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

Vaccine waning and booster protection across ages - data from Israel

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

Oct. 25th, 2021

Myocarditis & perimyocarditis cases and number of vaccinees by age group and sex

Proactive surveillance. All cases reported in Israel Dec. 2020 - Oct 10th, 2021

Sex	Age group	1st dose (0-21 days following vaccination)		2nd dose (0-30 days following vaccination)		3rd dose* (0-30 days following vaccination; in the minority of vaccinees not all 30 days have passed so far)	
		Number of vaccinees	Number of cases reported	Number of vaccinees	Number of cases reported	Number of vaccinees	Number of cases reported
Female	12-15	204,729	**0**	162,297	**1**	279	**0**
	16-19	248,881	**0**	222,067	**2**	97,807	**0**
	20-24	263,845	**1**	242,697	**6**	141,910	**0**
	25-29	247,365	**0**	229,189	**1**	130,283	**0**
	+30	2,127,538	**3**	2,029,074	**7**	1,542,142	**0**
Male	12-15	192,014	**1**	151,081	**10**	292	**0**
	16-19	254,497	**3**	223,079	**36****	96,238	**5**
	20-24	275,235	**6**	251,672	**26**	139,015	**5**
	25-29	257,713	**3**	239,319	**20**	133,650	**1**
	+30	1,983,230	**10**	1,897,067	**32**	1,448,745	**6**

* Two cases are still under investigation

** One case – first dose Pfizer, second dose Moderna

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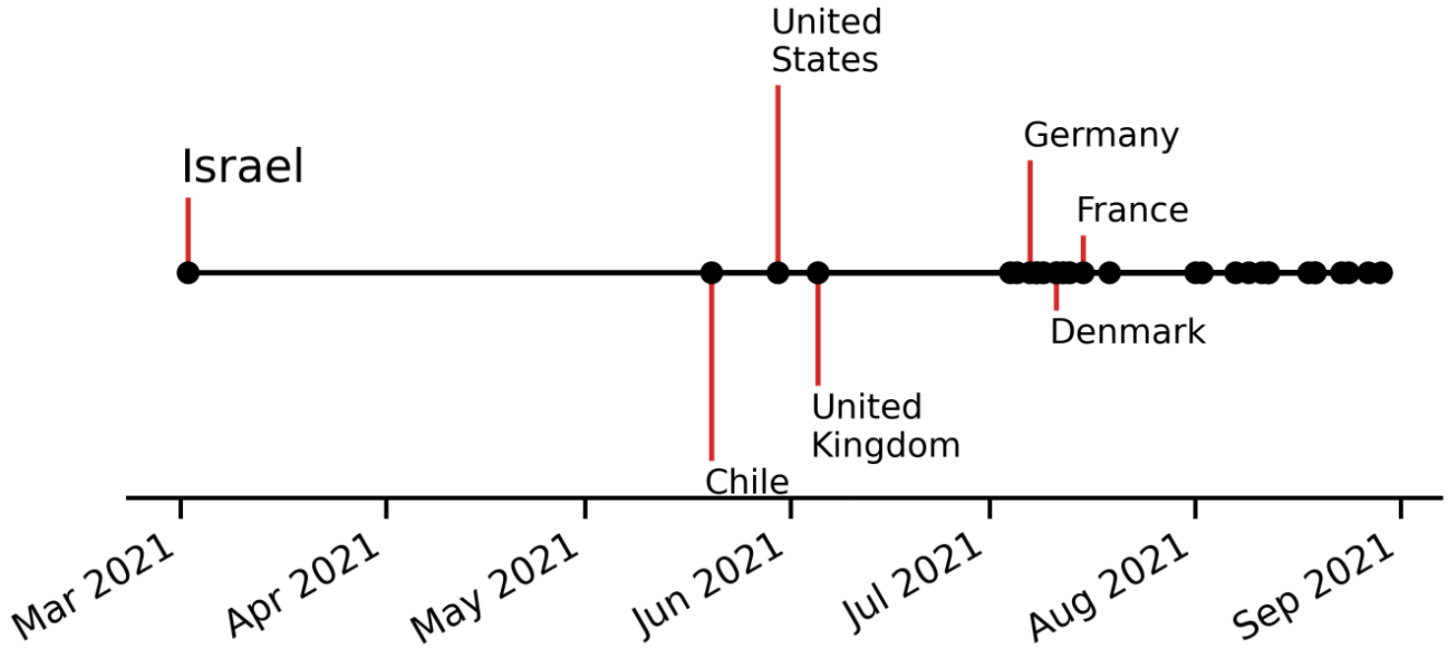
Israel reached high levels of population-wide immunization
≈3 months before most countries



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

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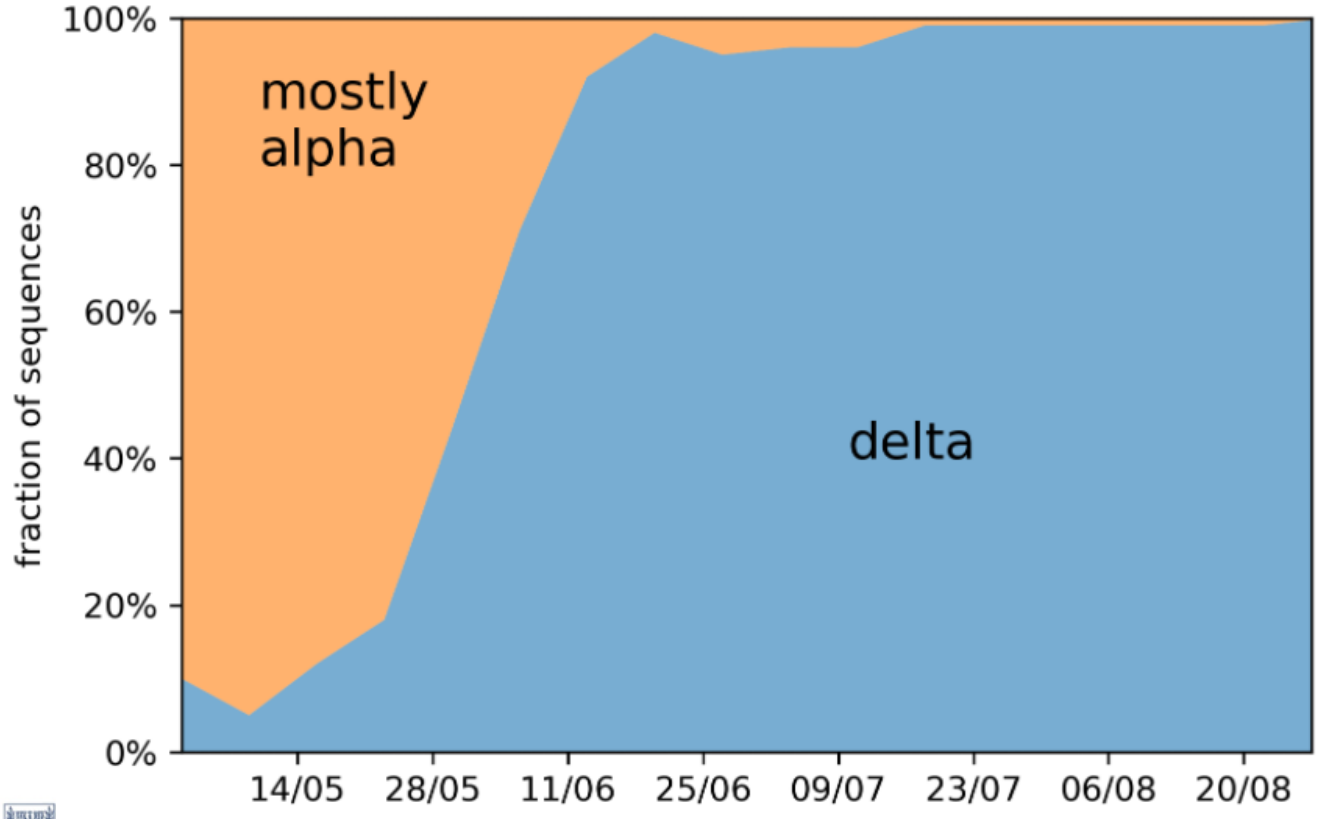
During June 2021 alpha was overtaken by delta variant in Israel



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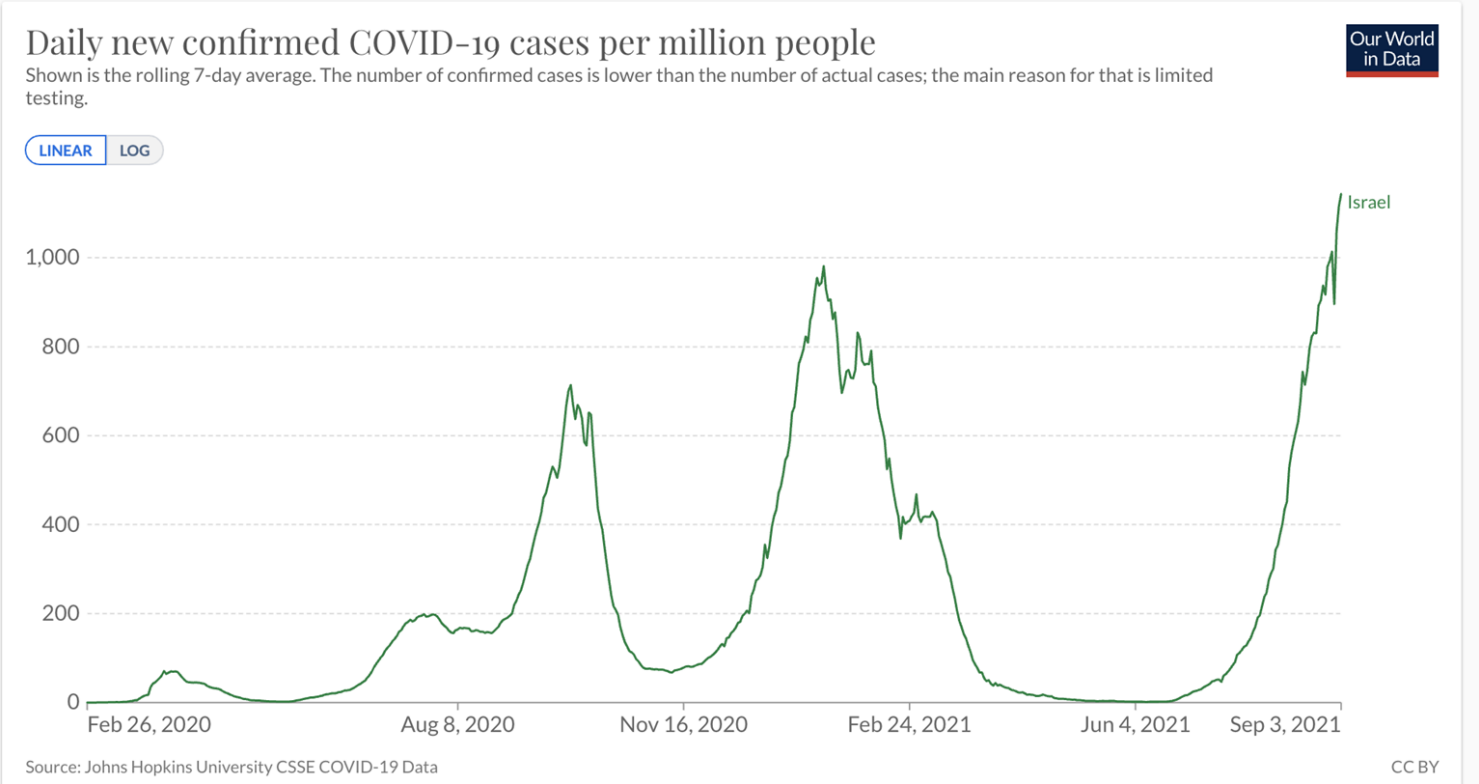
Israel experienced its **highest levels of infection** (delta variant) in spite of **widespread (>60%) 2nd dose** vaccination



