Vaccines and Related Biological Products Advisory Committee October 14-15, 2021 Meeting Presentation

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Ministry of Health
משרד הבריאות

WEIZMANN INSTITUTE OF SCIENCE

TECHNION
Israel Institute of Technology

The Gertner Institute

THE HEBREW UNIVERSITY OF JERUSALEM

Booster protection across ages - data from Israel

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

Oct. 12th, 2021

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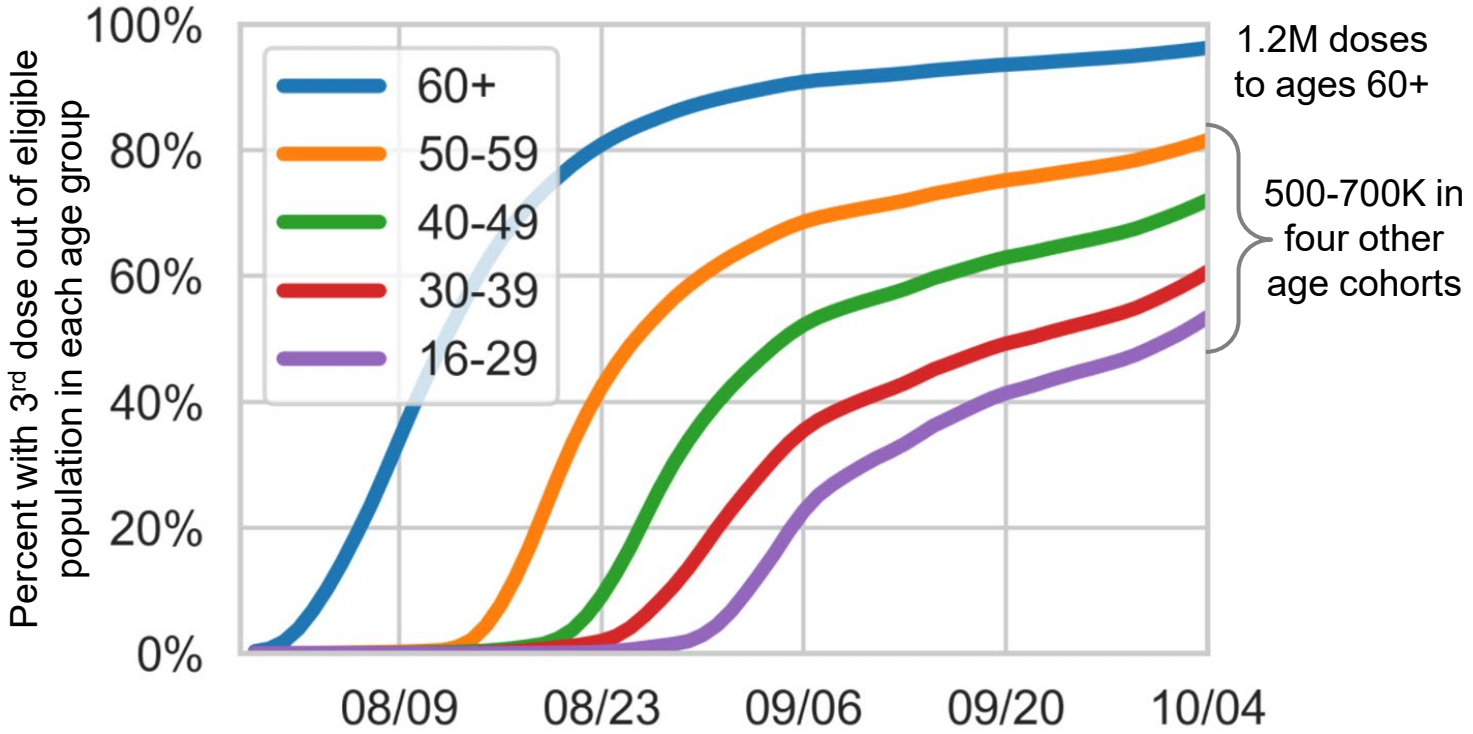
Sharon Alroy-Preis & Ron Milo have no competing financial interests to disclose.

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

Large majority of elderly population received a 3rd dose

Overall
3.7 million
booster doses
to date



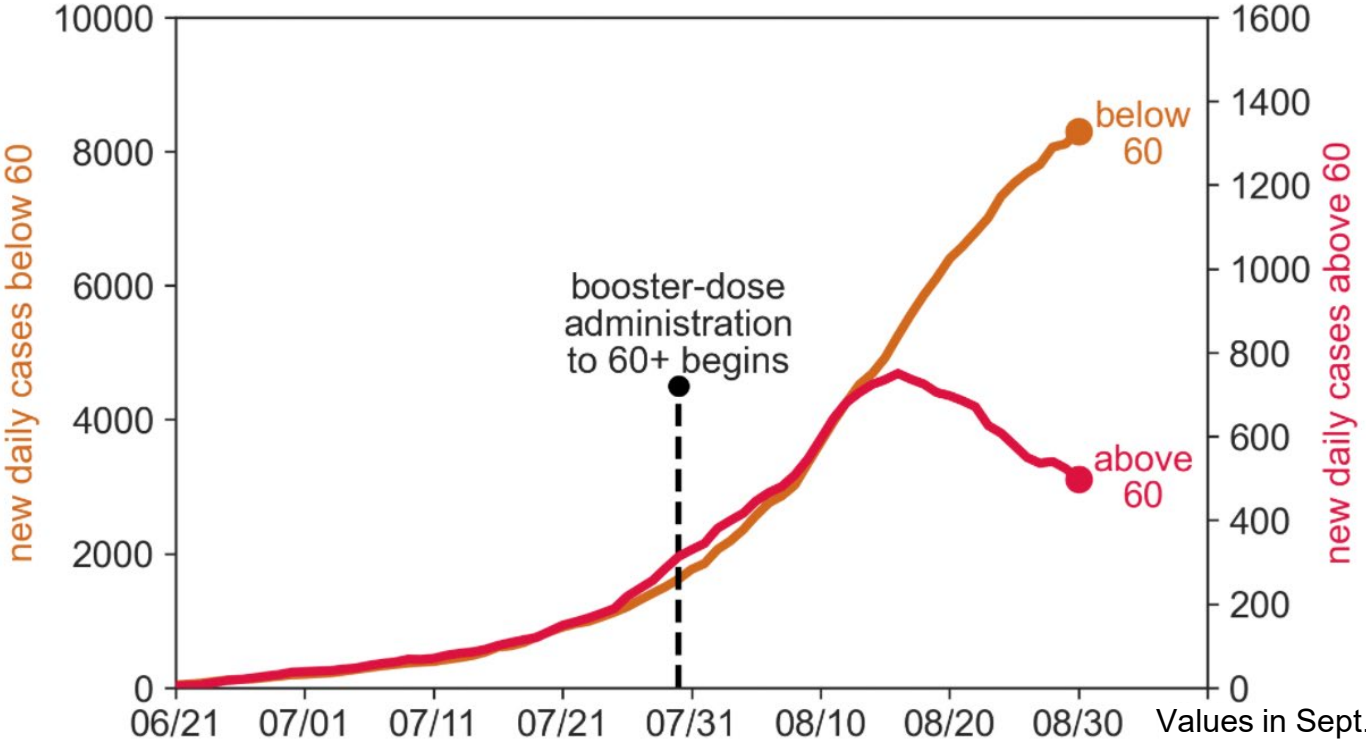
Booster campaign began on July 30th

MINISTRY OF HEALTH

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

Based on PCR testing.

