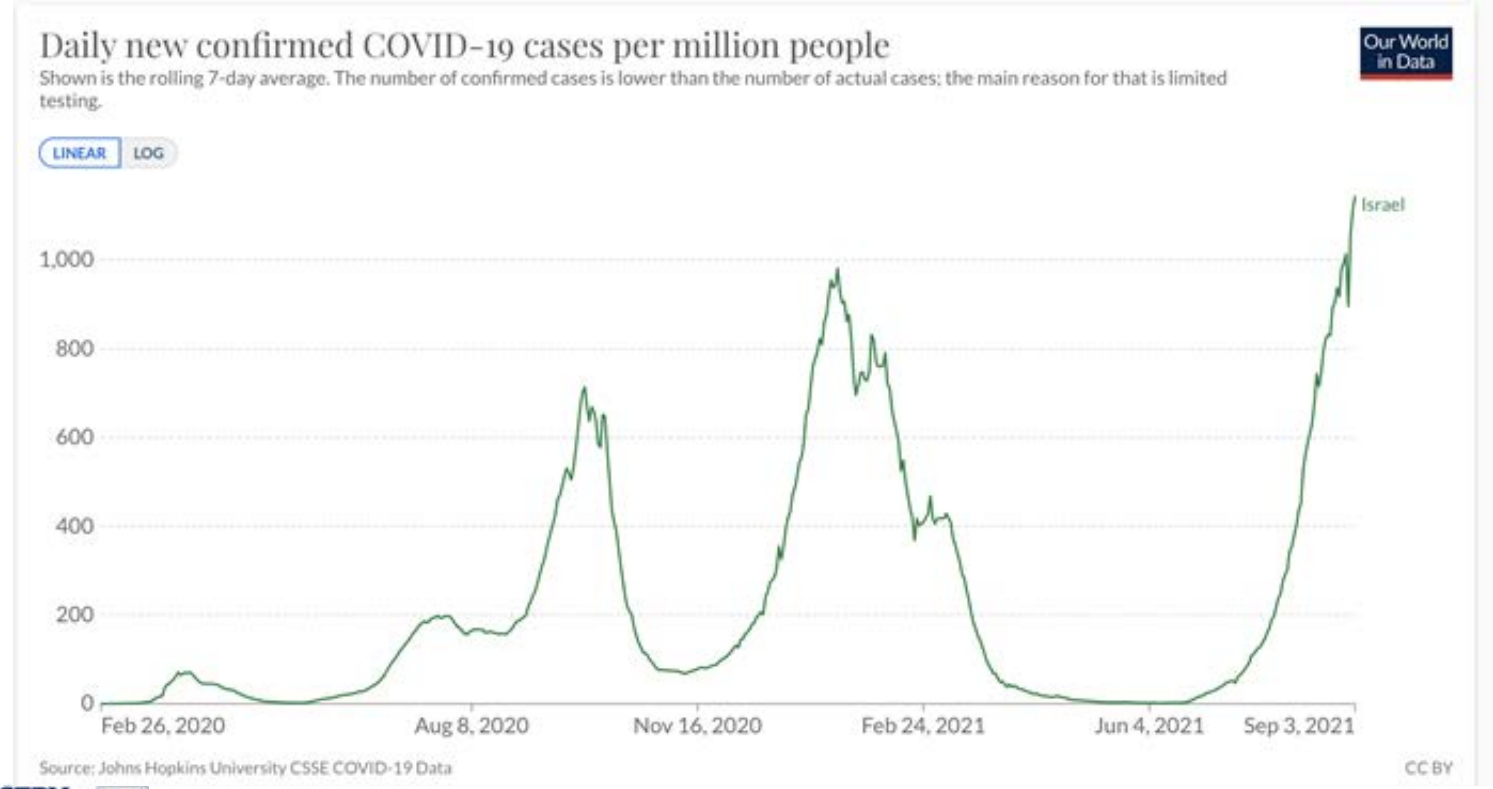
MINISTRY OF HEALTH

During June alpha was overtaken by the delta variant in Israel



MINISTRY OF HEALTH

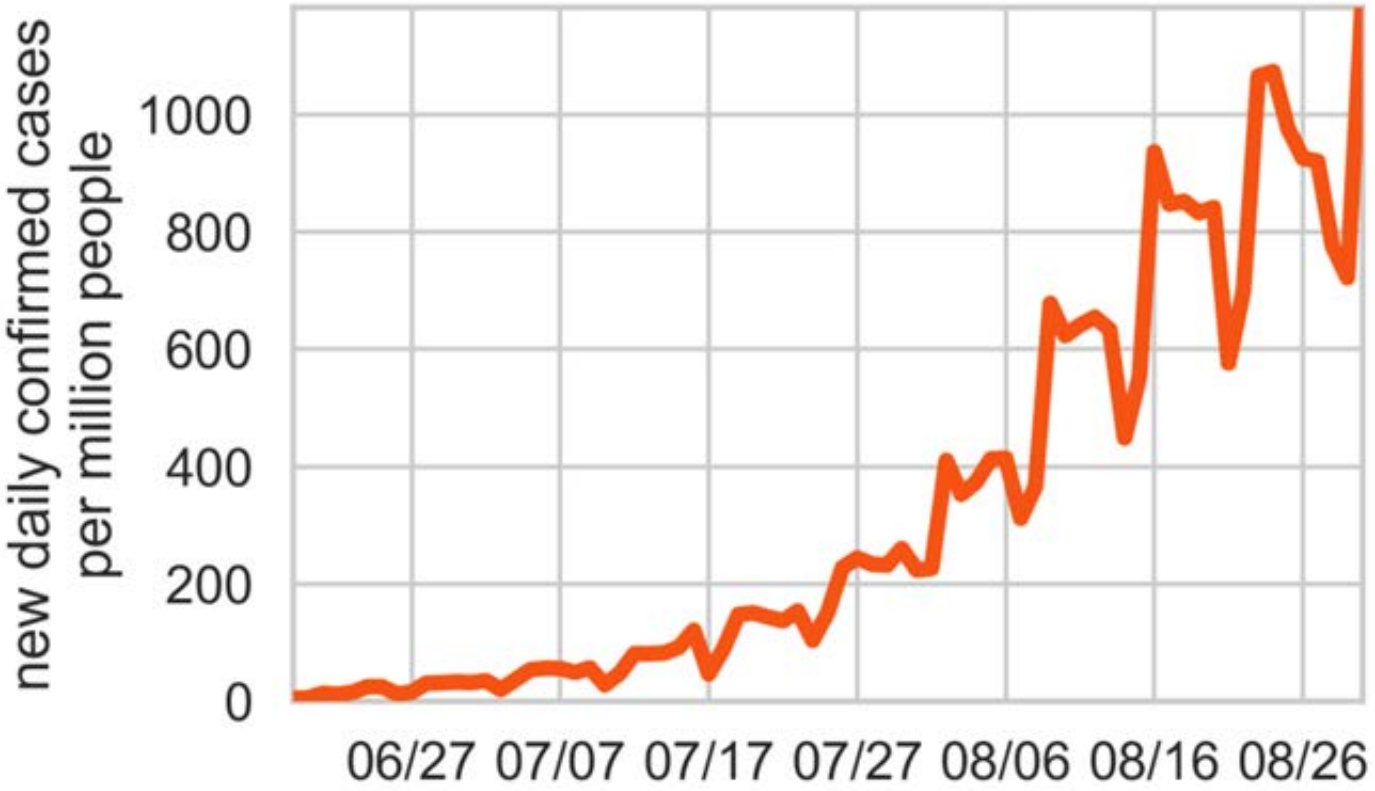
Israel now experiences its **highest levels of infection** (delta variant) in spite of **widespread (>60%) 2nd dose** vaccination



MINISTRY OF HEALTH

Daily cases rose by more than 100-fold in 1.5 months

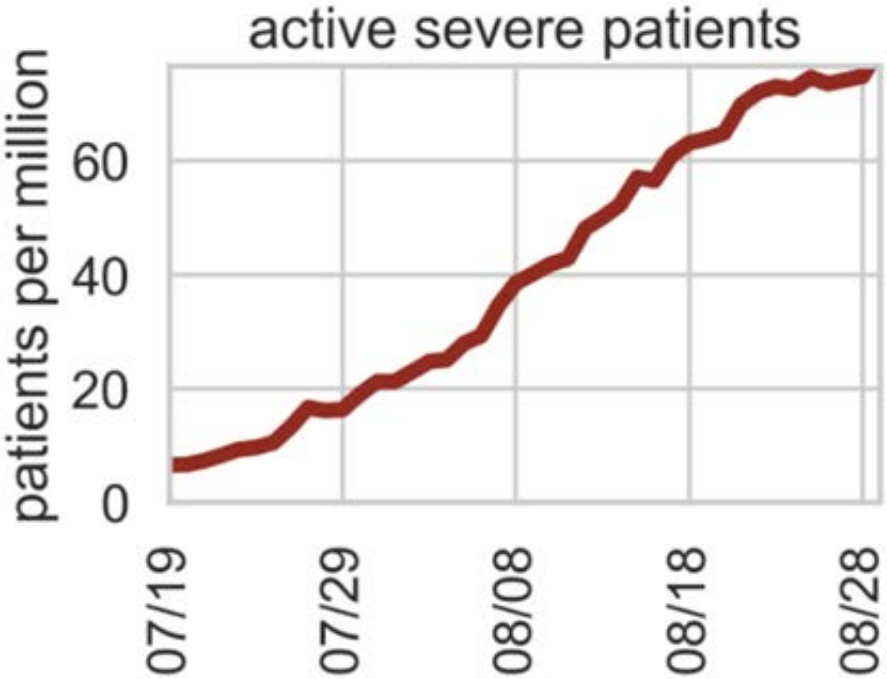
Based on PCR testing performed in Israel for both symptomatic and asymptomatic individuals



MINISTRY OF HEALTH

Severe active cases increased >10-fold in a month

Severe disease: resting respiratory rate >30 breaths per minute, or oxygen saturation <94%, or PaO2/FiO2 <300