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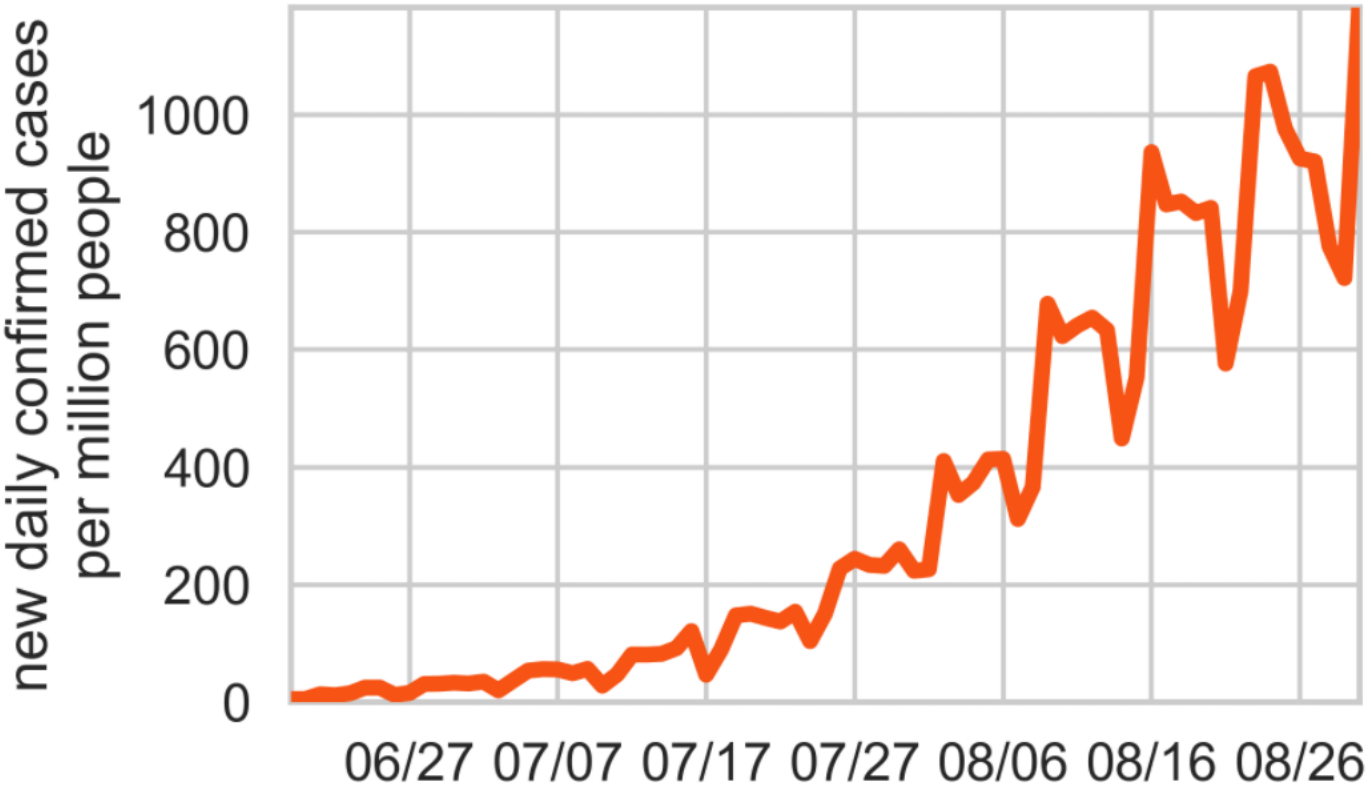
Daily cases rose by more than 100-fold in 1.5 months

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



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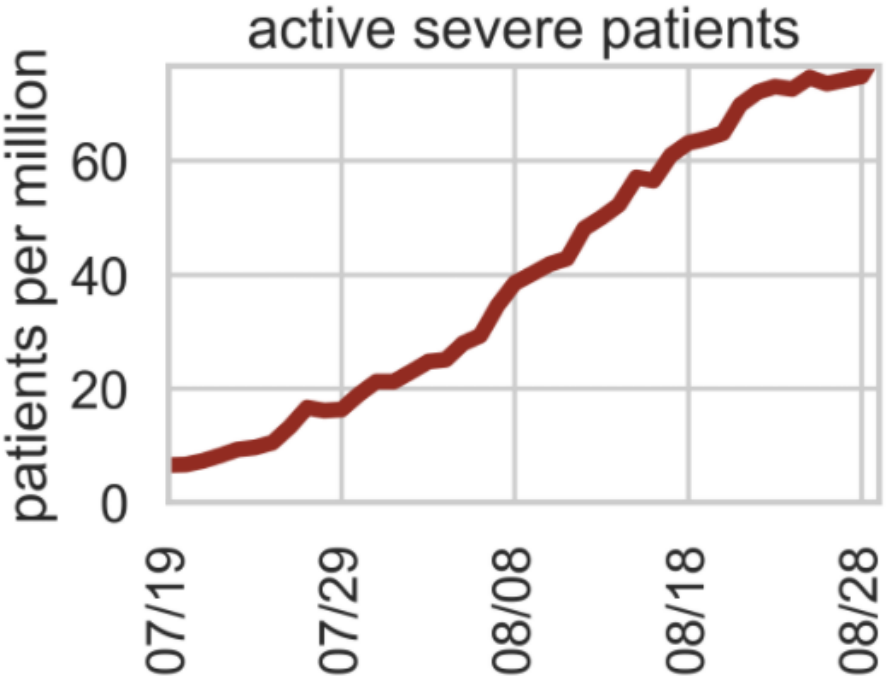
Severe active cases increased >10-fold in a month

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

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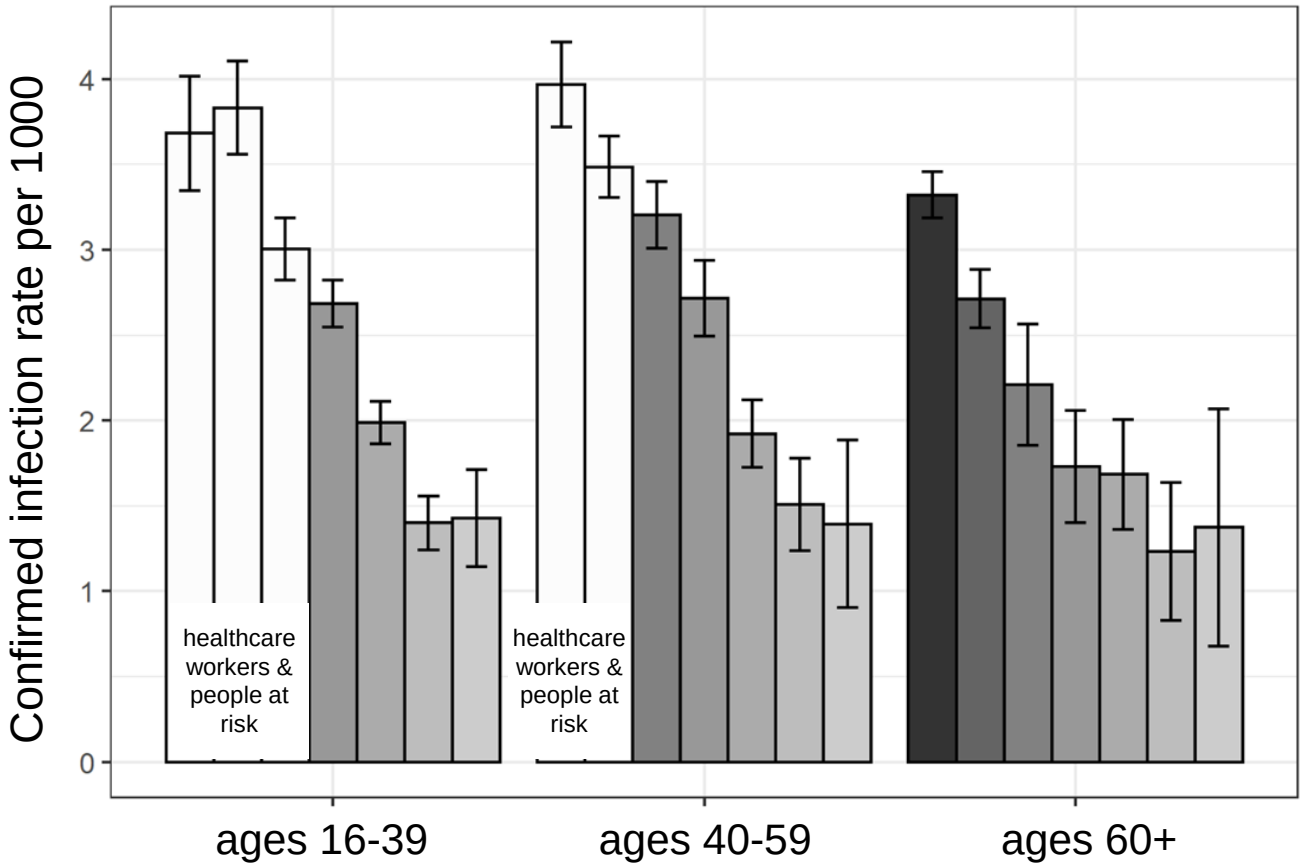
Waning immunity was observed across age groups