In Israel testing is performed either following symptoms or without symptoms for contact tracing and other reasons

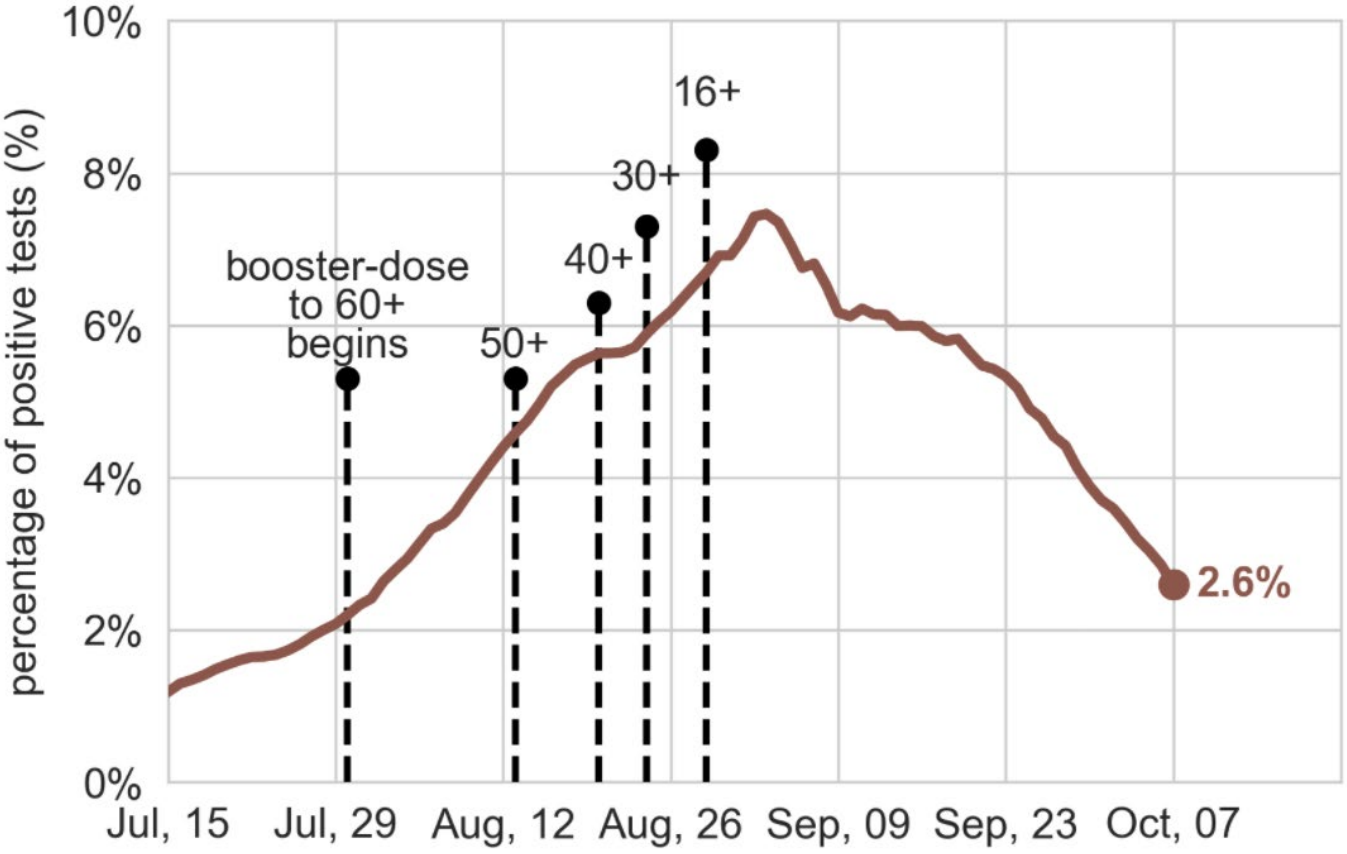


Values in Sept. are affected by booster administered to age groups below 60

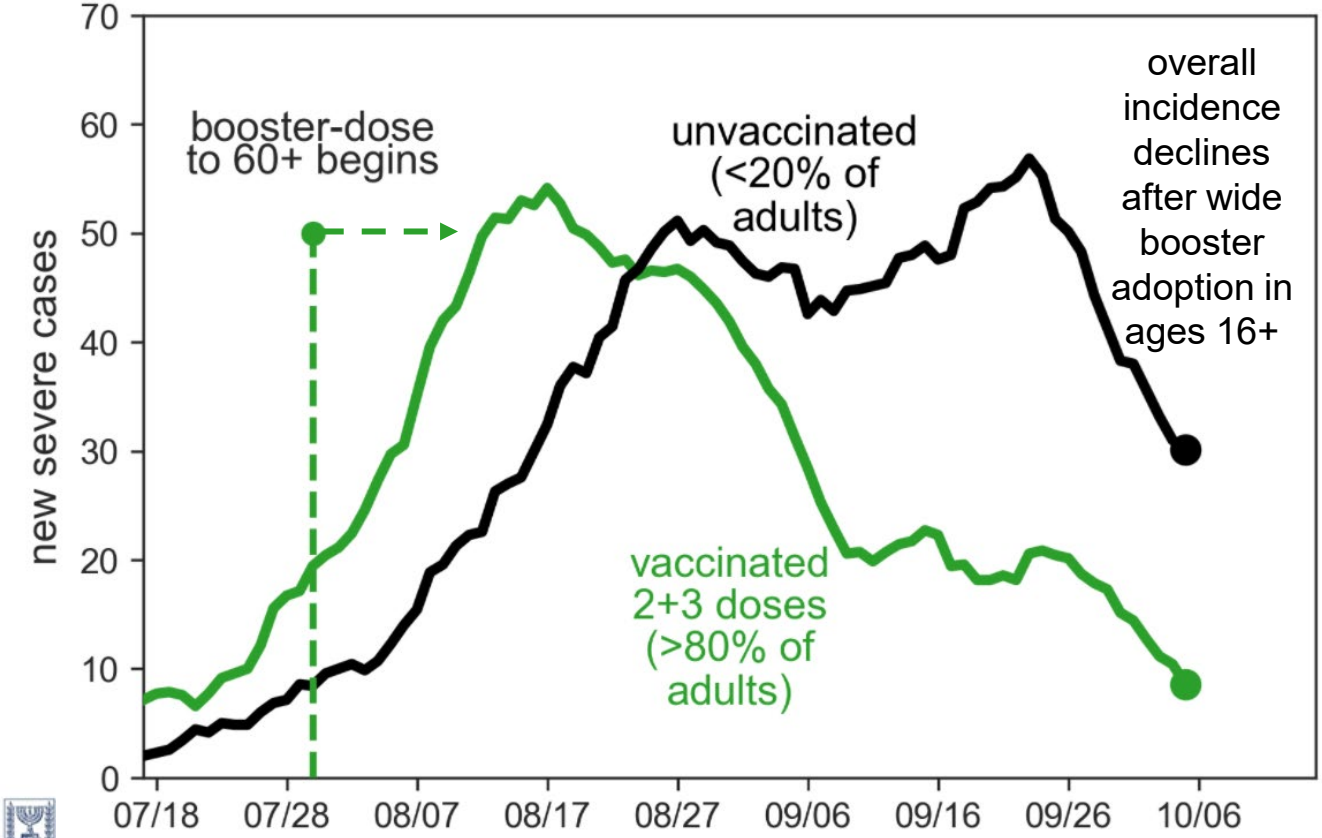
MINISTRY OF HEALTH

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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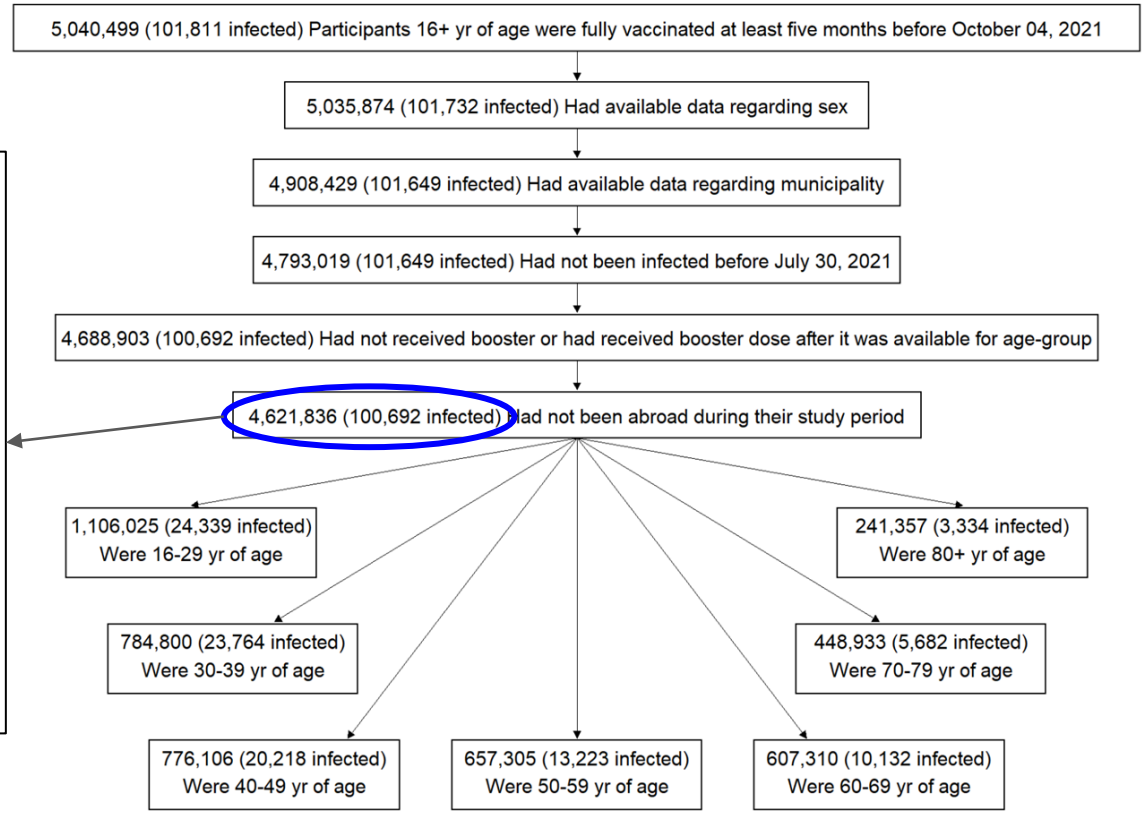
Our analysis covers most of the adult Israeli population

(data on those aged 16 and above who were fully vaccinated before May 2021)

4.6M people met study qualifications out of 4.9M who were fully vaxx'd by end of sept, i.e. 93% of the potential population

(**100k** confirmed infections;
>1000 severe illness;
>250 deaths
in Aug-Sept study period)