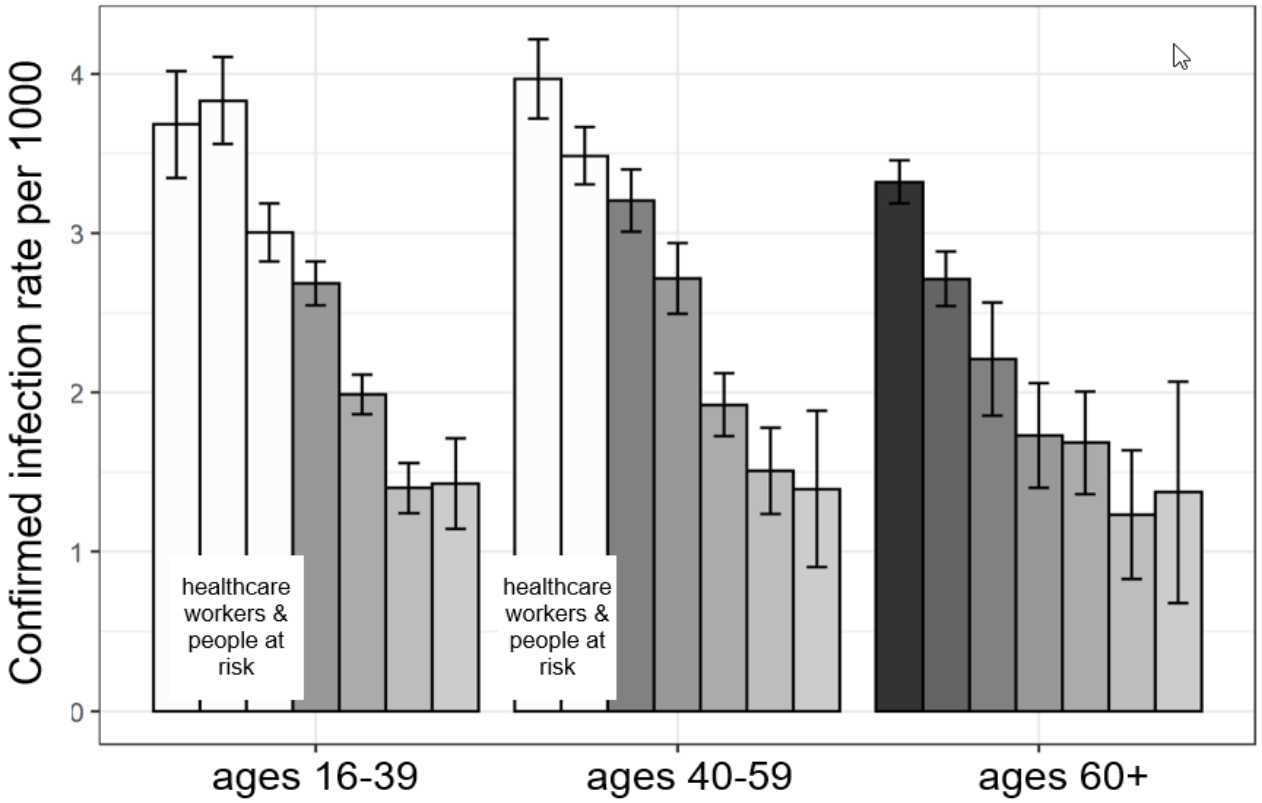


During July-early August:
60% vaccinated with 2 doses
40% unvaccinated

MINISTRY OF HEALTH

Waning immunity was observed across age groups

Rate of confirmed **SARS-CoV-2 infections** stratified by vaccination period and age group
Per 1000 persons, during July 11, 2021 and July 31, 2021



Goldberg et al.,
https://www.medrxiv.org/content/10.1101/2021.08.24.21262423v1

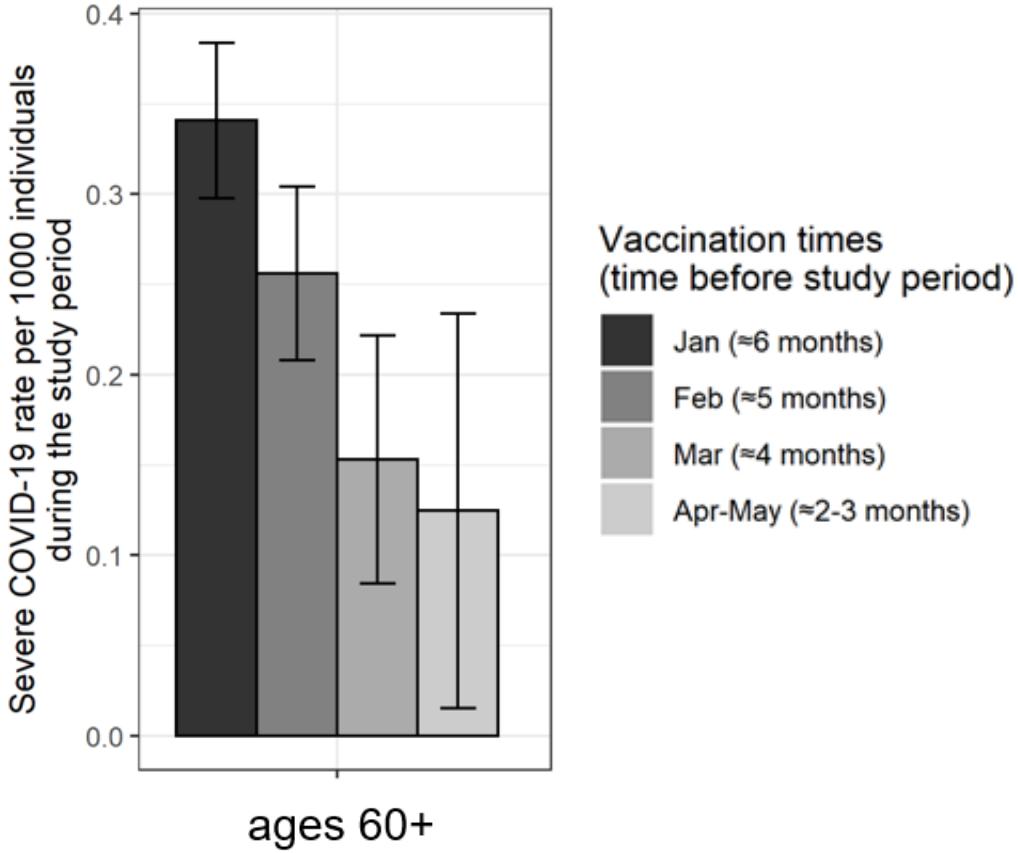
Vaccination times
(time before study period)

- Jan, 16-31 (≈6 months)
- Feb, 1-15 (≈5.5 months)
- Feb, 16-28 (≈5 months)
- Mar, 1-15 (≈4.5 months)
- Mar, 16-31 (≈4 months)
- Apr (≈3 months)
- May (≈2 months)

MINISTRY OF HEALTH

Waning immunity also observed for severe disease in 60+ group

Per 1000 persons, during July 11, 2021 and July 31, 2021

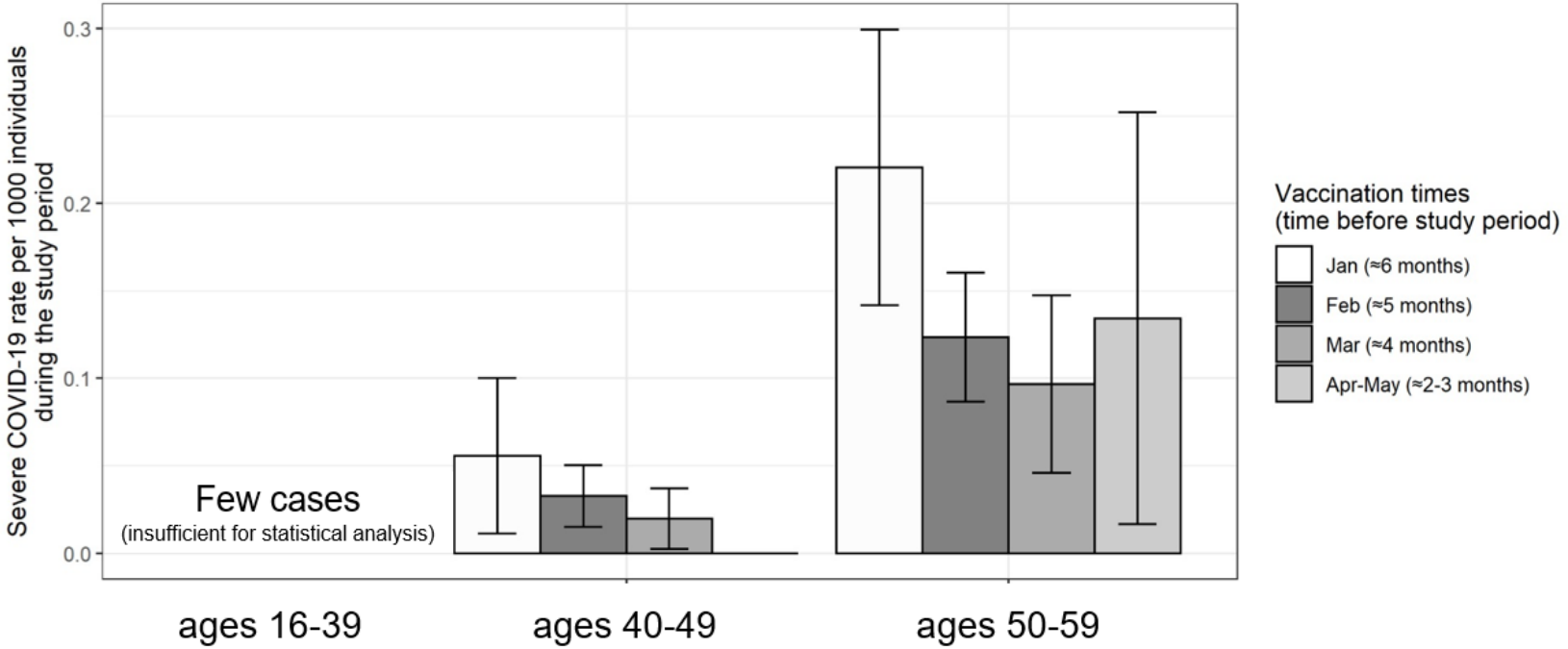


Goldberg et al.,
https://www.medrxiv.org/content/10.1101/2021.08.24.21262423v1

MINISTRY OF HEALTH

Waning immunity against severe disease may occur also in younger age groups

Rates of severe COVID-19 stratified by vaccination period and age group per 1000 persons, July 11 – Aug 15, 2021