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)

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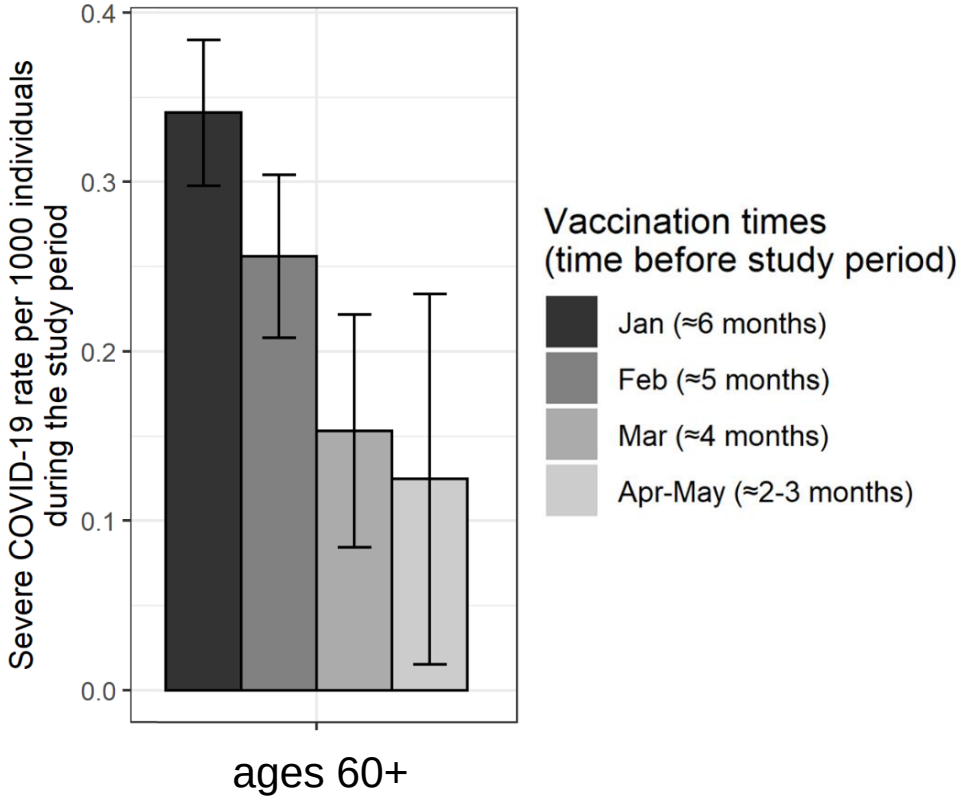
Waning immunity also observed for severe disease in 60+ group

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

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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.

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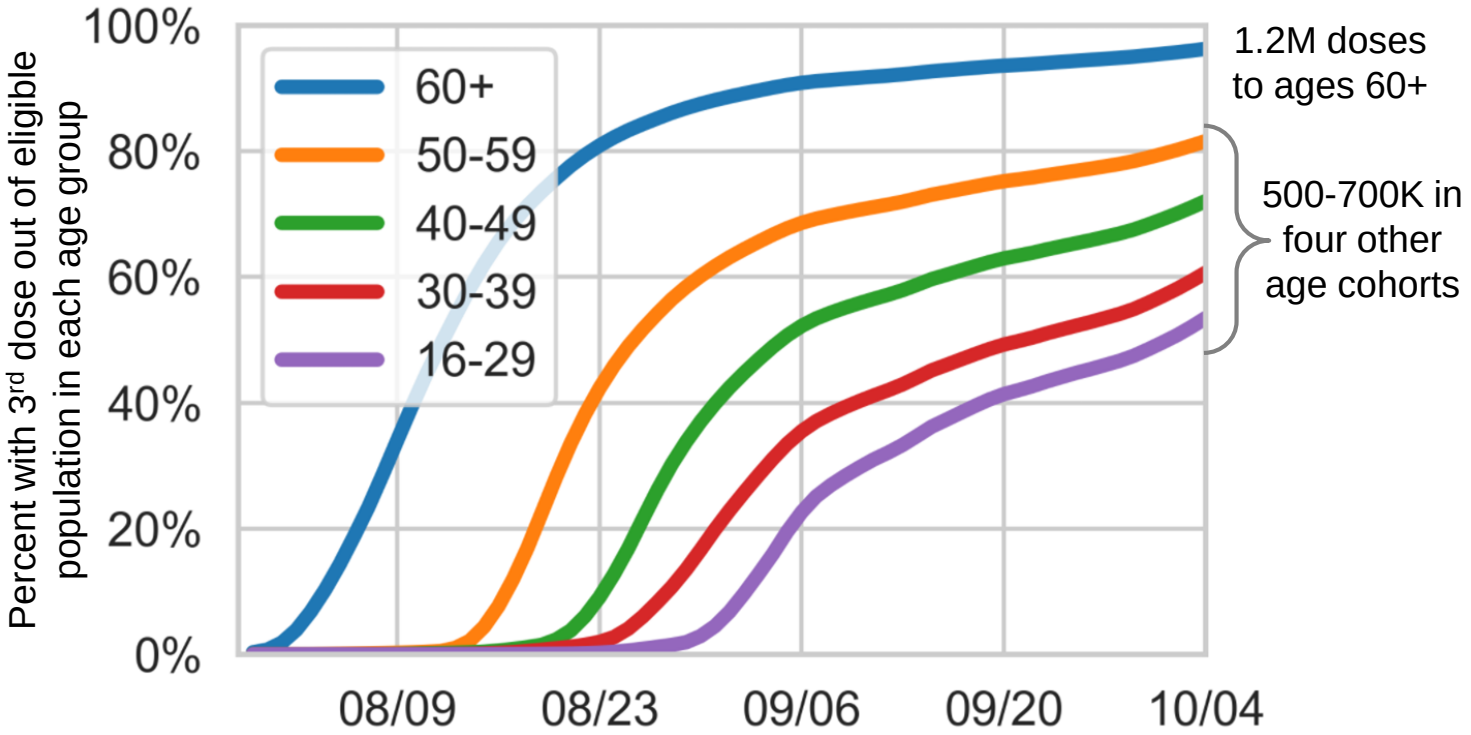
Large majority of elderly population received a 3rd dose

Overall
3.7 million
booster doses
to date



Booster campaign began on July 30th

Our analysis covers most of the adult Israeli population

- Data on those aged 16 and above who were fully vaccinated before May 2021
- 4.6M individuals
- Aug-Oct 2021 study period:
  - 100k confirmed infections
  - >1000 severe illness cases
  - >250 deaths

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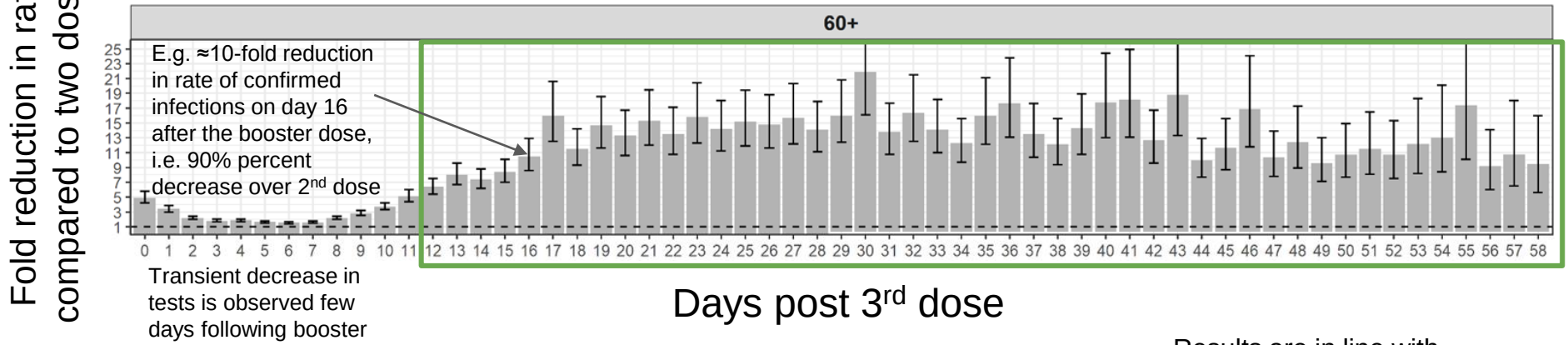
Protection against **confirmed infection** with booster versus 2nd dose only as a function of time post vaccination **ages 60+**

Poisson regression adjusted for age, gender, demographic group,
2nd dose period and incidence in area of residence. Based on data from July 30 to October 6



Results are in line with previous report: Bar-on et al., https://www.nejm.org/doi/full/10.1056/NEJMoa2114255

Bar-on et al., https://www.medrxiv.org/content/10.1101/2021.10.07.21264626v1.full.pdf

Protection against **confirmed infection** with booster versus 2nd dose only as a function of time post vaccination **ages 60+**