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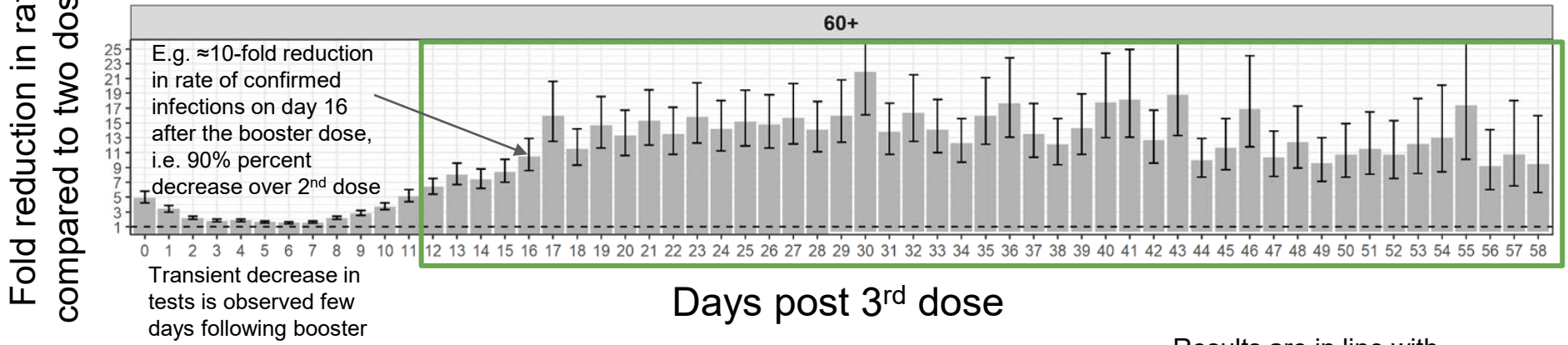
Protection against **confirmed infection** with booster versus 2nd dose only as a function of time post vaccination **ages 60+**

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 4.



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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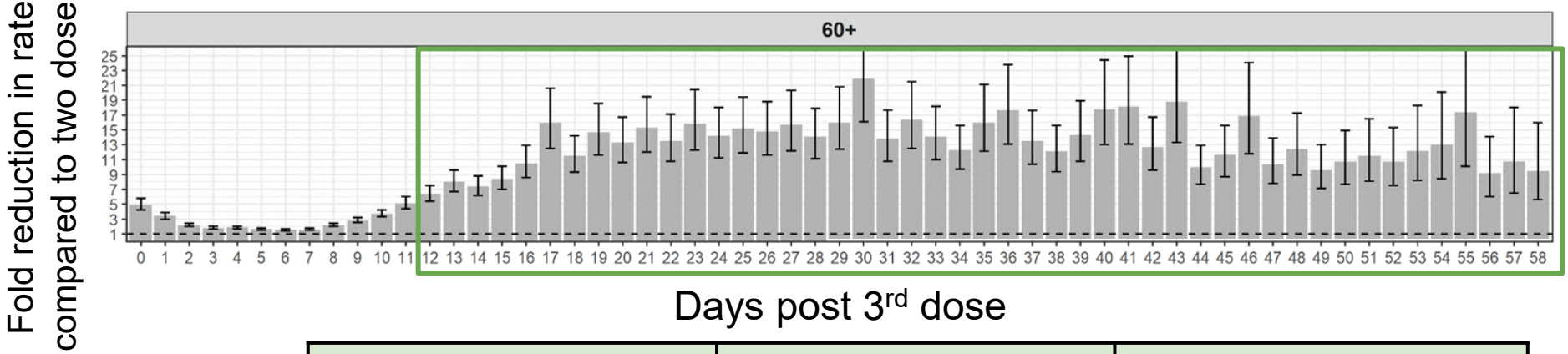


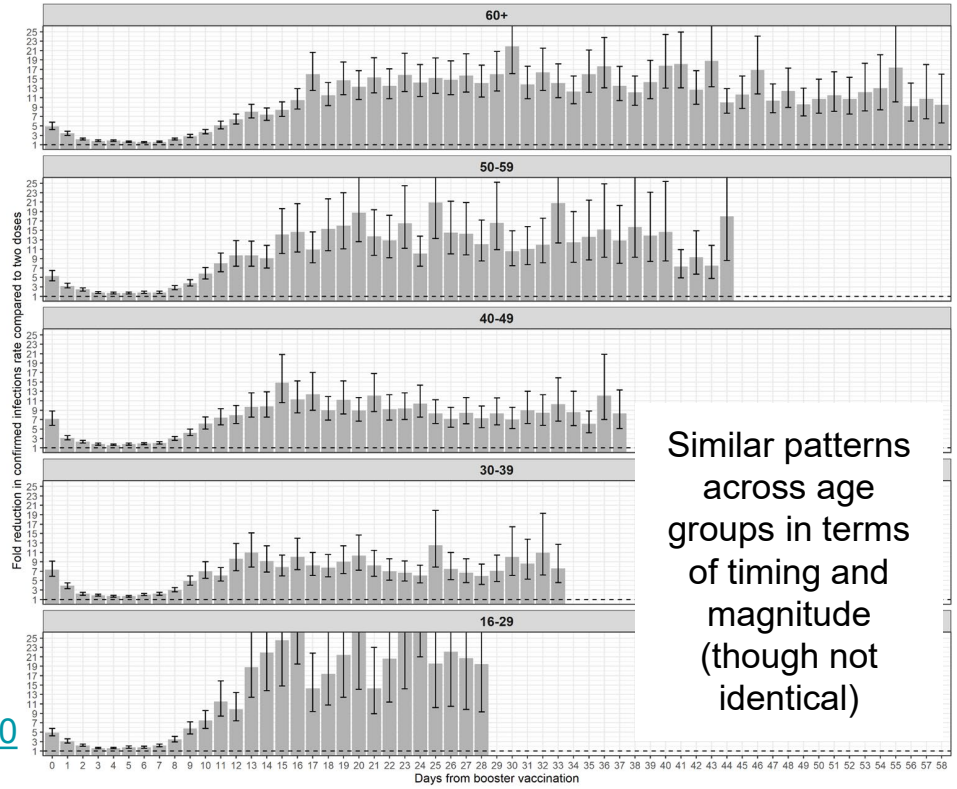
Cohort	Non-booster (2 doses only)	Following booster (12+ days)
Confirmed infections	12,225	2,694
Risk-days	21,660,770	46,201,515
Rate ratio, adj. via Poisson regression [95% CI]	-	**12.4** [11.9, 12.9]

MINISTRY OF HEALTH

Protection against confirmed infection 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. Based on data from booster eligibility in age group until 10/4.