MINISTRY OF HEALTH

Even a seemingly modest 12 percentage point decline in effectiveness could translate to a 5-fold increase in severe cases among the vaccinated

- Effectiveness in April for people vaccinated in Jan-March was high (e.g. 97%)
- Effectiveness in July for people vaccinated in January was reduced (e.g. 85%)

97% VE ⟶ 3% relative risk

85% VE ⟶ 15% relative risk

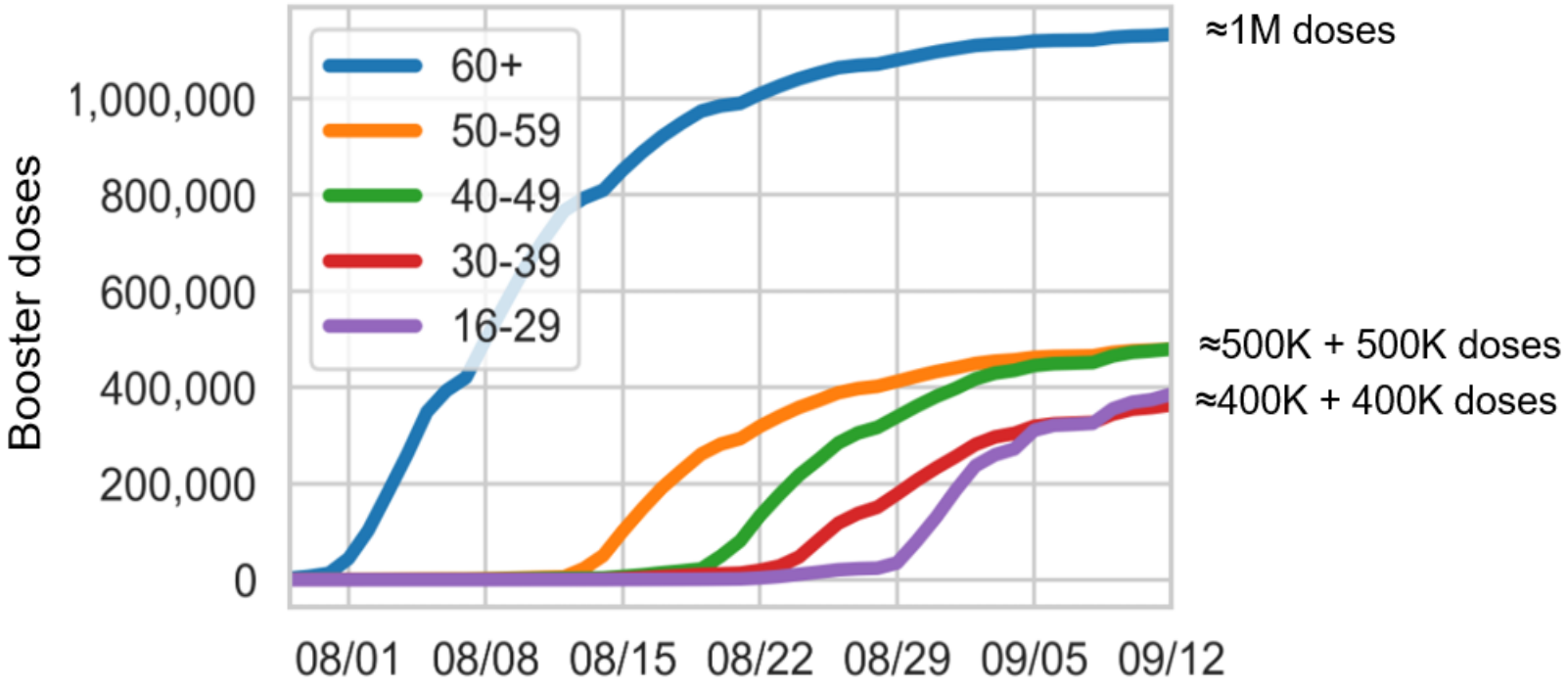
5-fold increase in relative risk

MINISTRY OF HEALTH

Based on evidence for waning in Israel, and the trajectory towards exceeding national hospitalization capacity given the rapid rise in severe cases, Israel decided to begin a 3rd vaccination campaign on July 30th, starting with the elderly.

MINISTRY OF HEALTH

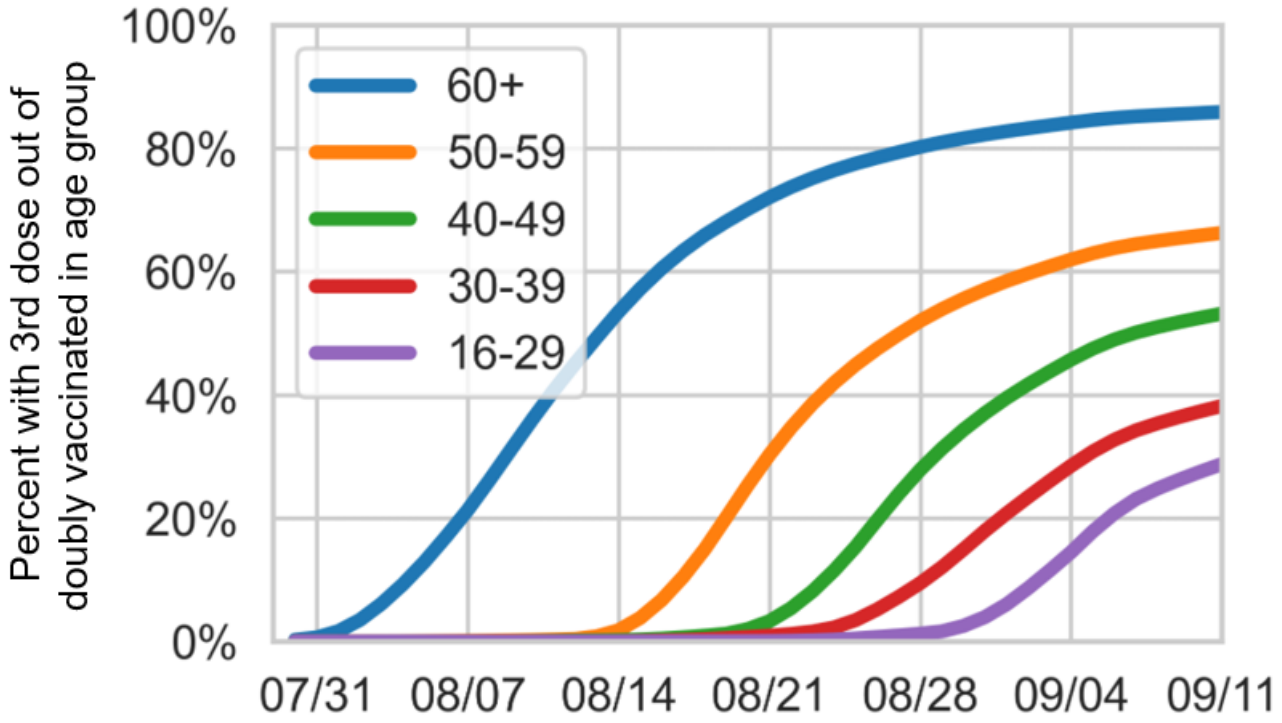
Booster campaign began in Israel on July 30th



>2.8 million booster doses to date

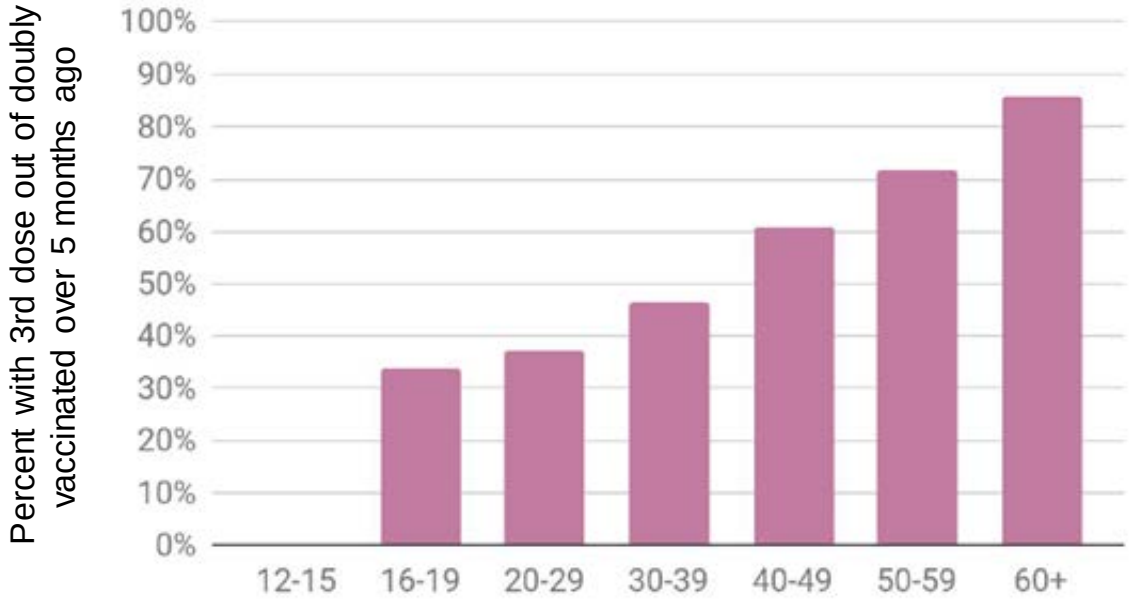
MINISTRY OF HEALTH

Large majority of elderly population received a 3rd dose



MINISTRY OF HEALTH

Overall half of the eligible population received a 3rd dose
(eligibility begins 5 months after the second dose)