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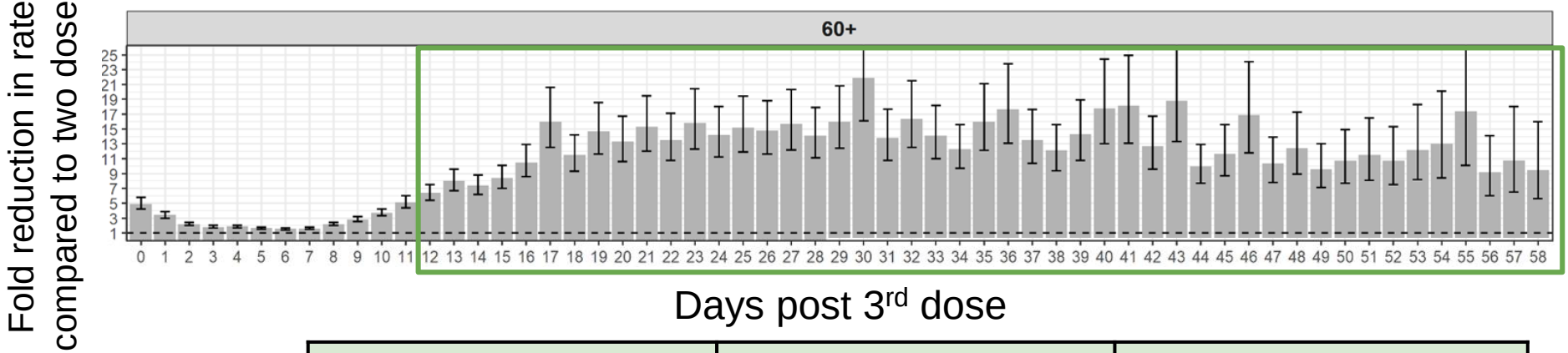

Cohort	Non-booster (2 doses only)	Following booster (12+ days)
Confirmed infections	12,225	2,694
Risk-days	21,660,770	46,201,515
Rate ratio, adj. via Poisson regression [95% CI]	-	**12.4** [11.9, 12.9]

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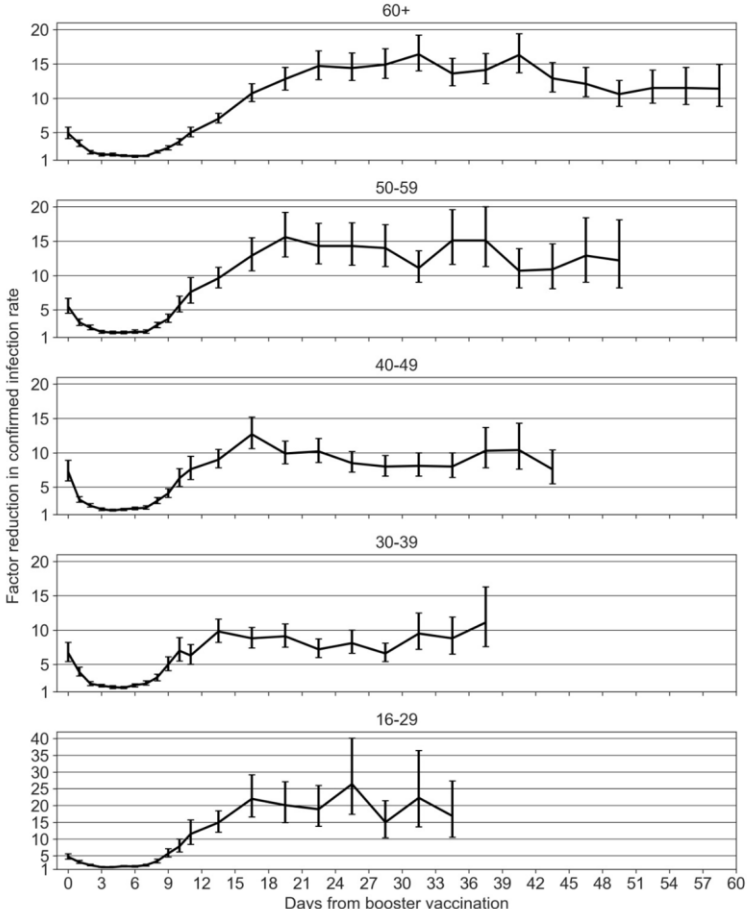
Protection with booster versus 2nd dose only as a function of time post vaccination **by age group**

Poisson regression adjusted for age, gender, demographic group, 2nd dose period and incidence in area of residence

Age	Non-booster group infections (person-days at risk)	Booster group infections - day 12+ (person-days at risk)	Rate ratio day 12+ relative to non-booster [95% CI]
60+	12,225 (21,660,770)	2,694 (46,201,515)	**12.4** [11.9, 12.9]
50-59	9,912 (11,887,725)	935 (14,204,942)	**12.2** [11.4, 13.1]
40-49	16,378 (15,416,326)	1,054 (11,409,730)	**9.7** [9.2, 10.4]
30-39	20,736 (17,757,731)	758 (7,228,945)	**8.8** [8.2, 9.5]
16-29	21,649 (23,985,406)	267 (7,060,384)	**17.6** [15.6, 19.9]



Bar-on et al.,
https://www.medrxiv.org/content/10.1101/2021.10.07.21264626v1.full.pdf

Similar patterns across age groups in terms of timing and magnitude (though not identical)

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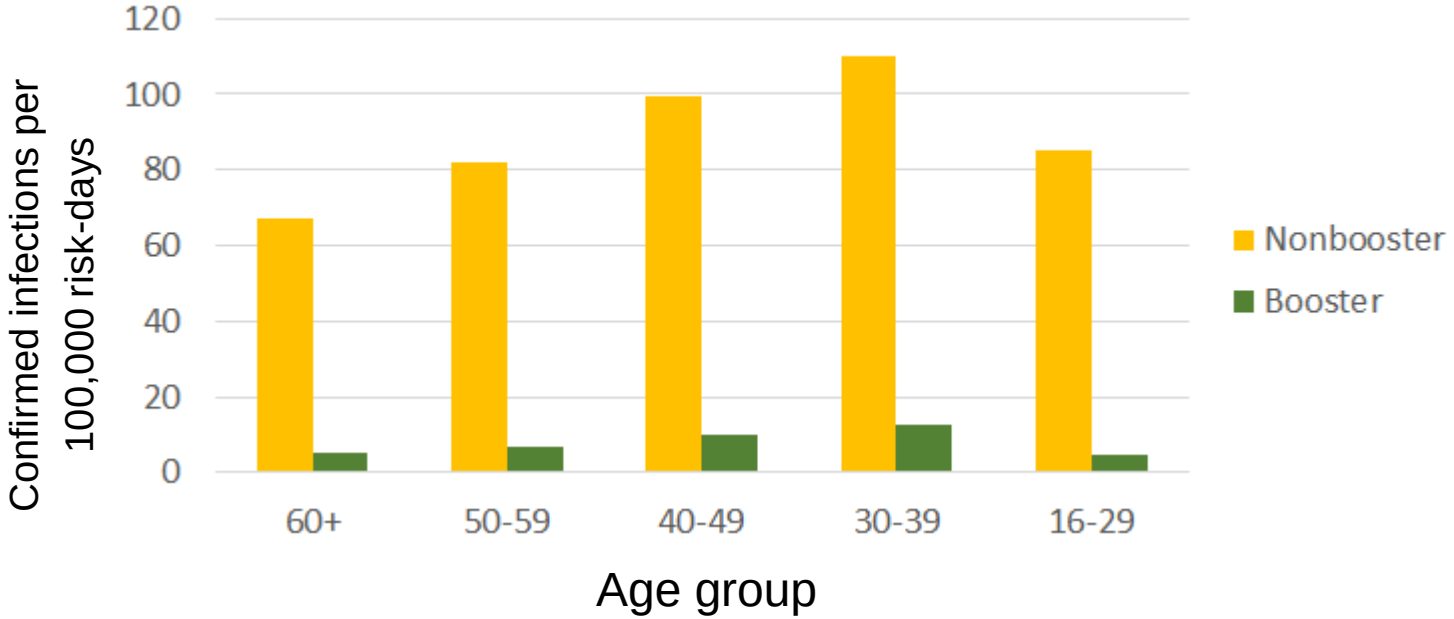
Absolute rates of confirmed infections per 100,000 risk-days

12+ days following booster versus 2nd dose only. Based on data from July 30 to October 6



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Bar-on et al., https://www.medrxiv.org/content/10.1101/2021.10.07.21264626v1.full.pdf

Using matching yields similar results

- Matching of booster-vaccinated people with corresponding 2-dose only vaccinated individuals (similar to Dagan et al.).

Matching was performed based on the following characteristics: age group (16-29, 30-39, 40-49, 50-59, 60-69, 70-79 and 80+), gender, week of second vaccine dose and demographic group (general Jewish, Arab, ultra-Orthodox).

Age	Rate ratio day 12+ relative to non-booster, using matching [95% CI]
60+	**9.7** [7.6, 12.8]
50-59	**10.0** [7.9, 12.6]
40-49	**8.6** [6.8, 10.2]
30-39	**7.7** [5.3, 9.4]
16-29	**16.4** [11.8, 22.1]

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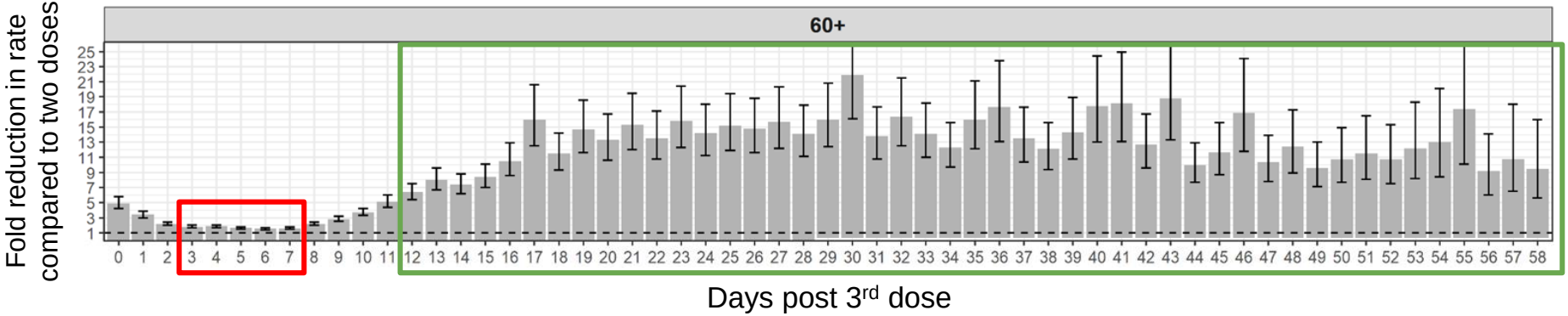
Bar-on et al., https://www.medrxiv.org/content/10.1101/2021.10.07.21264626v1.full.pdf