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]



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

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

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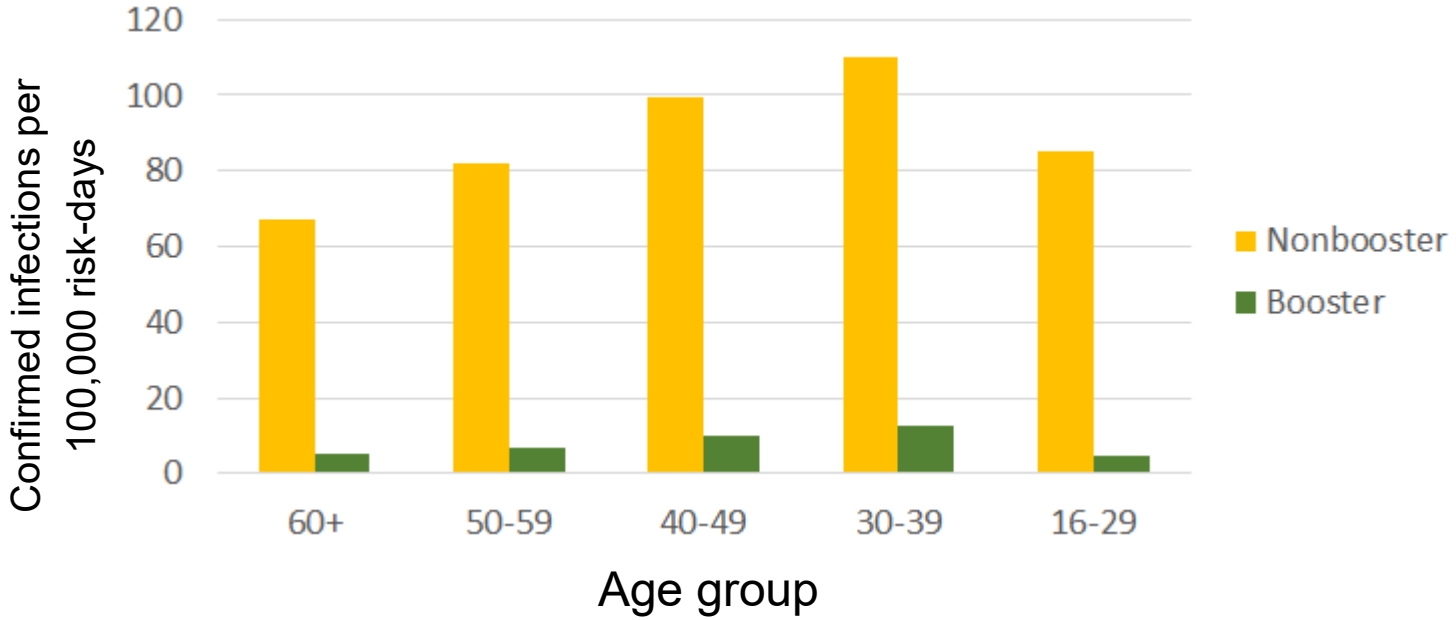
Absolute rates of confirmed infections per 100,000 risk-days

12+ days following booster versus 2nd dose only.

Based on data from booster eligibility in age group until 10/4.



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

Results were tested by various methods

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

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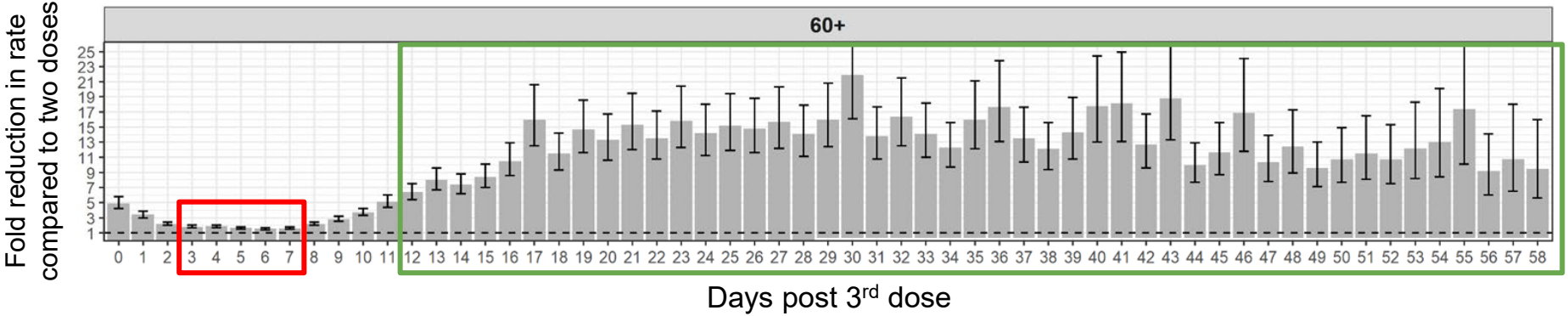
Bar-on et al., https://www.medrxiv.org/content/10.1101/2021.10.07.21264626v1.full.pdf

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)



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. Based on data from booster eligibility in age group until 9/29)

*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]
16-39	23 (36,907,240)	1 (9,761,068)	too few cases to estimate reliably

MINISTRY OF HEALTH

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

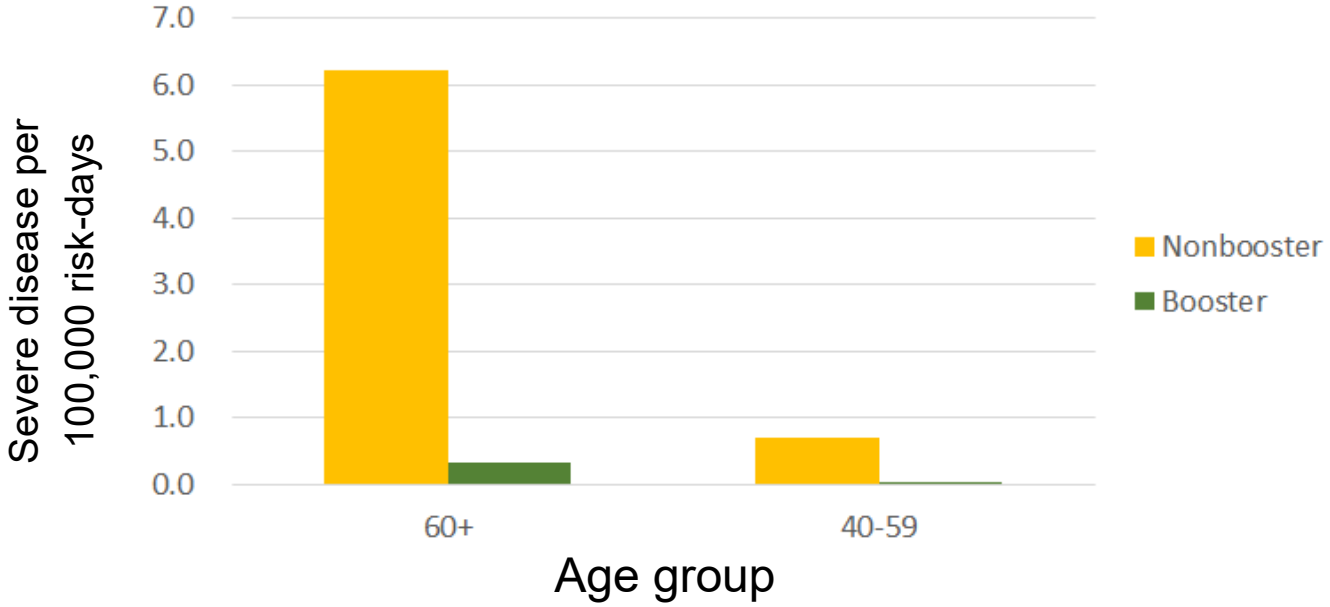
(**Poisson regression** controlling for age, gender, demographic group, 2nd dose period, and incidence in area of residence.
Based on data from booster eligibility in age group until 9/29)