Updated: Sep. 13, 2021

MINISTRY OF HEALTH

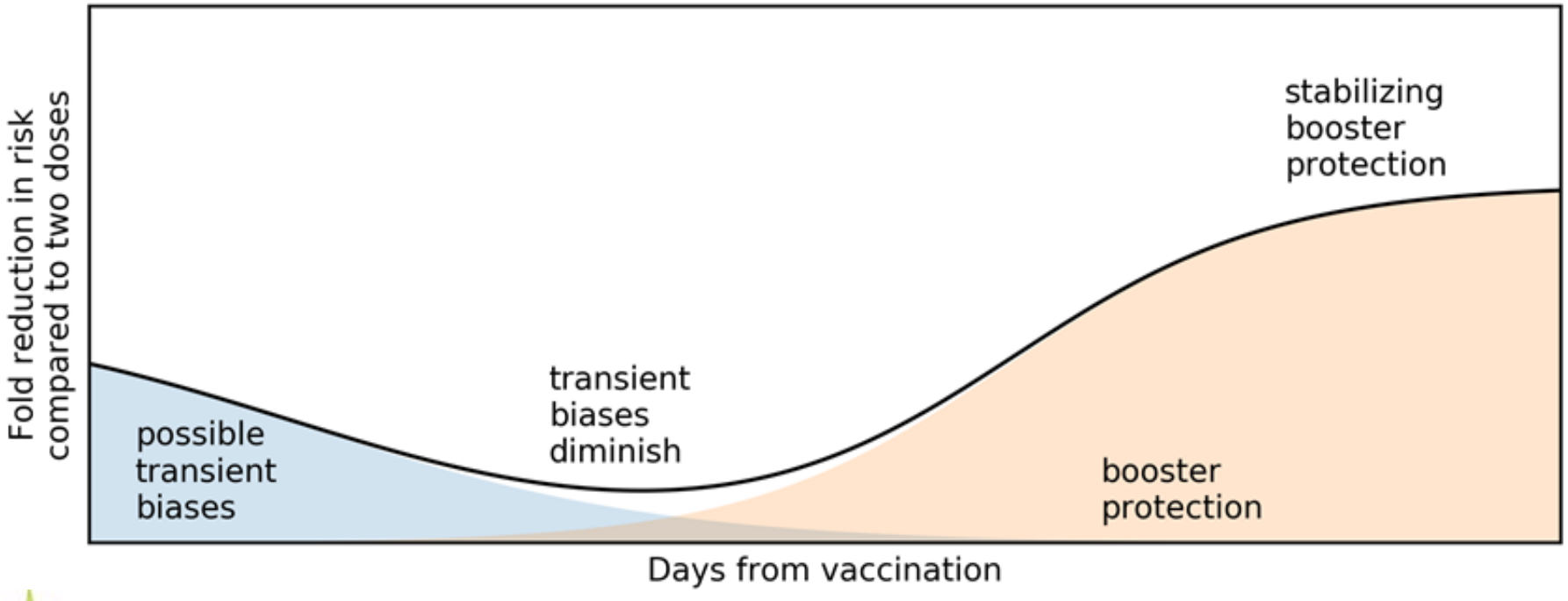
Booster analysis covers most of the 60+ population

Data on 60+ who were fully vaccinated before March 2021
Analysis period from August 10 to August 31

More than 1.1M people in the analysis (13K confirmed infections).

MINISTRY OF HEALTH

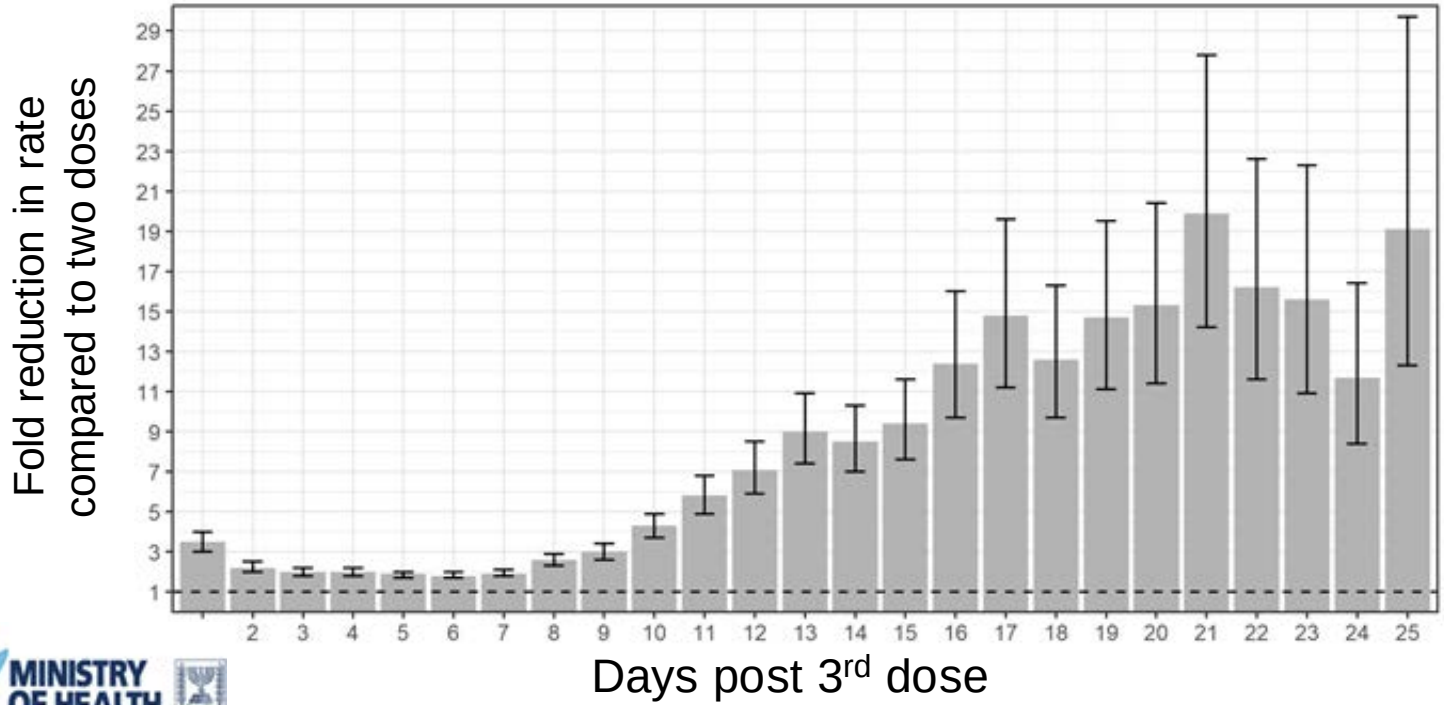
Reduction in risk due to booster is expected to be observed after ≈2 week delay



MINISTRY OF HEALTH

Booster protection against confirmed **infection** as a function of time post vaccination **ages 60+**

Poisson regression adjusted for age, gender, demographic group, 2nd dose period and calendar day.
Based on data from August 10 to August 31

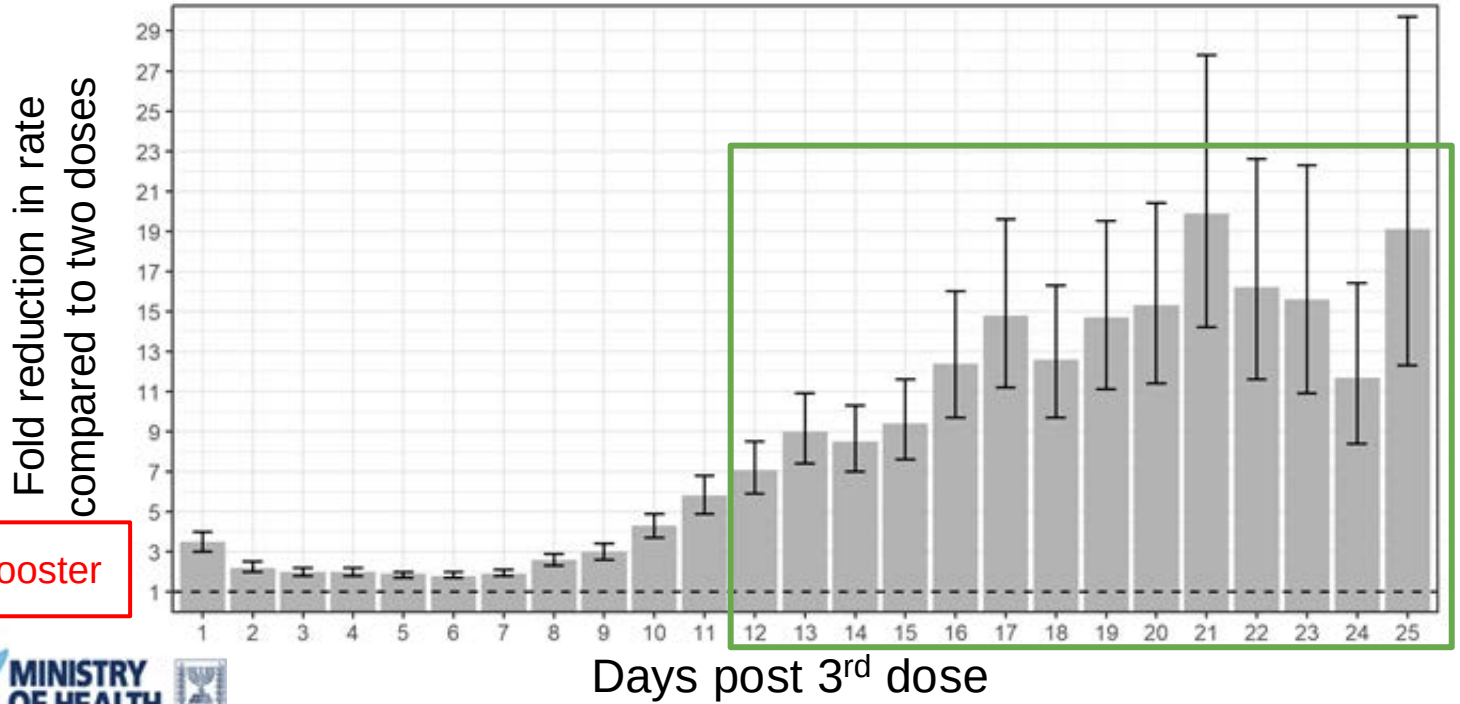


Bar-on et al.,
https://www.medrxiv.org/content/10.1101/2021.08.27.21262679v1

MINISTRY OF HEALTH

Booster protection against confirmed **infection** as a function of time post vaccination **ages 60+**