Temporal comparison within the booster cohort

(comparison within the group who chose to receive the booster dose)

- Alternative control **comparing 12+ days to 3-7 days** post vaccination (rationale: little effect of booster on confirmed infections in days 3-7)



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Bar-on et al., https://www.medrxiv.org/content/10.1101/2021.10.07.21264626v1.full.pdf

Temporal comparison within the booster cohort shows high protection factor

- **Alternative control group** - comparing **12+** days to **3-7** days post vaccination (when booster has little effect on confirmed infections)

Age	Rate ratio day 12+ relative to day 3-7 [95% CI]
60+	**7.4** [7.0, 7.8]
50-59	**7.3** [6.7, 7.9]
40-49	**5.4** [5.0, 5.8]
30-39	**4.8** [4.4, 5.2]
16-29	**11.2** [9.9, 12.8]

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Bar-on et al., https://www.medrxiv.org/content/10.1101/2021.10.07.21264626v1.full.pdf

Booster reduces the rate of severe disease* in 60+ and 40-60 age groups

(**Poisson regression** controlling for age, gender, demographic group, 2nd dose period, and incidence in area of residence)

*Severe disease (NIH definition): resting respiratory rate >30 breaths per minute, or O2 saturation <94%, or PaO2/FiO2 <300

Age	Non-booster severe cases (person-days at risk)	Booster group severe cases - day 12+ (person-days at risk)	Rate ratio for **severe** cases day 12+ relative to non-booster [95% CI]
60+	957 (20,894,746)	150 (39,630,040)	**18.7** [15.7, 22.4]
40-59	160 (25,243,100)	7 (20,202,835)	**22** [10.3, 47]

Too few cases to compare the rates of severe disease in ages 16-39 (19 in the nonbooster; one in the 12+ days post booster and none in the alternative control groups).

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Bar-on et al., https://www.medrxiv.org/content/10.1101/2021.10.07.21264626v1.full.pdf

Booster reduces the rate ratio of severe disease in 60+ and 40-60 age groups also in alternative control group

(**Poisson regression** controlling for age, gender, demographic group, 2nd dose period, and incidence in area of residence)

Age	Non-booster severe cases (person-days at risk)	Booster group severe cases - day 12+ (person-days at risk)	Rate ratio for **severe** cases day 12+ relative to non-booster [95% CI]		Booster control group severe cases - day 3-7 (person-days at risk)	Rate ratio for **severe** cases day 12+ relative to day 3-7 [95% CI]
60+	957 (20,894,746)	150 (39,630,040)	**18.7** [15.7, 22.4]		127 (5,548,778)	**6.5** [5.1, 8.3]
40-59	160 (25,243,100)	7 (20,202,835)	**22** [10.3, 47]		6 (4,704,467)	**3.2** [1.1, 9.6]

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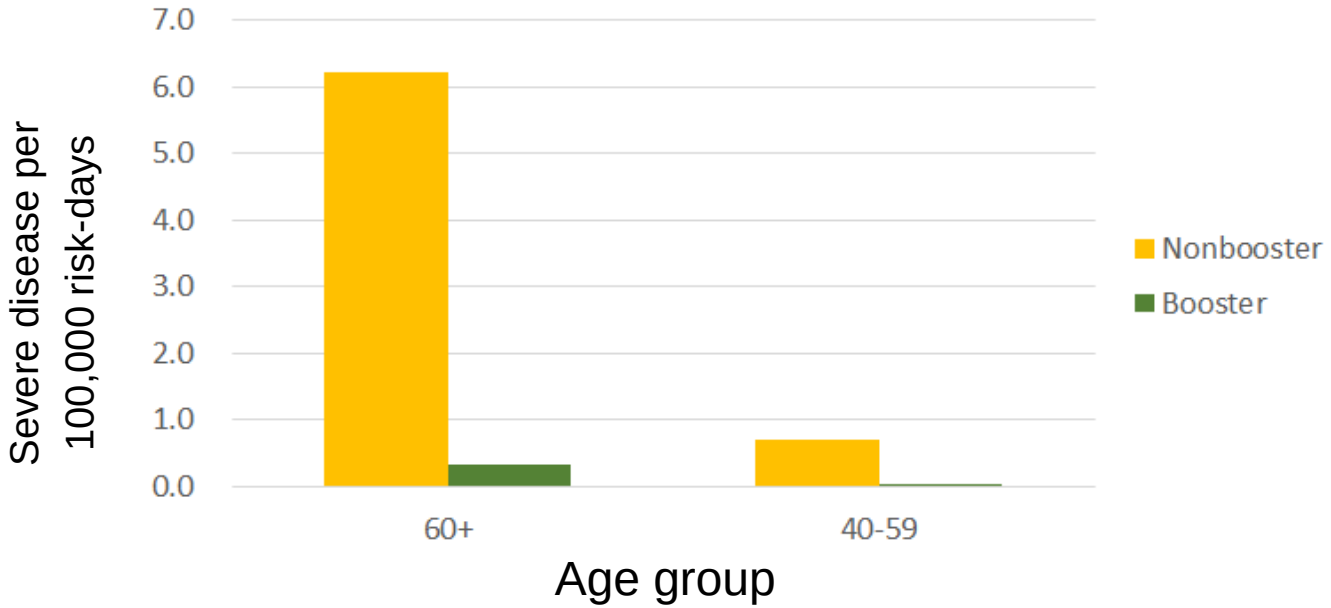
Bar-on et al., https://www.medrxiv.org/content/10.1101/2021.10.07.21264626v1.full.pdf

Absolute rates of severe disease per 100,000 risk-days

*Severe disease (NIH definition): resting respiratory rate >30 breaths per minute, or O2 saturation <94%, or PaO2/FiO2 <300

12+ days following booster versus 2nd dose only. Based on data from July 30 to October 6



Bar-on et al., https://www.medrxiv.org/content/10.1101/2021.10.07.21264626v1.full.pdf

Booster reduces the rate ratio of death in 60+ age group

(**Poisson regression** controlling for age, gender, demographic group, 2nd dose period, and incidence in area of residence)

Age	Non-booster deaths (person-days at risk)	Booster group deaths - day 12+ (person-days at risk)	Booster control group deaths - day 3-7 (person-days at risk)	Rate ratio for **death** day 12+ relative to non-booster [95% CI]	Rate ratio for **death** day 12+ relative to day 3-7 [95% CI]
60+	270 (16,395,473)	23 (10,600,038)	46 (5,074,461)	**14.7** [9.4, 23.1]	**4.8** [2.8, 8.2]

Not enough cases to compare the rate ratio of death in ages 16-59 (7 in the nonbooster; none in the 12+ days post booster and alternative control groups).

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Bar-on et al., https://www.medrxiv.org/content/10.1101/2021.10.07.21264626v1.full.pdf

Nationwide observations following booster campaign

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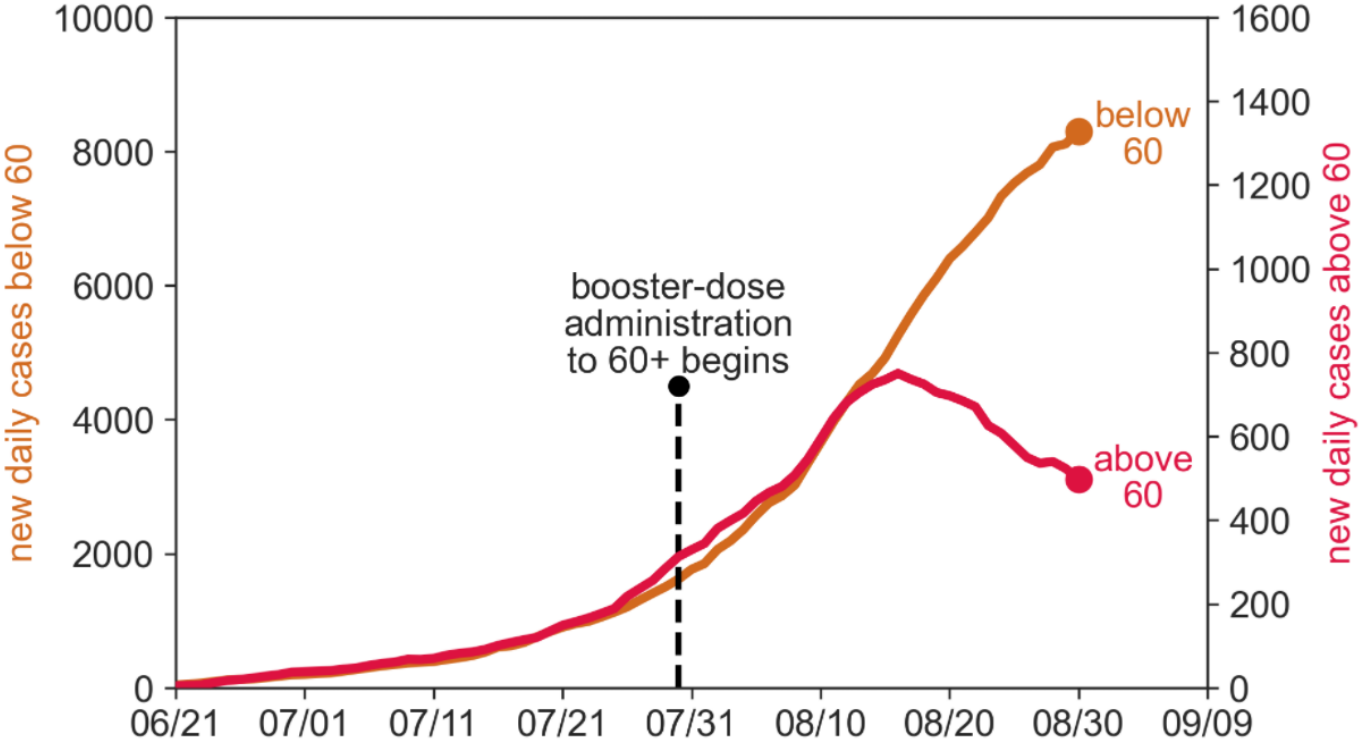
Following the booster a decrease in confirmed infections was observed among people aged 60+