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]		Alternative 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]
16-39	23 (36,907,240)	1 (9,761,068)	too few cases to estimate reliably		0 (4,096,522)	too few cases to estimate reliably

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

12+ days following booster versus 2nd dose only.
Based on data eligibility in age group until 9/29

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



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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 death in 60+ age group

(**Poisson regression** controlling for age, gender, demographic group,
2nd dose period, and incidence in area of residence.
Based on data from booster eligibility in age group until 9/1)

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]
40-59	7 (11,923,351)	0 (874,068)	0 (2,917,068)	Too few cases to estimate	

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

Summary: Booster dose shows improved effectiveness over 2nd dose across all tested age groups

- Booster dose shows ≈10 fold improved protection over 2nd dose against confirmed infection across age groups 16 years old and above.
- Booster dose is also effective against severe COVID19
  - For ages 60+ between 6 to 20-fold reduction (i.e. over 80% decrease in rate ratio over 2nd dose)
  - For ages 40-60 between 3 to 20-fold reduction (i.e. over 60% decrease in rate ratio over 2nd dose)
- Booster dose decreases COVID19 associated death rate 3 to 10-fold among the elderly

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Nationwide observations following booster campaign

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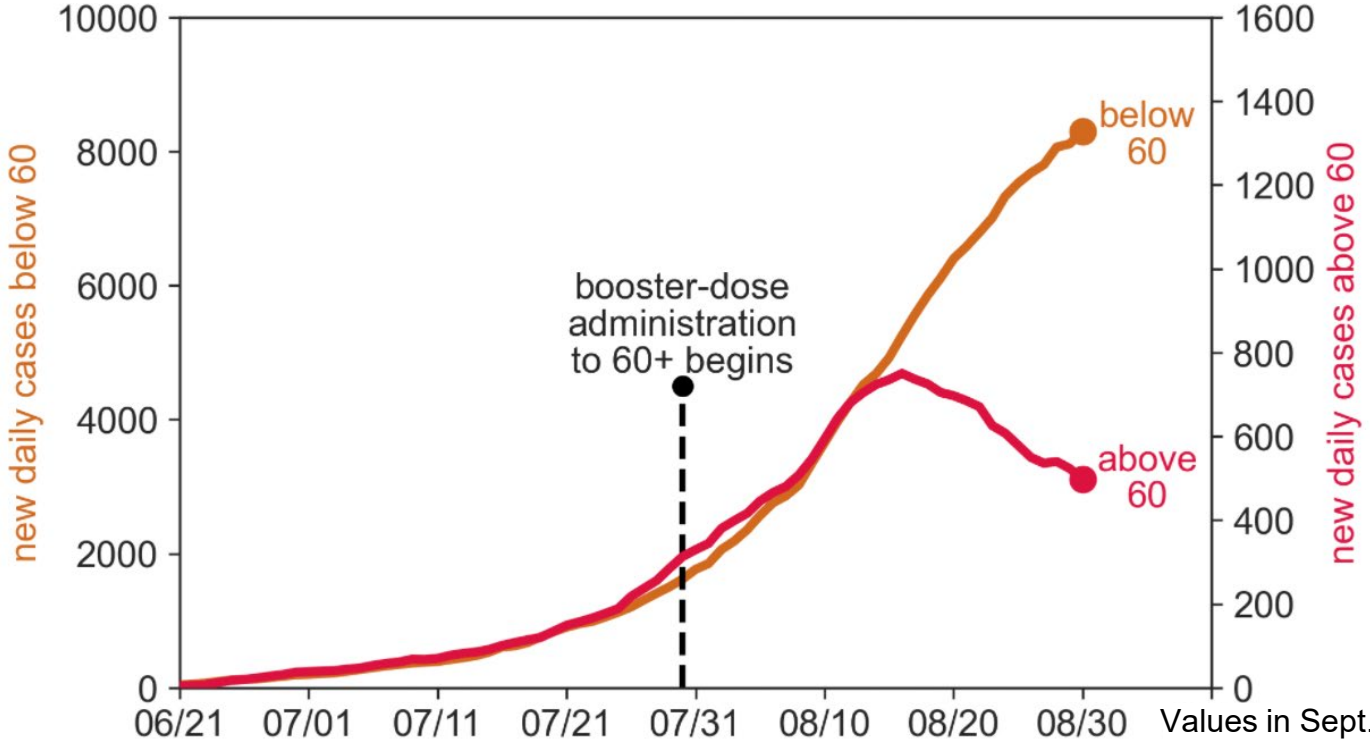
Following the booster a decrease in confirmed infections was observed among people aged 60+

Based on PCR testing.

In Israel testing is performed either following symptoms or without symptoms for contact tracing and other reasons



Values in Sept. are affected by booster administered to age groups below 60

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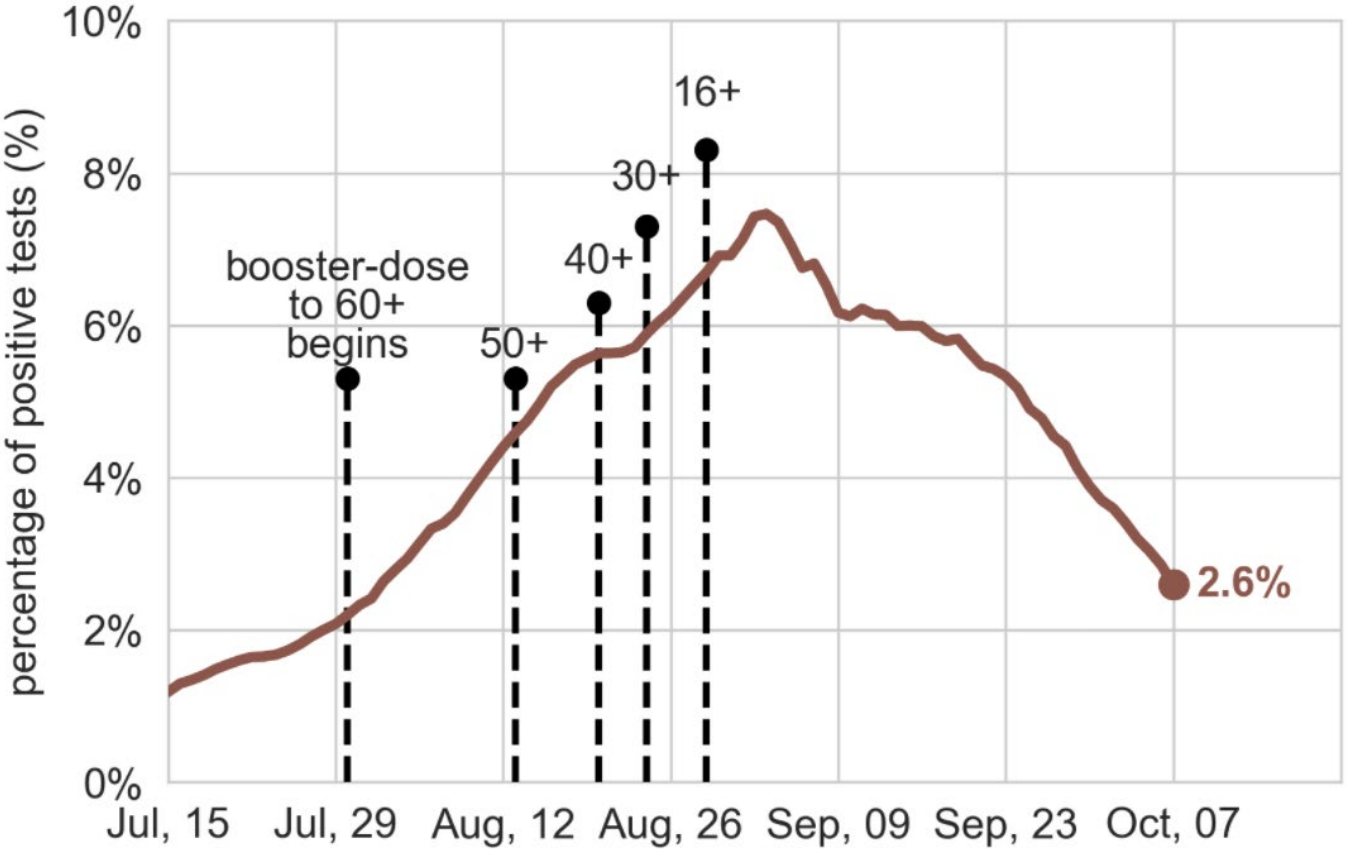