Poisson regression adjusted for age, gender, demographic group, 2nd dose period and calendar day.
Based on data from August 10 to August 31



no booster

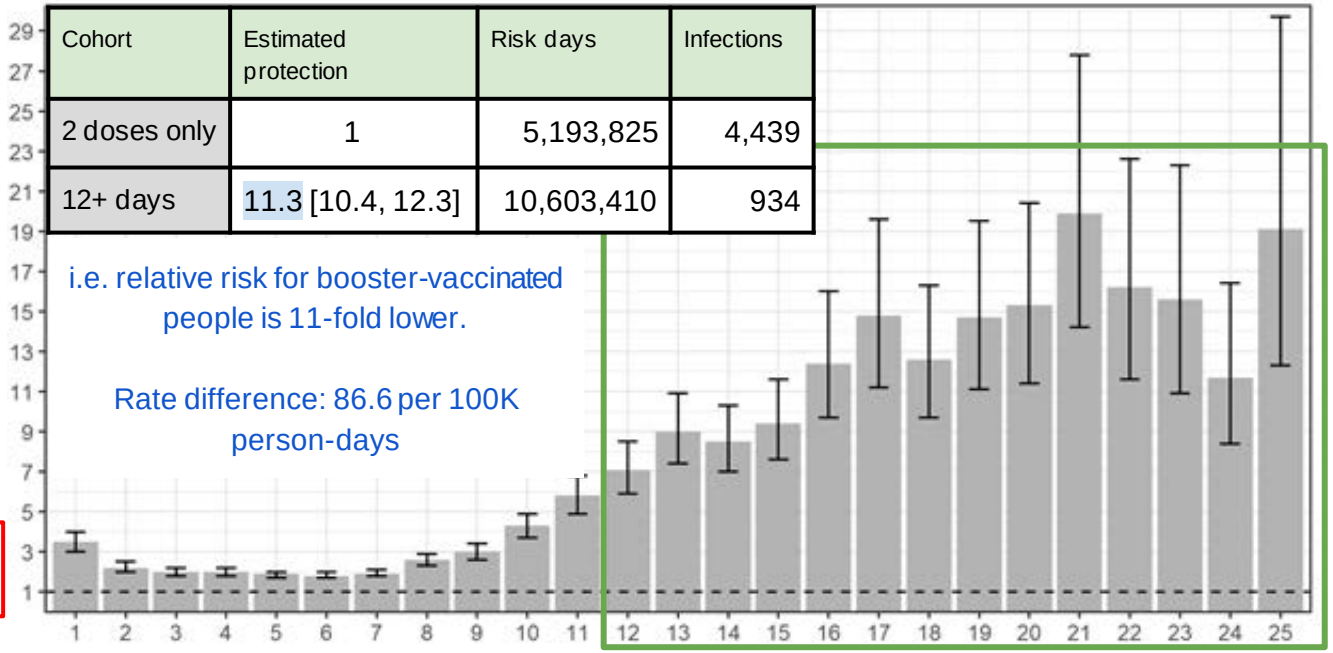
MINISTRY OF HEALTH

Bar-on et al.,
https://www.medrxiv.org/content/10.1101/2021.08.27.21262679v1

Relative risk for booster vaccinated is ≈11-fold lower against confirmed infection for ages 60+

Poisson regression adjusted for age, gender, demographic group, 2nd dose period and calendar day.
Based on data from August 10 to August 31

Cohort	Estimated protection	Risk days	Infections
2 doses only	1	5,193,825	4,439
12+ days	11.3 [10.4, 12.3]	10,603,410	934

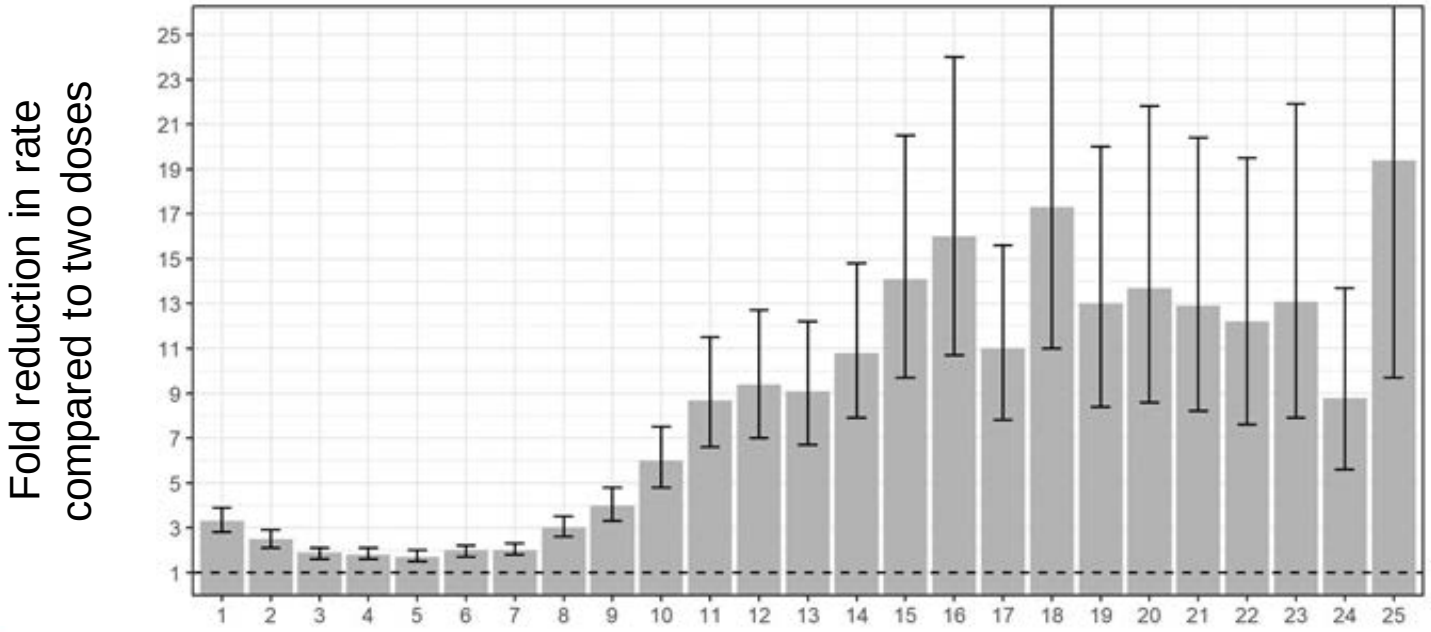


Bar-on et al.,
https://www.medrxiv.org/content/10.1101/2021.08.27.21262679v1

MINISTRY OF HEALTH

Similar booster protection against confirmed **infection** is observed for **ages 50-59**

Poisson regression adjusted for age, gender, demographic group, 2nd dose period and calendar day.
Based on data from August 13 to Sept 10

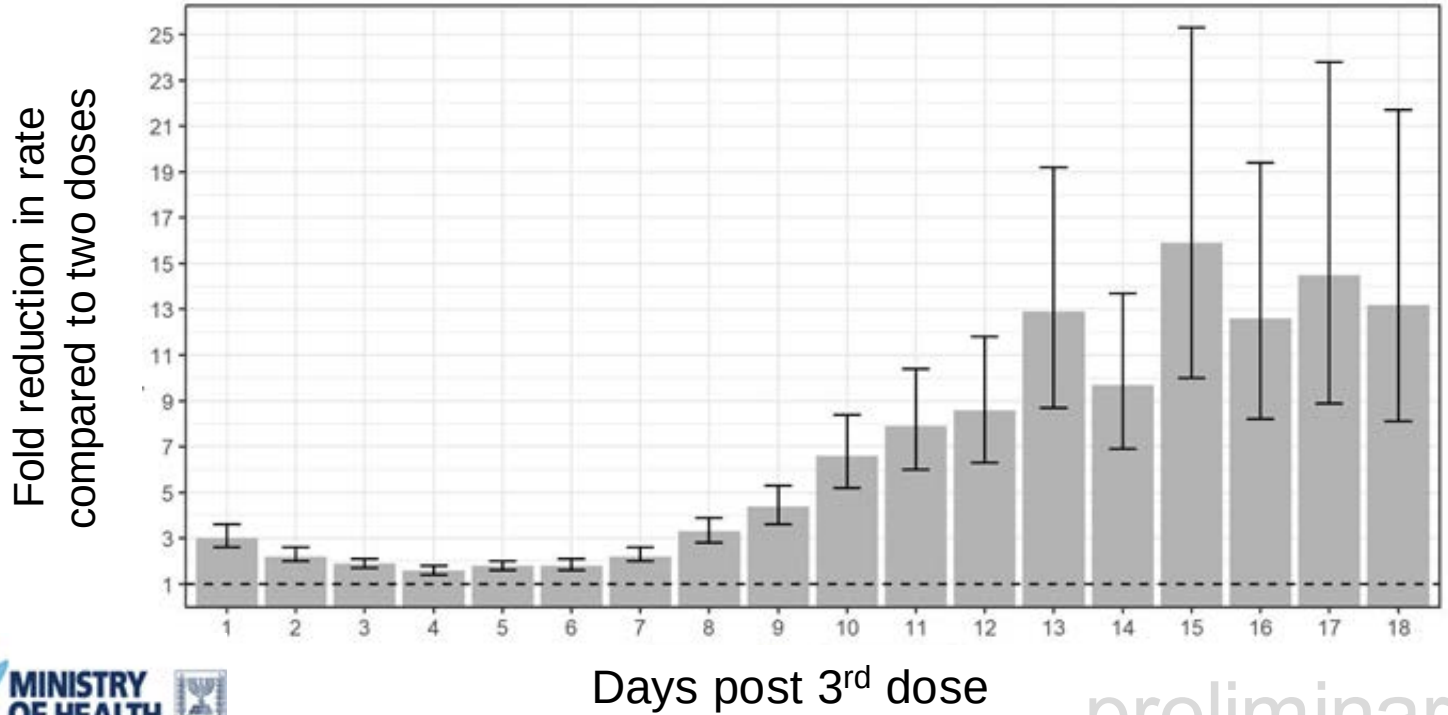


MINISTRY OF HEALTH

preliminary results

Similar booster protection against confirmed **infection** is observed for **ages 40-49**

Poisson regression adjusted for age, gender, demographic group, 2nd dose period and calendar day.
Based on data from August 20 to Sept 10