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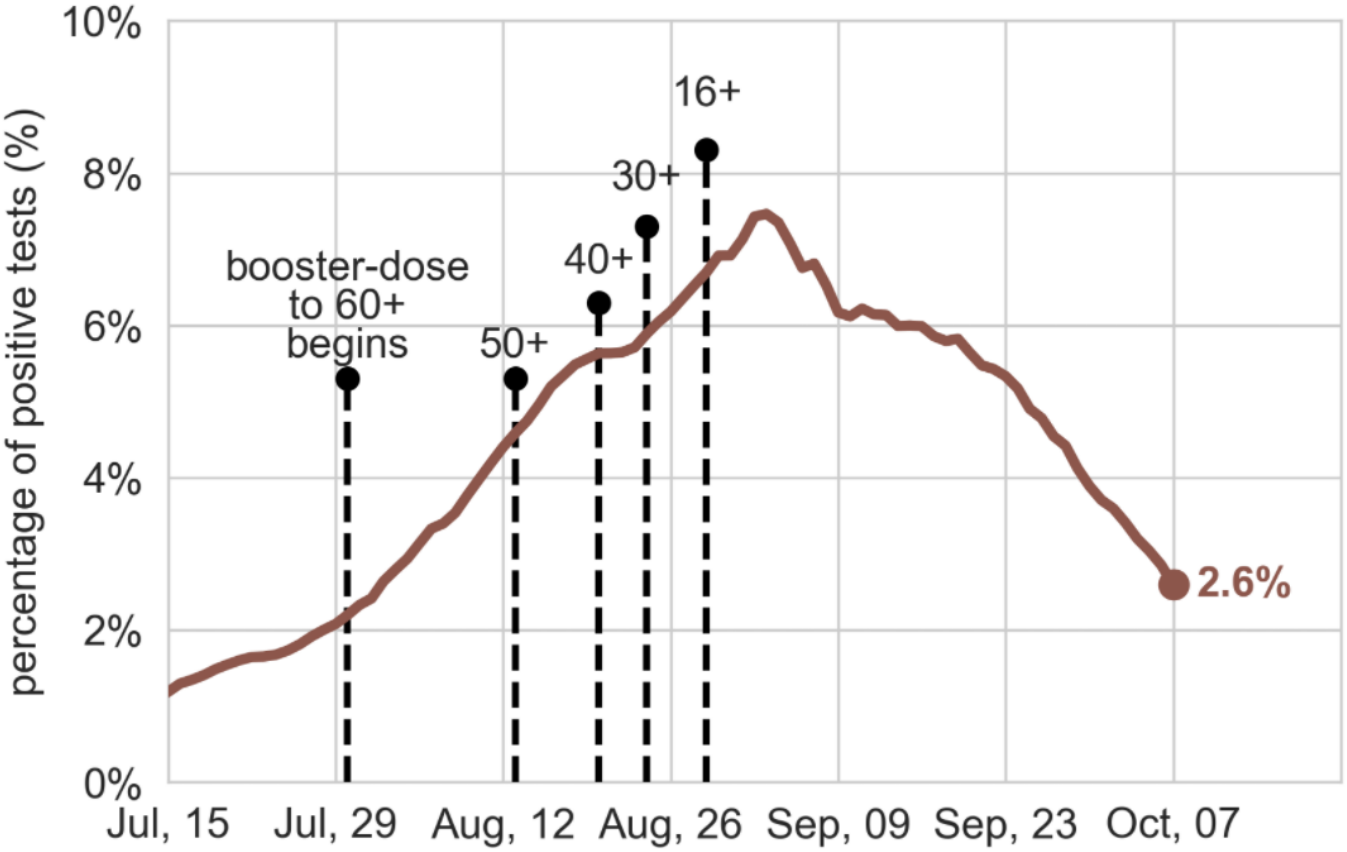
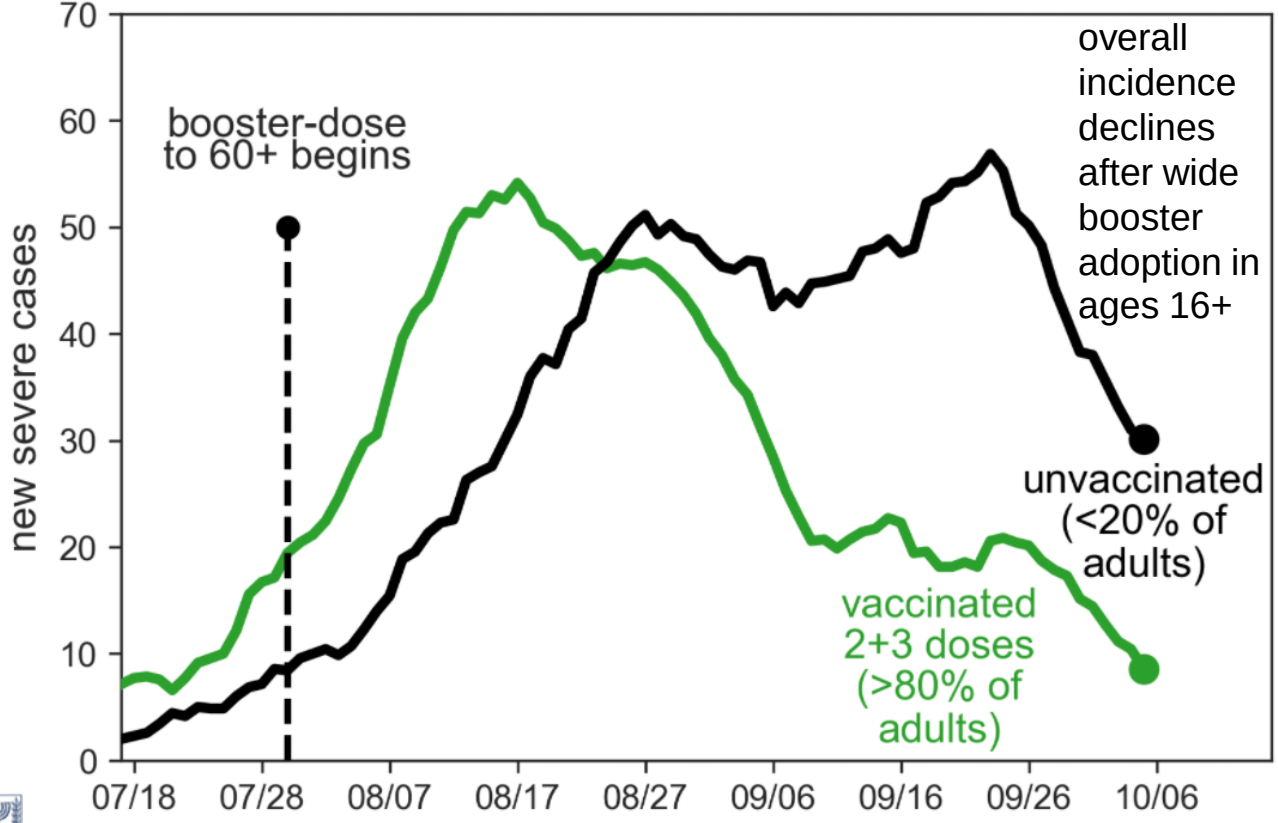
In sept. effects of booster at ages below 60

Nationwide decrease in percentage of positive tests began only after boosters were administered to most age groups

Percentage of positive tests is more reliable than number of cases due to high-holidays in Israel during Sept.



Following the third dose, severe cases among vaccinated decreased sharply



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Safety results from nationwide booster campaign

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- Rates of adverse events per million doses within 30 days
- Updated up to Oct. 10th
- For youngest age groups ≈half had >30 days since booster
- Limitation: Reporting based on passive surveillance (proactive for myocarditis), and therefore subject to underreporting

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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.

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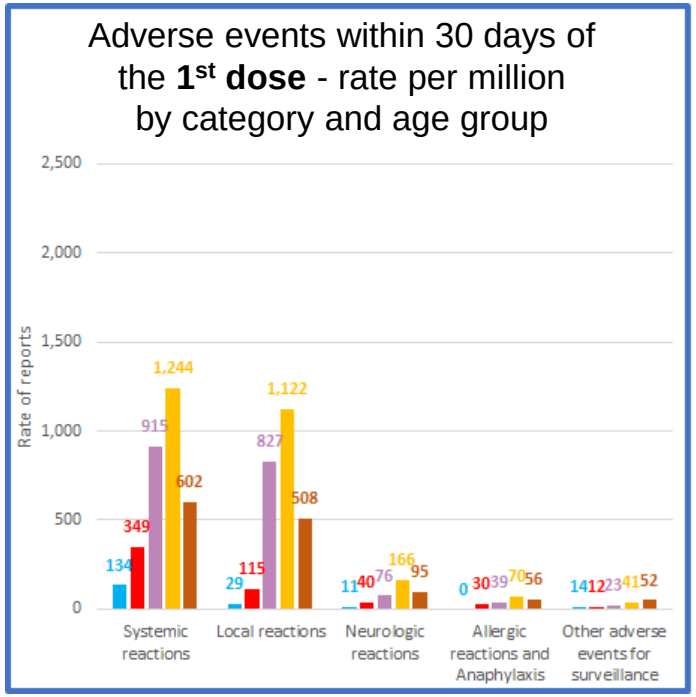
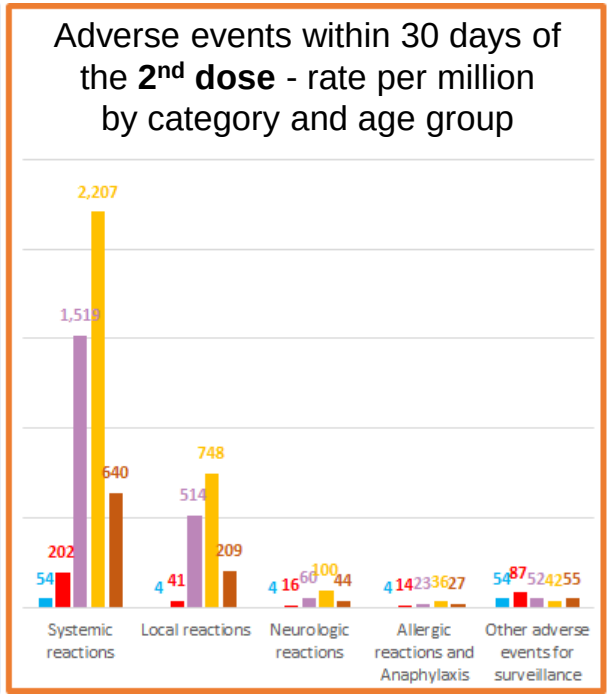
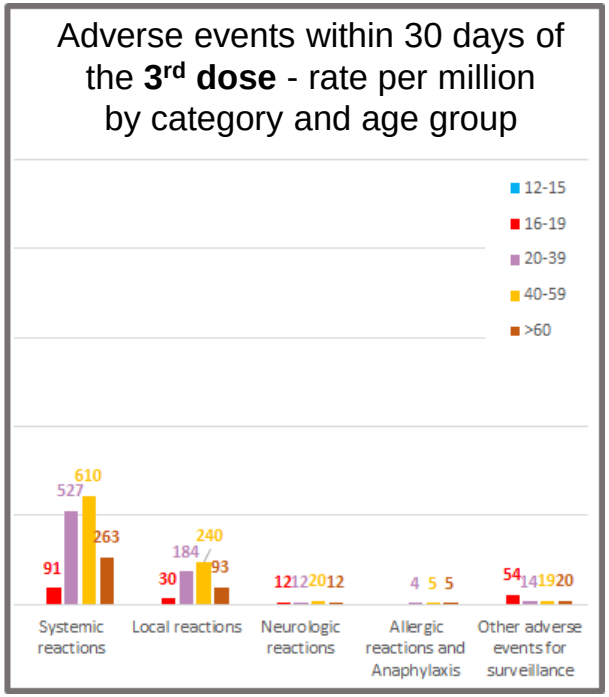
Rate of adverse events by category and age group