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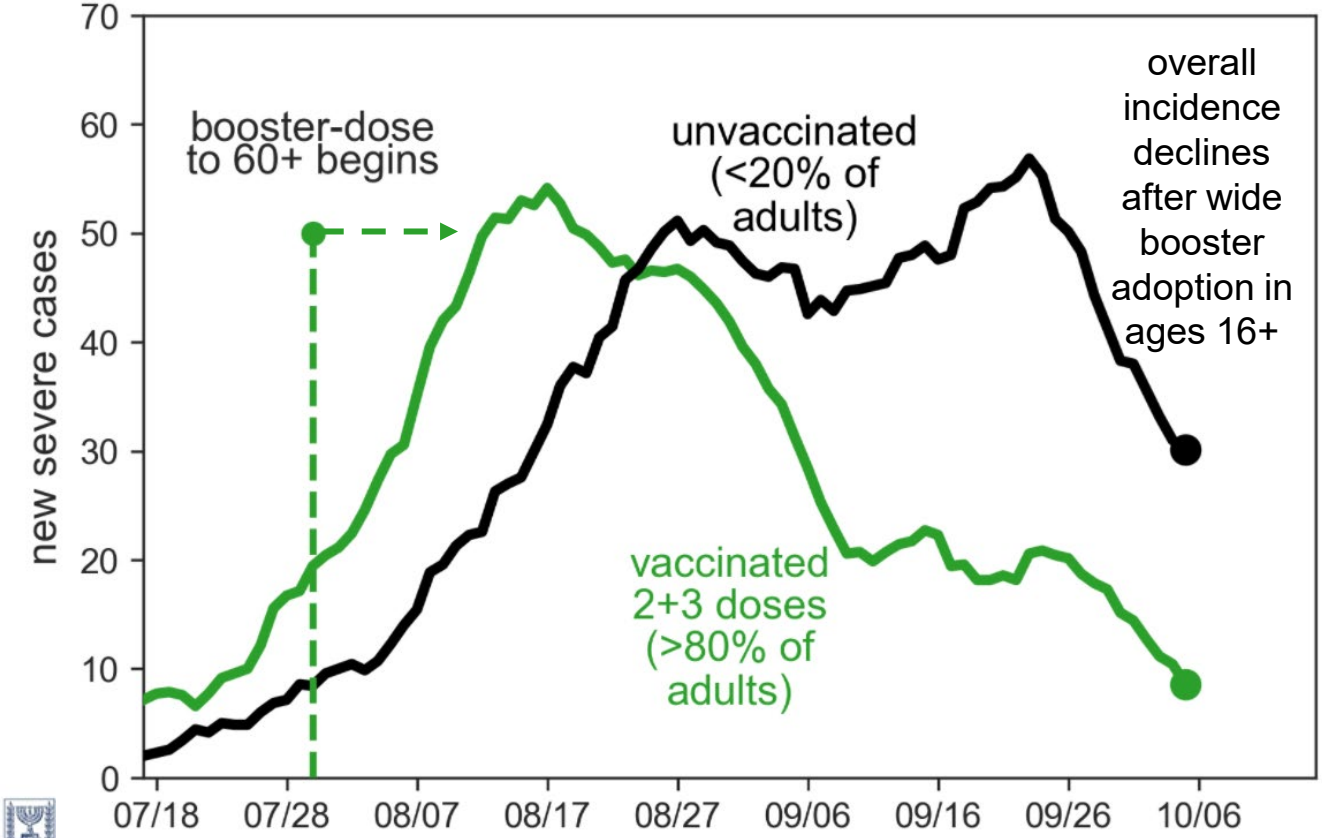
Following the third dose, severe cases among vaccinated decreased sharply



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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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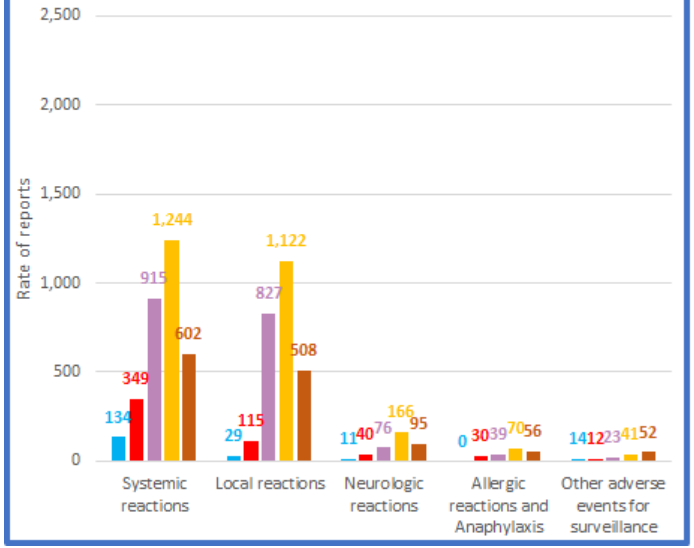
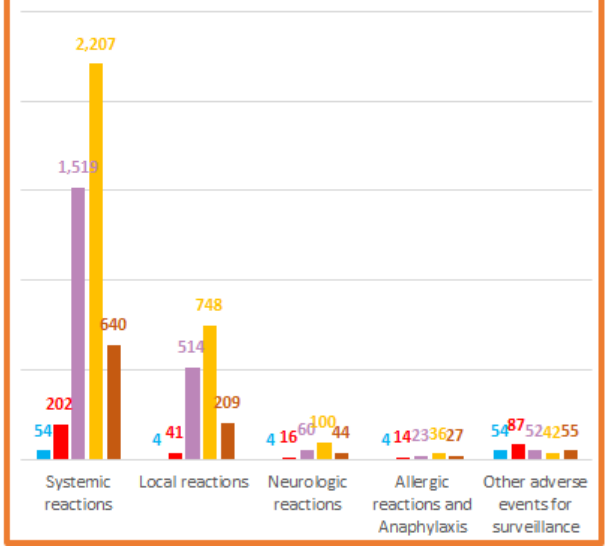
Rate of adverse events by category and age group