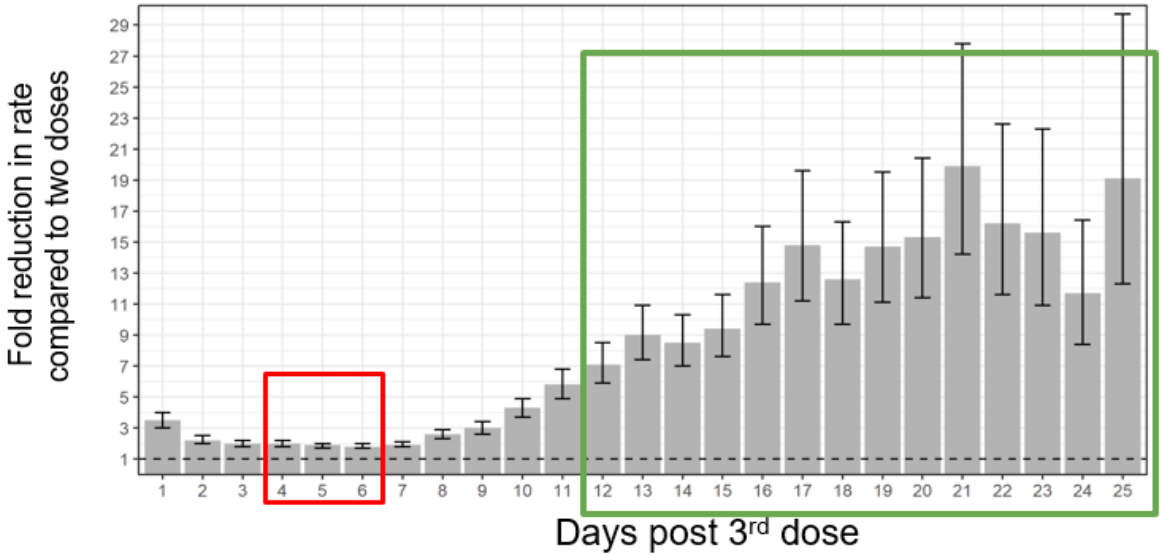


MINISTRY OF HEALTH

preliminary results

Results were tested by various methods and show high protection

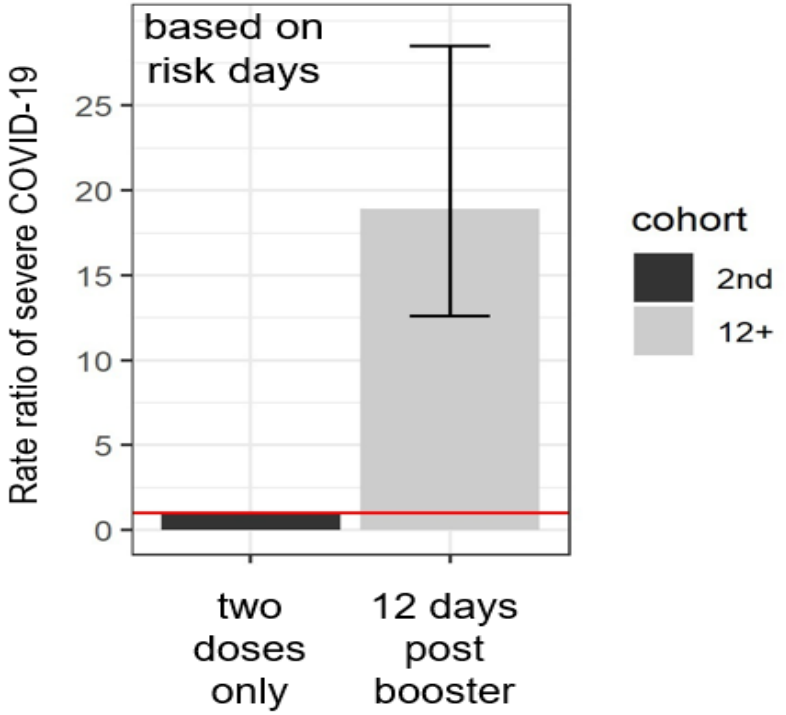
- **Using matching** of booster-vaccinated people with corresponding 2-dose vaccinated individuals (similar to Dagan et al.) → we got **11.6-fold** reduction
- **Comparing 12+ days to 4-6 days** post vaccination (when booster has little effect on confirmed infections) → we got **5.4-fold** reduction



MINISTRY OF HEALTH

Booster provides >10-fold reduction in relative risk of severe disease in 60+ age group

(**Poisson regression** controlling for age, gender, demographic group, 2nd dose period, and calendar day)



absolute rate difference
of 7.5 severe cases
per 100K person-days

MINISTRY OF HEALTH

Vaccine effectiveness (VE) **against delta** after **booster dose** returns to VE levels similar to **recent 2nd dose against alpha**

- If VE after waning is 50% for infection and increases 10-fold it becomes 95%
- If VE after waning is 80% for severe and increases 10-fold it becomes >97%

→ similar to reported values in first few months after 2nd dose
(e.g. Dagan et al., Polack et al.)

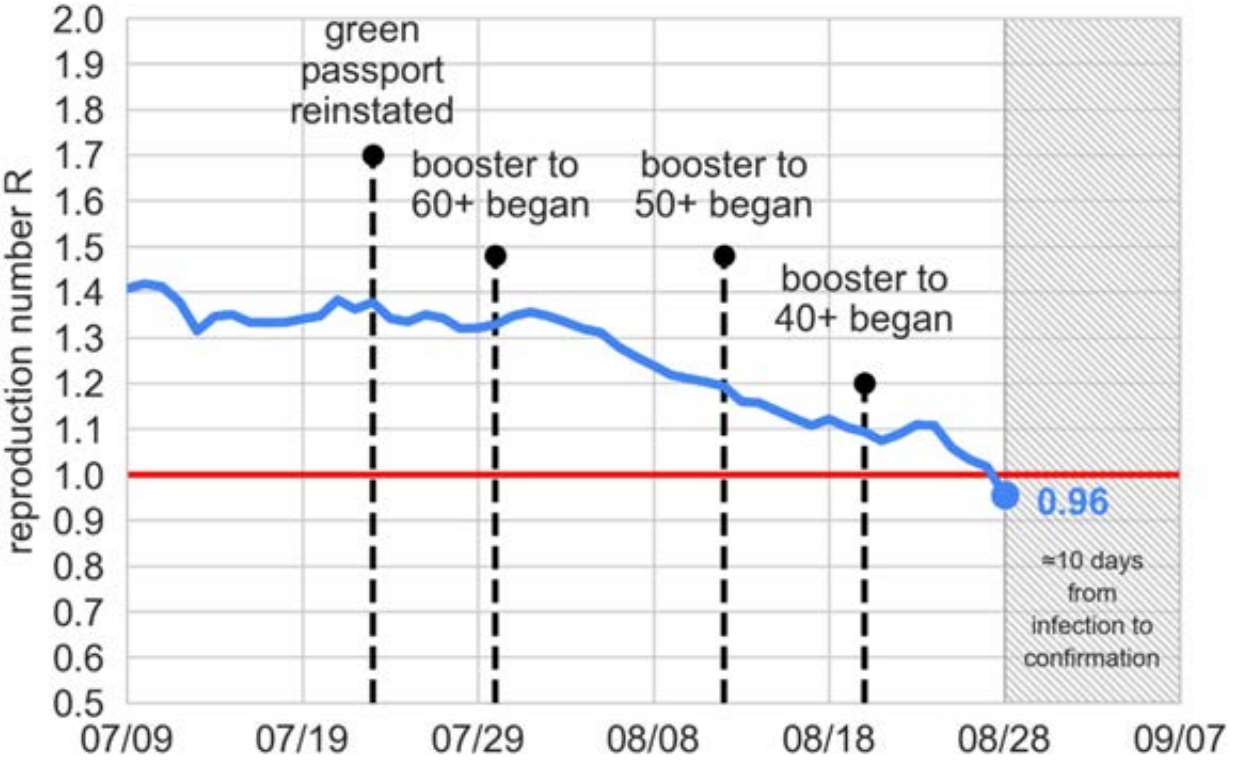
MINISTRY OF HEALTH

The reproduction number was high in the two months prior to decision on booster dose, with fully vaccinated cases rising rapidly