Limitation: Reporting based on passive surveillance, and therefore subject to underreporting







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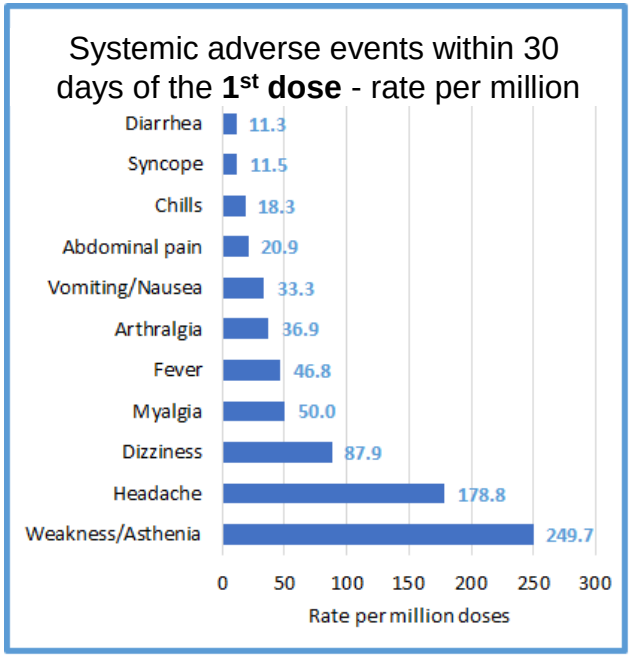
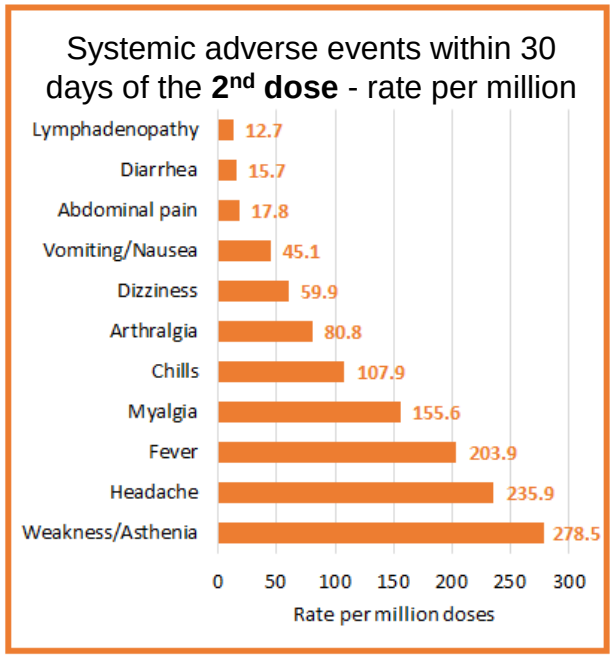
Data is based on adverse events reported to the MoH | Individuals may report more than 1 adverse event | There is an estimated under reporting

Rate of systemic adverse events by dose

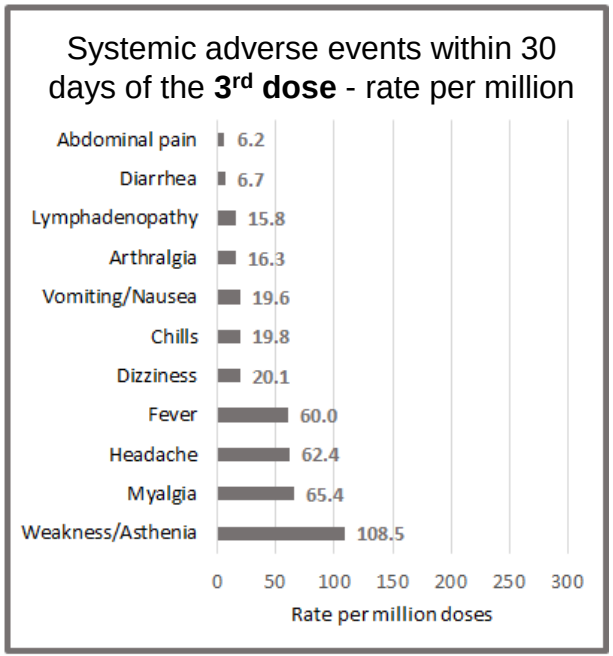
Limitation: Reporting based on passive surveillance, and therefore subject to underreporting



1st dose – 6,178,847 vaccinees



2nd dose – 5,679,655 vaccinees



3rd dose – 3,732,923 vaccinees

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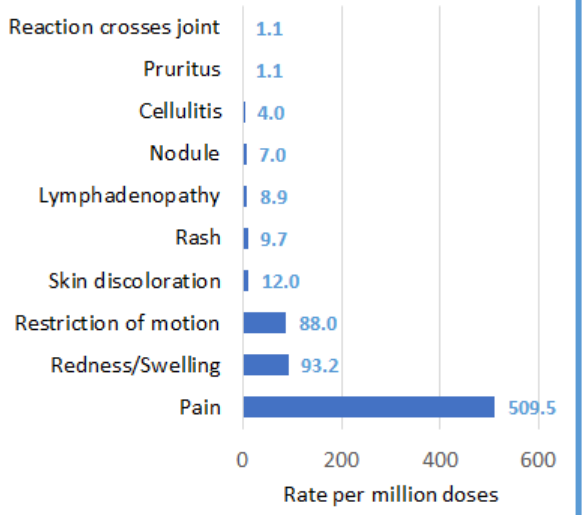
Data is based on adverse events reported to the MoH | Individuals may report more than 1 adverse event | There is an estimated under reporting

Rate of local adverse events by dose

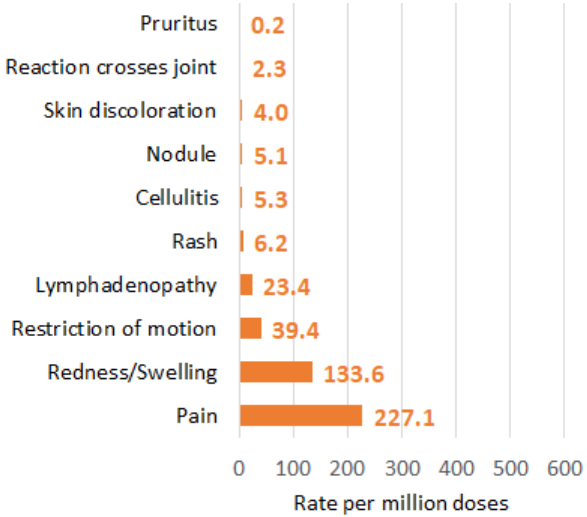
Limitation: Reporting based on passive surveillance, and therefore subject to underreporting