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

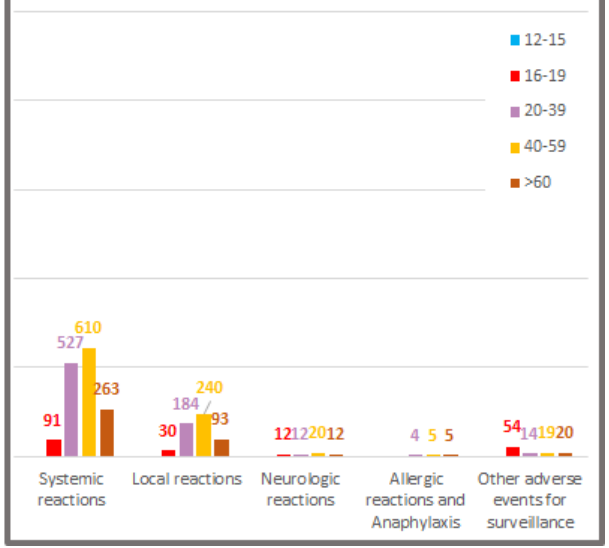
Adverse events within 30 days of the **1st dose** - rate per million by category and age group



Adverse events within 30 days of the **2nd dose** - rate per million by category and age group



Adverse events within 30 days of the **3rd dose** - rate per million by category and age group



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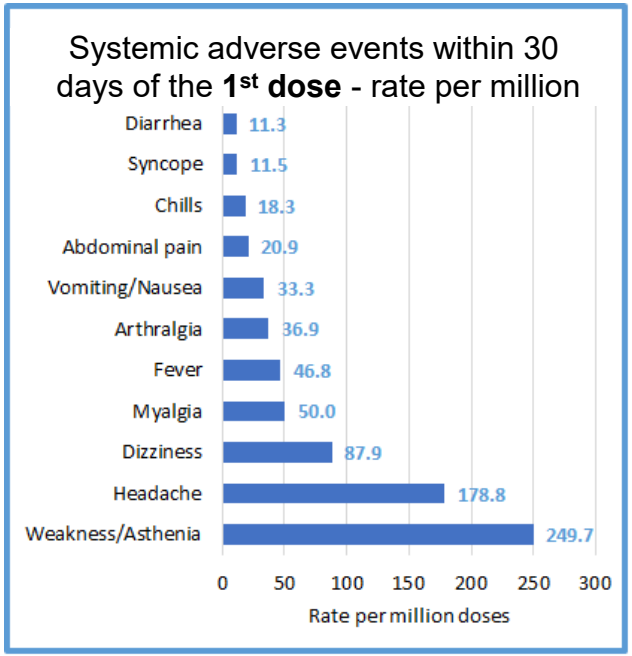
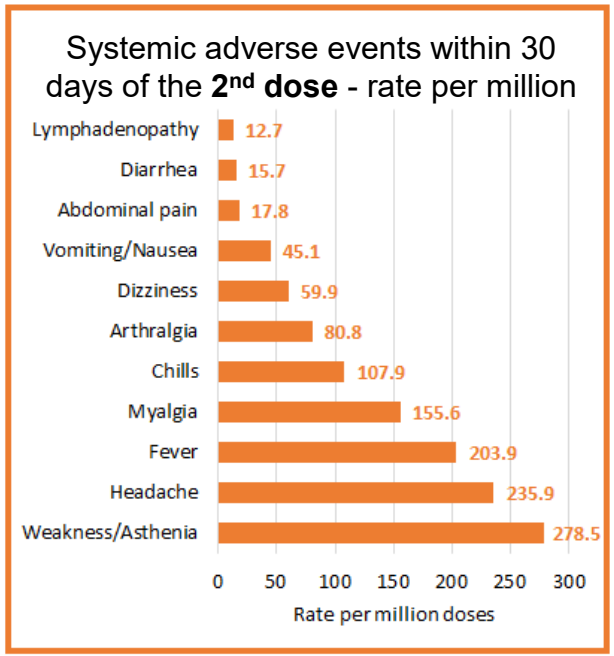
Data is based on adverse events reported to the MoH | Individuals may report more than 1 adverse event | There is an estimated under reporting

Rate of systemic adverse events by dose

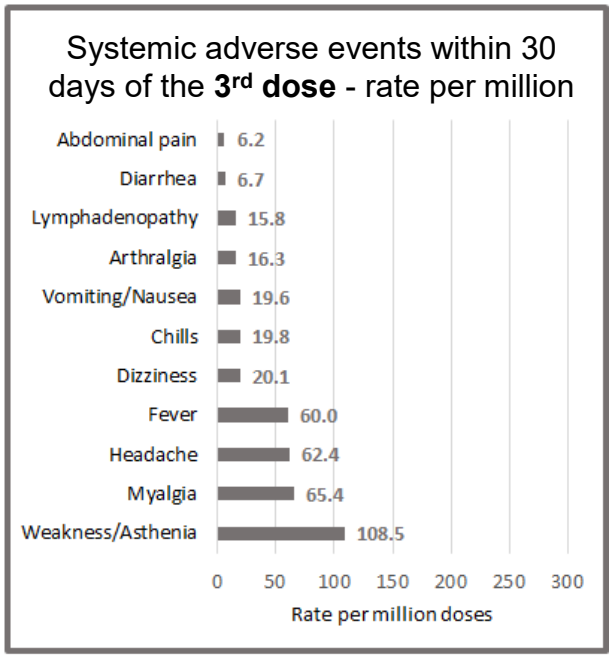
Limitation: Reporting based on passive surveillance, and therefore subject to underreporting



1st dose – 6,178,847 vaccinees



2nd dose – 5,679,655 vaccinees



3rd dose – 3,732,923 vaccinees

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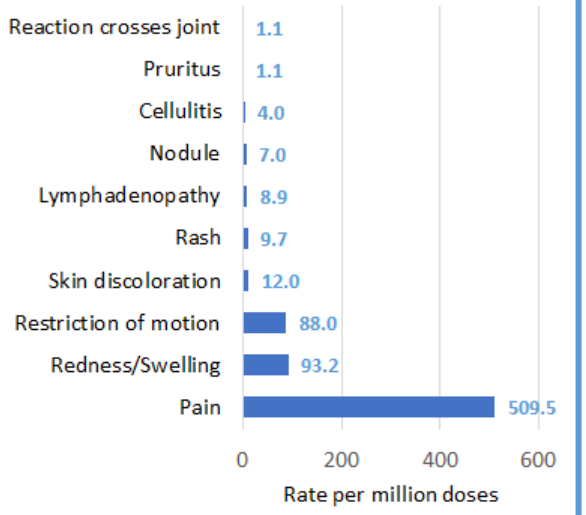
Data is based on adverse events reported to the MoH | Individuals may report more than 1 adverse event | There is an estimated under reporting

Rate of local adverse events by dose

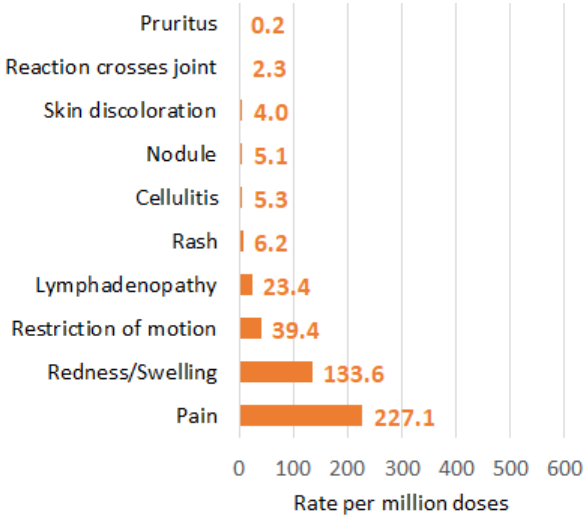
Limitation: Reporting based on passive surveillance, and therefore subject to underreporting