→ doubling every 10 days

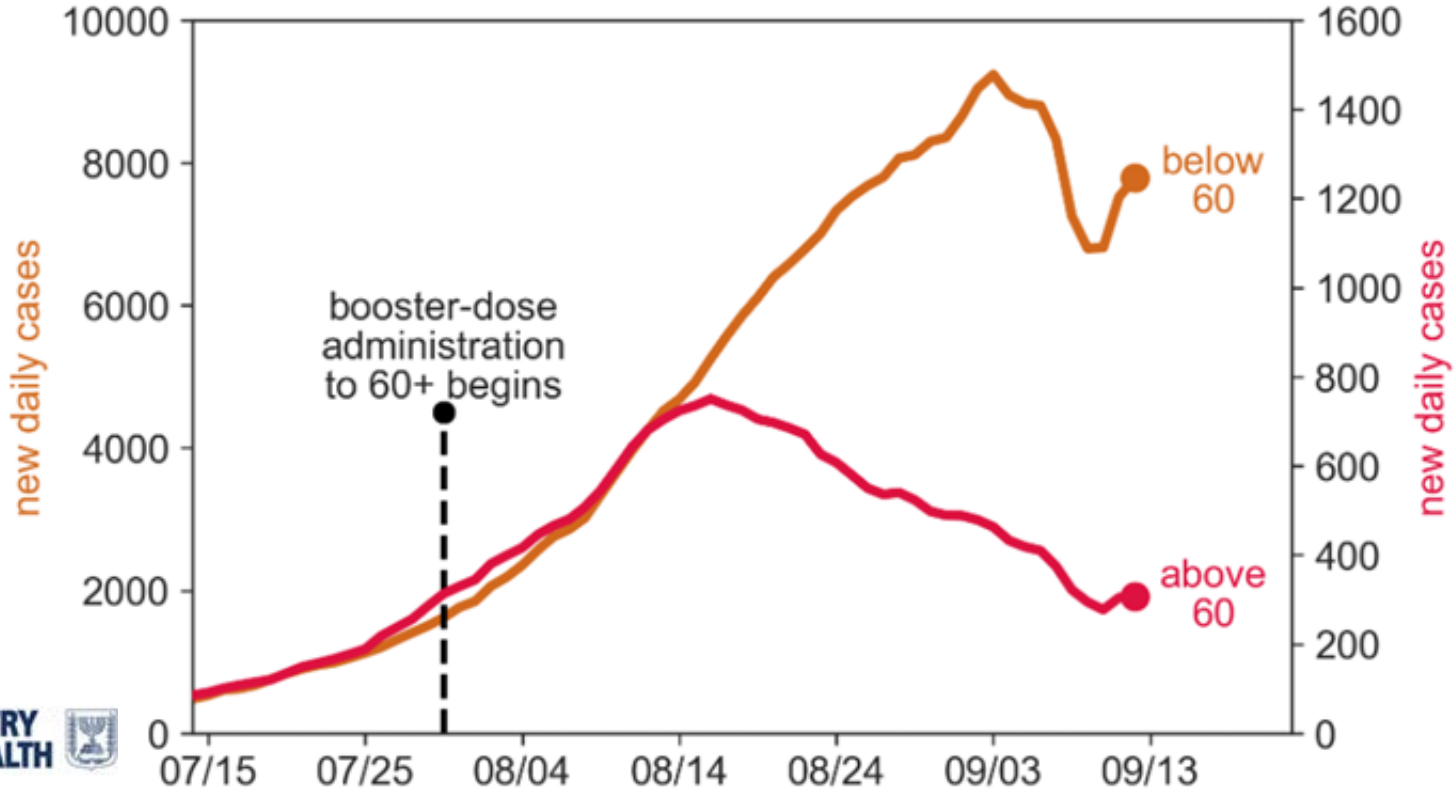
MINISTRY OF HEALTH

The reproduction number started decreasing in sync with the expected timing of the booster effect



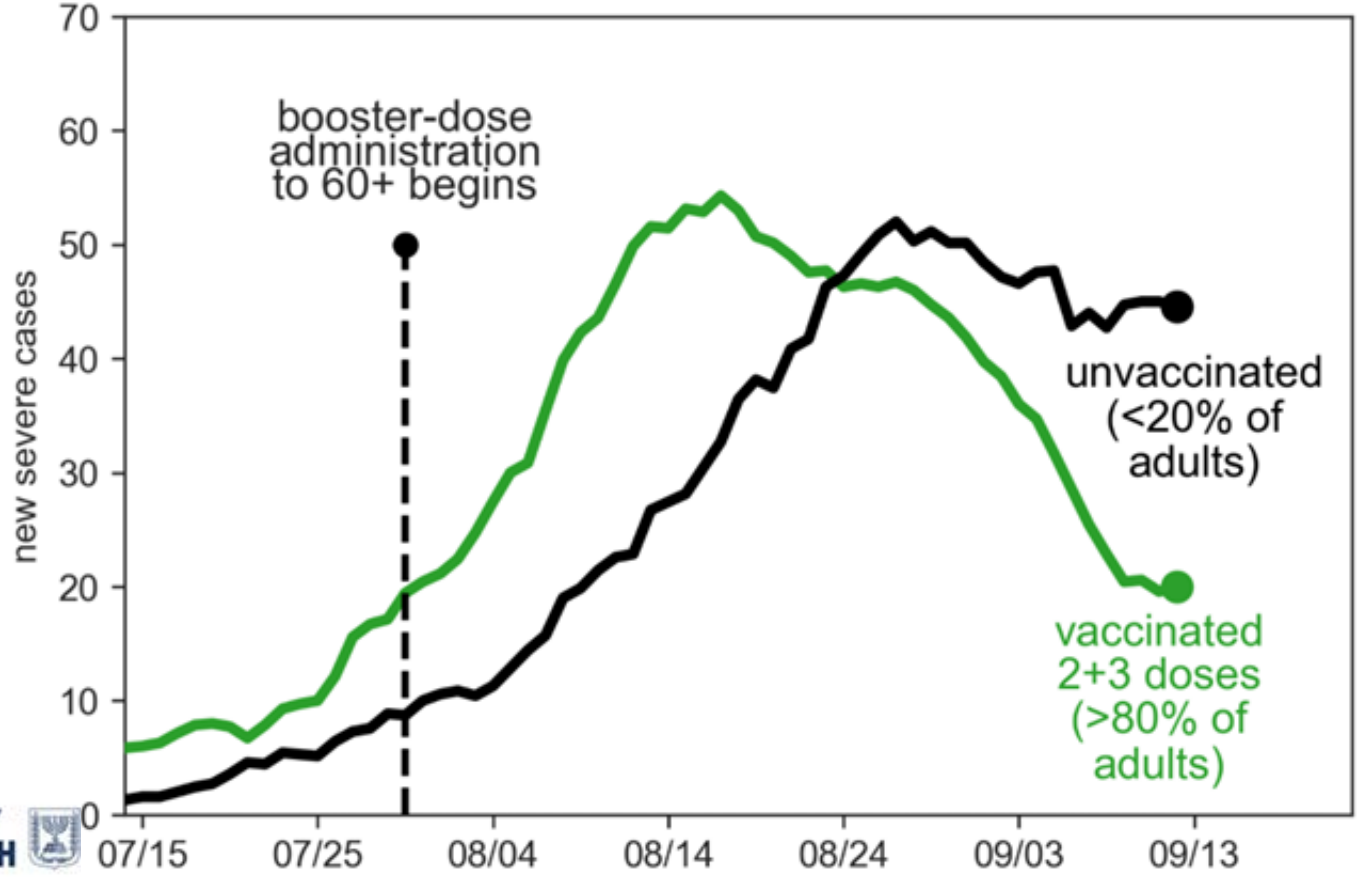
MINISTRY OF HEALTH

Large fraction of the older population received a third dose, leading to a substantial decrease in confirmed infections among people over 60y



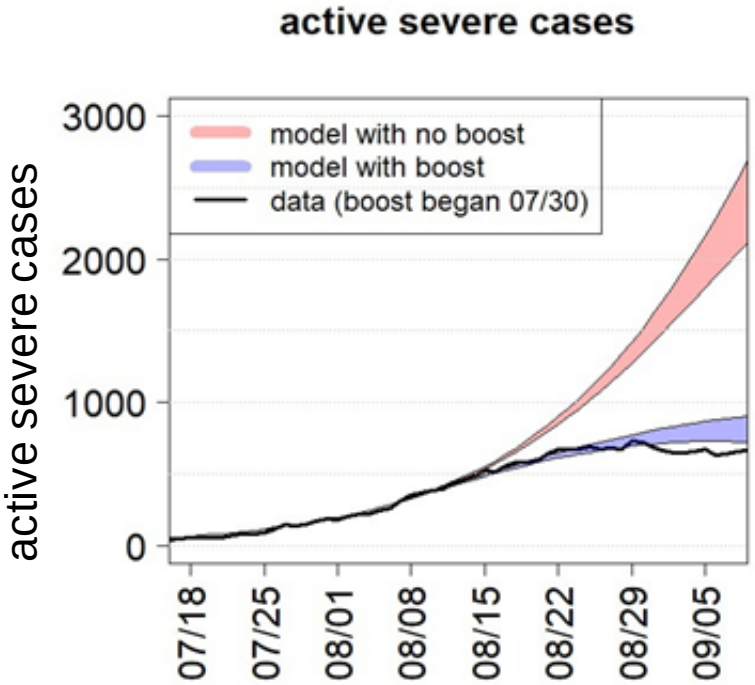
MINISTRY OF HEALTH

Following the third dose, severe cases sharply decreased



MINISTRY OF HEALTH

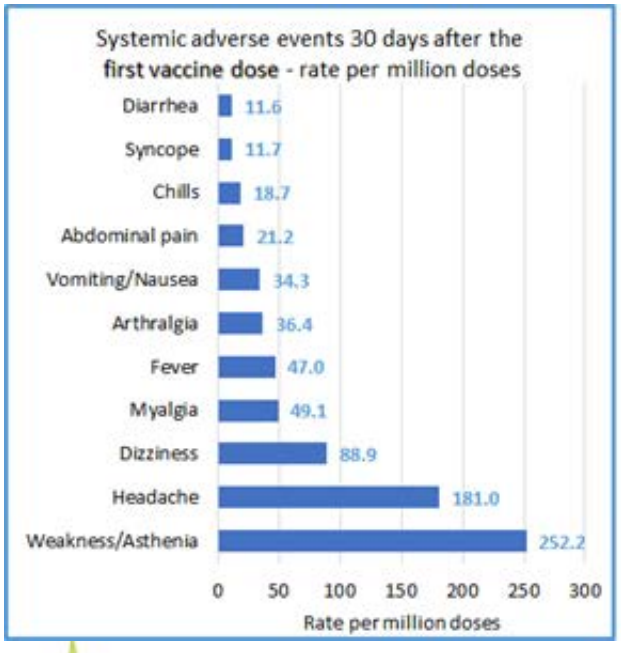
Our model's projections are that without the booster, or if the booster was administered a few weeks later, hospitalization could have significantly exceeded the national capacity



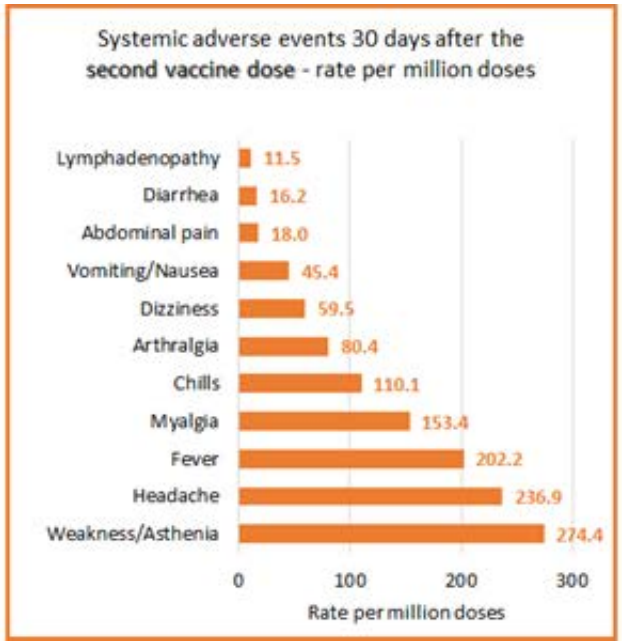
MINISTRY OF HEALTH

Rate of systemic adverse events by dose
(under-reporting expected in all cases)