Local adverse events within 30 days of the **1st dose** - rate per million



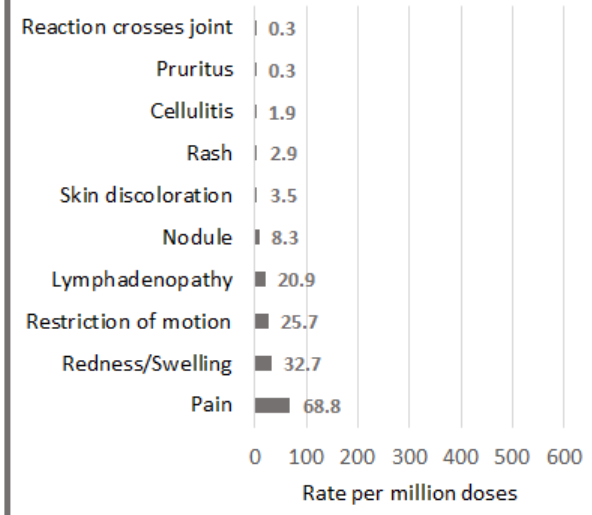
1st dose – 6,178,847 vaccinees

Local adverse events within 30 days of the **2nd dose** - rate per million



2nd dose – 5,679,655 vaccinees

Local adverse events within 30 days of the **3rd dose** - rate per million



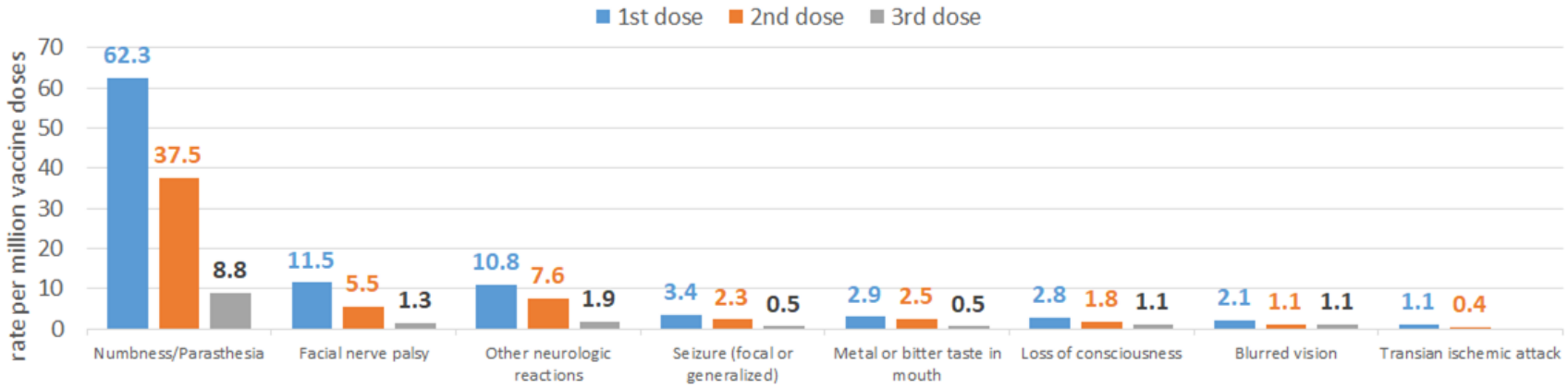
3rd dose – 3,732,923 vaccinees

MINISTRY OF HEALTH

Data is based on adverse events reported to the MoH | Individuals may report more than 1 adverse event | There is an estimated under reporting

Rate of neurologic adverse events by dose within 30 days of vaccination

Limitation: Reporting based on passive surveillance, and therefore subject to underreporting



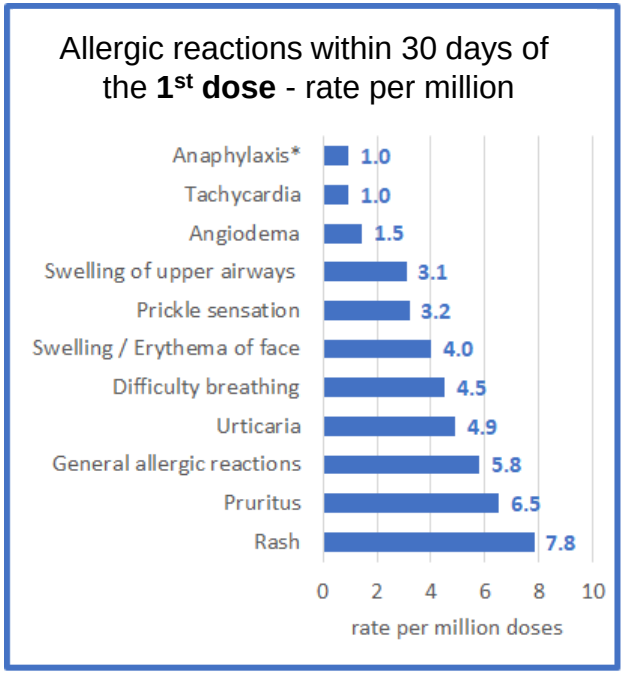
1st dose – 6,178,847 vaccinees

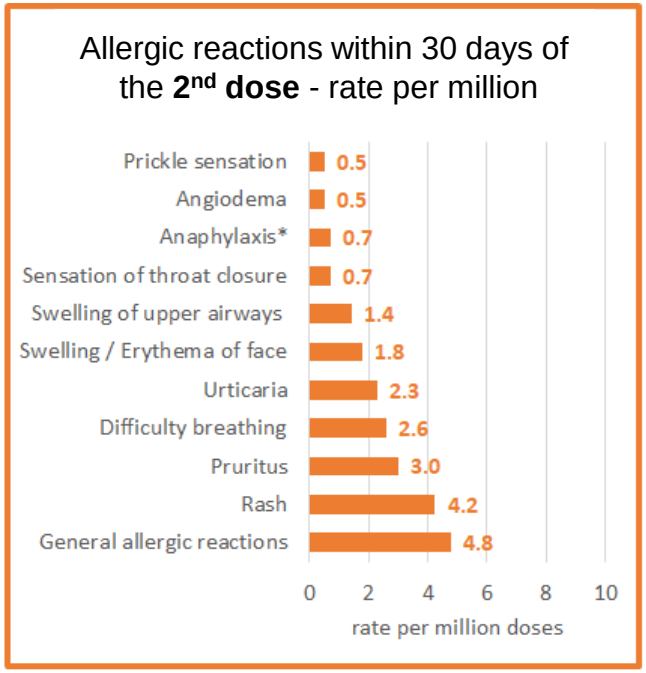
2nd dose – 5,679,655 vaccinees

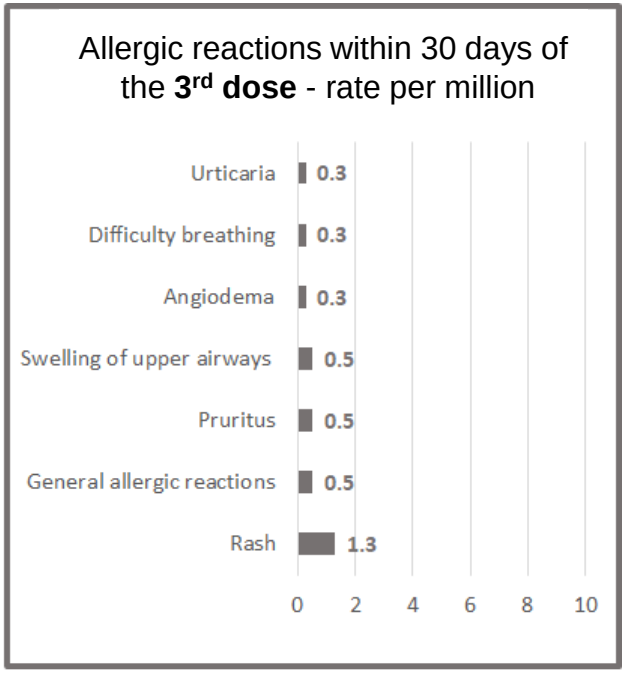
3rd dose – 3,732,923 vaccinees

Rate of allergic adverse events by dose

Limitation: Reporting based on passive surveillance, and therefore subject to underreporting







1st dose – 6,178,847 vaccinees

2nd dose – 5,679,655 vaccinees

3rd dose – 3,732,923 vaccinees

MINISTRY OF HEALTH

Data is based on adverse events reported to the MoH | Individuals may report more than 1 adverse event | There is an estimated under reporting

Adverse events reported following 3rd dose
(>3.5 million booster doses administered)

Non serious reports	Serious reports
2,394	43

Serious Adverse event (SAE) definition*

Any adverse event that:

- Results in death
- Is life-threatening
- Requires hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability or incapacity
- Results in congenital anomaly
- Other important medical events which required intervention

*https://www.fda.gov/safety/reporting-serious-problems-fda/what-serious-adverse-event

Hospitalization and death reports following vaccination are examined by an independent clinical work group using available clinical data

Serious adverse events

Ages 12-59, out of 2,515,675 vaccinees

Event type	Num. of events	Deceased
Myocarditis	9	0
Perimyocarditis	8	0
Pericarditis	3	0
Guillain barre syndrome	2	0
Allergic reaction	2	0
DVT	2	0
Other events	4	0

- In total 30 events out of which:
  - 8 cases are still under investigation.
  - For 17 myocarditis and perimyocarditis cases causality is probable, cases will be reviewed by special committee
  - For two cases no causality to the vaccine was found.
  - For one case causality is possible.
  - For two cases causality to the vaccine was found.

Ages 60+, out of 1,216,955 vaccinees

Event type	Num. of events	Deceased
CVA	4	3
UTI	3	0
pneumonia	1	0
thrombocytopenia	1	0
Other events	7	2

- In total 14 events out of which:
  - One case (1 death) is still under investigation.
  - For 12 cases (4 deaths) no causality to the vaccine was found.
  - For one case causality is possible.

MINISTRY OF HEALTH

Myocarditis & perimyocarditis cases and number of vaccinees by age group and sex

Proactive surveillance. All cases reported in Israel Dec. 2020 - Oct 10th, 2021

Sex	Age group	1st dose (0-21 days following vaccination)		2nd dose (0-30 days following vaccination)		3rd dose* (0-30 days following vaccination; in the minority of vaccinees not all 30 days have passed so far)	
		Number of vaccinees	Number of cases reported	Number of vaccinees	Number of cases reported	Number of vaccinees	Number of cases reported
Female	12-15	204,729	**0**	162,297	**1**	279	**0**
	16-19	248,881	**0**	222,067	**2**	97,807	**0**
	20-24	263,845	**1**	242,697	**6**	141,910	**0**
	25-29	247,365	**0**	229,189	**1**	130,283	**0**
	+30	2,127,538	**3**	2,029,074	**7**	1,542,142	**0**
Male	12-15	192,014	**1**	151,081	**10**	292	**0**
	16-19	254,497	**3**	223,079	**36****	96,238	**5**
	20-24	275,235	**6**	251,672	**26**	139,015	**5**
	25-29	257,713	**3**	239,319	**20**	133,650	**1**
	+30	1,983,230	**10**	1,897,067	**32**	1,448,745	**6**

* Two cases are still under investigation

** One case – first dose Pfizer, second dose Moderna

MINISTRY OF HEALTH

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

- Booster dose shows improved protection against confirmed infection in all age groups tested.
- Booster dose shows improved protection against severe disease in ages 40 and above.
- Booster dose adverse events not more acute than first or second dose.
- Administration of booster dose helped Israel dampen infections and severe cases in the 4th wave.

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