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



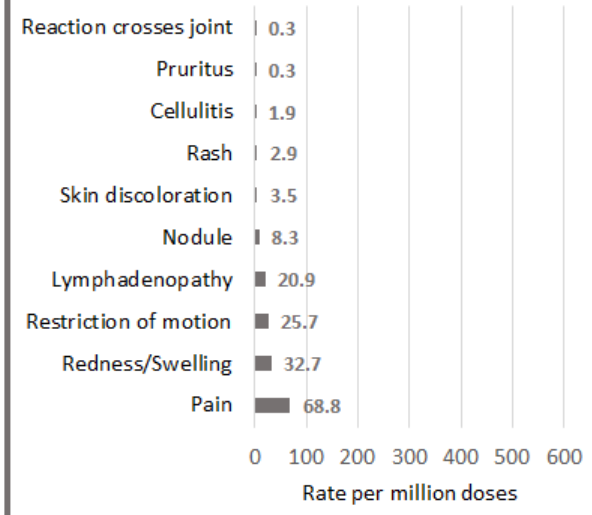
1st dose – 6,178,847 vaccinees

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

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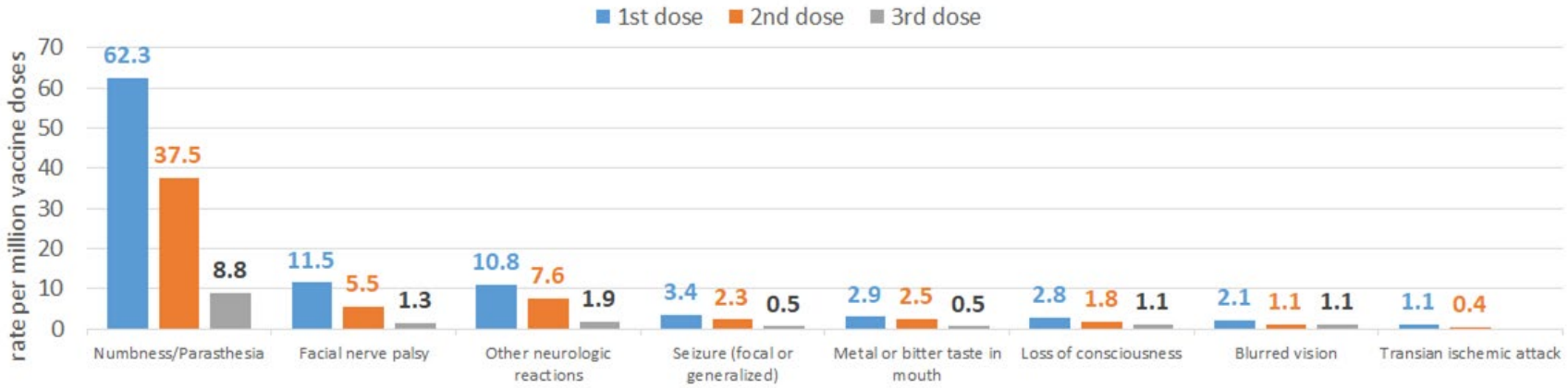
Rate of neurologic adverse events by dose within 30 days of vaccination

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



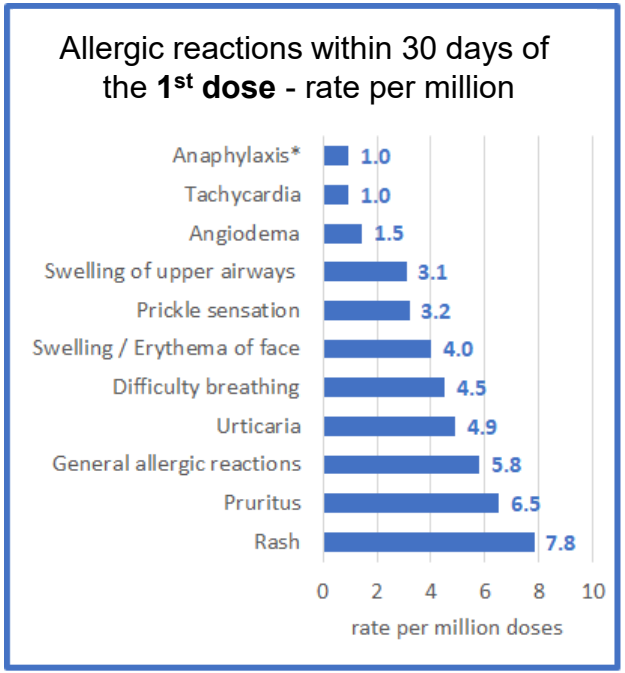
1st dose – 6,178,847 vaccinees

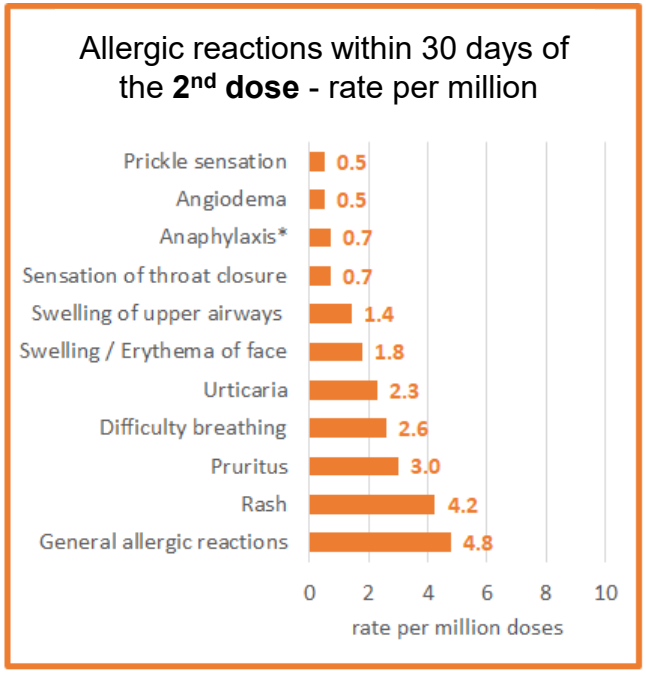
2nd dose – 5,679,655 vaccinees

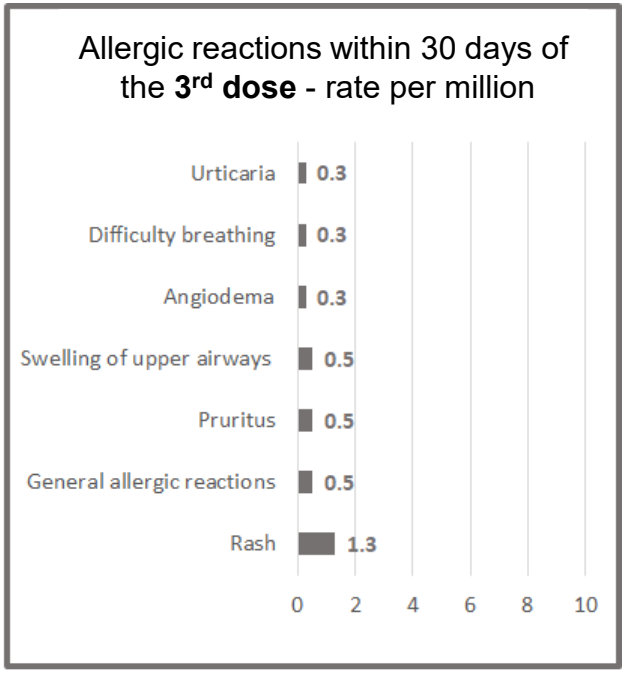
3rd dose – 3,732,923 vaccinees

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
(3.7 million booster doses administered)

Non serious reports	Serious reports
2,394	44

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 reported following 3rd dose

Ages 16-59, out of 2.5 million 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:
  - For 17 myocarditis and perimyocarditis cases causality is probable, cases will be reviewed by special committee
  - For two cases causality to the vaccine was found.
  - For one case causality is possible.
  - For two cases no causality to the vaccine was found.
  - 8 cases are still under investigation.

Ages 60+, out of 1.2 million vaccinees

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

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

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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; For ages 30+, 80% with 30 days; For ages 16-29, 48% with 30 days)	
		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**

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* Two more cases are currently under diagnosis review; For 2,548 individuals without gender information there were zero cases reported.

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

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 ages 16 years and above.
- Booster dose shows improved protection against severe disease in ages 40 years 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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