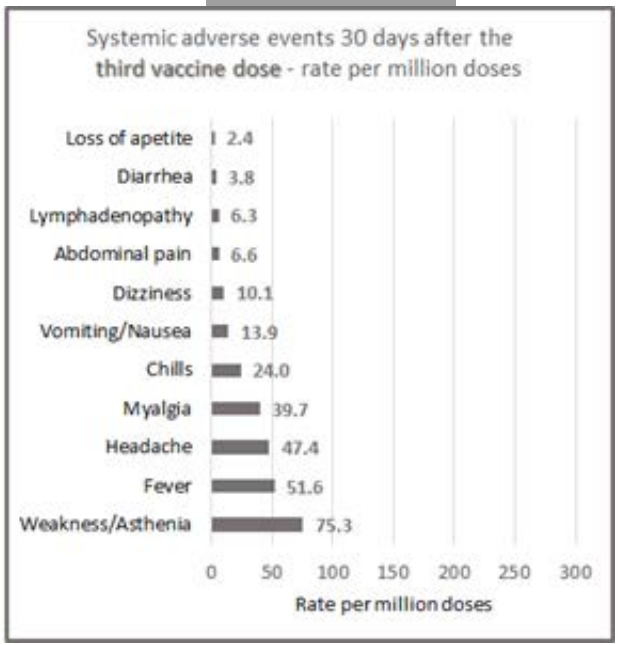
1st dose



2nd dose



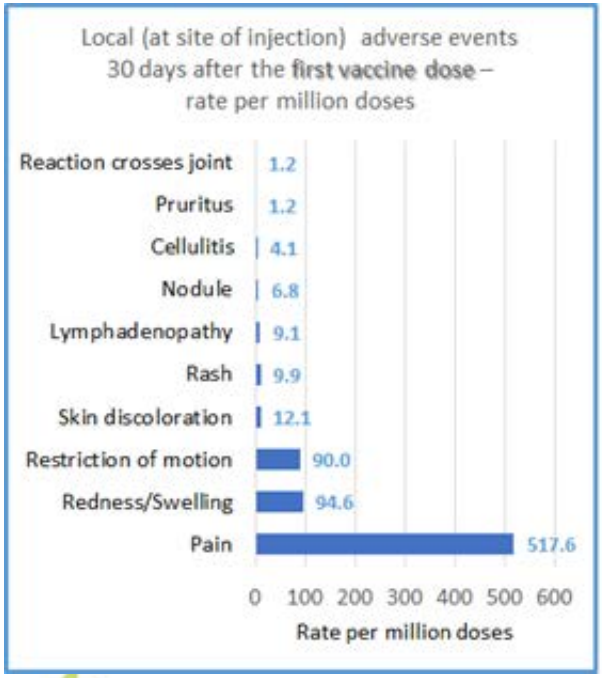
3rd dose



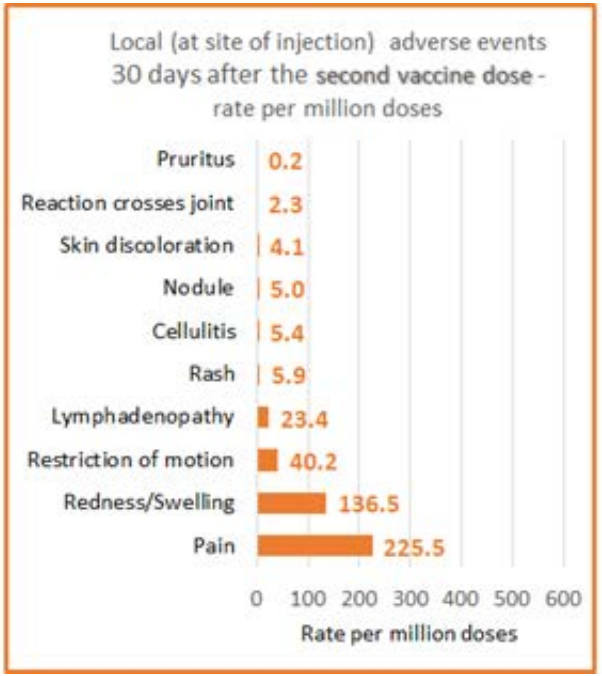
MINISTRY OF HEALTH

Rate of local adverse events by dose
(under-reporting expected in all cases)

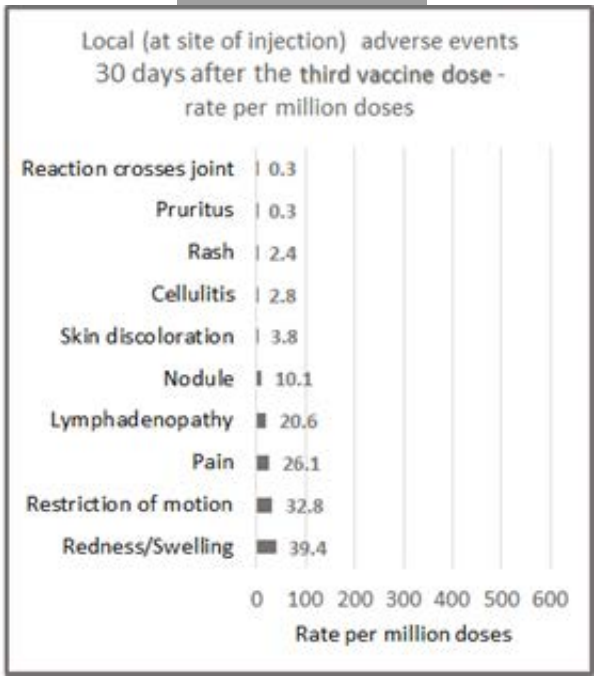
1st dose



2nd dose



3rd dose



MINISTRY OF HEALTH

Adverse events reported following 3rd dose
(>2.8 million booster doses administered)
under-reporting expected

Non serious reports	Serious reports
1,328	19

All hospitalized and deceased patients were investigated by independent clinical workgroup using all clinical data

MINISTRY OF HEALTH

Serious adverse events following 3rd dose ages 12-64 out of 2,004,064 vaccinees

#	Age group	Sex	Time post dose	Case details	Deceased	Causality
A	55-59	F	immediately	**Allergic reaction** Dyspnea, tongue swelling, palpitations, also has allergies and carries an epipen		Yes
B	50-54	F	2.5h	**Allergic reaction** edema in vocal chords, prophylactic intubation (h/o difficulty breathing and swelling of tongue following 1st dose, no allergic reaction following 2nd dose)		Yes
C	30-34	M	3d	**Myocarditis** Chest pain, fever and ECG changes.		Under investigation
D	55-59	F	6d	**Guillian barre syndrome followed by bells palsy.** Proximal weakness in lower limbs		possible
E	25-29	M	1d	**DVT, PE** coagulation disorder in family, symptoms started 1 month before vaccination, APLA r/o		No
F	60-64	F	immediately	**TIA /CVA** (Normal brain CT)		No
G	60-64	M	7d	**VT during a routine stress test** (runner) , released on beta blockers		No

MINISTRY OF HEALTH

Serious adverse events following 3rd dose ages 65+ out of 866,208 vaccinees

case	Age group	Sex	Time post dose	Case details	Deceased	Causality
A	75-79	M	4d	**Suspected encephalitis** fever and confusion, occurred after I & III dose		Possible
B	65-69	M	24h	**Vitreous hemorrhage** Loss of vision in left eye		Possible
C	70-74	M	24h	**CVA** h/o Erythromycin sensitivity	V	Under investigation
D	65-69	M	6d	**Septic shock** lung transplant recipient	V	No
E	80-84	F	2d	**Thrombocytopenia, m/p sepsis induced** COVID-19 Recovered individual, Multiple comorbidities		No
F	80-84	M	24h	**UTI** CRF HTN		No
G	80-84	F	24h	**UTI** Multiple co-morbidities		No
H	85-89	M	2d	**UTI** Multiple co-morbidities		No
I	85-89	F	8d	**Pneumonia** Multiple comorbidities		No
J	75-79	M	7d	MM, bone marrow transplant, arrhythmia, ablation, Coumadin, sudden death	V	No
K	75-79	M	24h	CRF, IHD, CHF, CVA, DM, dementia, PEG	V	No
L	85-89	F	12-24h	DM, CVA, Parkinson's, obesity	v	No

Myocarditis cases and number of vaccinees by age group and sex

Gender	Age group	1st dose (0-21 days after vac.)		2nd dose (0-30 days after vac.)		3rd dose (0-30 days after vac. but in many vaccinees less days so far)	
		Number of vaccinees	Myocarditis cases	Number of vaccinees	Myocarditis cases	Number of vaccinees	Myocarditis cases
Female	12-15	186,655	0	134,637	1	163	No cases observed
	16-19	242,497	0	215,725	2	55,107	
	20-24	260,693	1	239,427	6	79,174	
	25-29	244,705	0	226,471	1	74,222	
	30+	2,116,016	3	2,013,329	8	1,273,773	
Male	12-15	174,597	1	126,723	9	142	
	16-19	248,673	3	217,006	33	57,195	
	20-24	272,641	6	248,747	26	85,961	
	25-29	255,426	3	236,913	20	77,325	
	30+	1,973,238	10	1,882,588	32	1,211,543	1

* All cases reported in Israel Dec, 2020 - Sep 13, 2021

Most young vaccinees received booster only in last two weeks

Summary: Booster dose in Israel was effective and so far had safety profile similar to the other doses

- Booster dose shows ≈10 fold improved protection against confirmed infection and severe COVID19.
- Post-booster efficacy against delta similar to pre-waning efficacy against alpha.
- Booster dose adverse events not more acute than first or second dose.
- Based on the above for ages 60+ (and then 50+), the vaccine safety & effectiveness committees in Israel approved booster dose 5 months after 2nd dose for ages 12+.
- Administration of booster dose helped Israel dampen severe cases in the 4th wave.

MINISTRY OF HEALTH