How effective are single doses of vaccines with the currently available Covid-19 vaccine options?

TOM BECKER

NORTHWEST PORTLAND AREA INDIAN HEALTH BOARD

Game plan

- Review some recent articles on responses to one dose of vaccine (Pfizer and Moderna), in Israel….and, among HCW in Maryland with and without history of Covid-19 (three short articles)
- Review the ‘family case report’ from last sessions, as a potential launching point for further discussion about patient compliance with both doses

Objectives

- Cite evidence related to effectiveness of one dose of currently available vaccines in different situations, and implications for patients and populations

Take home messages

- We do not have adequate data on antibody levels, population-based effectiveness, or public health consequences of single-dose strategies among previously-infected persons…based on well-done studies (with currently approved vaccines) in real world settings
- Some analyses suggest that a single dose of the currently approved vaccines in the US, will be effective at the individual and population or community levels
- Previously infected Covid-19 patients (health care workers) who get immunized with a single dose appear to develop a strong antibody response in small study/ies

Background

- Vaccine shortages nationwide and worldwide have stimulated discussions about ensuring everyone who wants to be vaccinated can get one dose, at least
- The two currently available vaccines in the US have been tested in trials that require both doses at prescribed intervals
- Some observational data now available (short term view) on protection from single dose
- Substantial complaints about side effects from first dose, though most of us would likely not consider them very serious (several days of fatigue, malaise, fever, sore arm, headache, etc)

Chodick et al, Israel study on Covid-19 occurrence post single dose of Pfizer vaccine

- 503,875 vaccines provided
- 351,000 people followed to 13-21 days post inoculation
- Electronic follow up for all vaccinees for Covid-19 diagnoses, including any PCR positive persons
- Investigators looked at occurrence of disease in two time periods, 1-12 days and 13-21 days, by age, co-morbidities, sex, special interest groups

Results, Chodick et al, Israel study

- Cumulative incidence of infection/disease decreased by about half from first 12 days, to days 13-21
- Investigators note 50% effectiveness in Israel of single dose, consistent with Phase 3 drug trials for Pfizer vaccine
- Investigators suggest that second dose is still critical for personal and public health reasons and Israel is in compliance with approved dosing strategies

Implications of all the available evidence The study results indicate that in real life the first dose of the new BNT162b2 mRNA COVID-19 vaccine confers around 50% protection against overall SARS-CoV-2 infections (symptomatic or asymptomatic). Together our findings and the 95% efficacy shown in the phase III trial, suggest that the BNT162b2 vaccine should be administered in two doses to achieve maximum protection and impact in terms of disease burden reduction and possibly reducing SARS-CoV-2 transmission. COVID-19 vaccines should be urgently deployed globally.

Limitations of Chodick study

- Not all persons followed out to day 21
- Disease history changed over the period of vaccination, with rapid increase in cases nationwide and worldwide during the time of vaccine rollout
- They concentrated their observations only on relatively long time periods
- An unknown proportion of asymptomatic cases would have been missed due to experimental design (no antibody testing or antigen testing for all recipients…only about 10% had PCR tests post vaccine)

Hunter, Brainard, re-analysis of Israel data using math models

- Authors able to secure the Israel data from authors who concluded that the UK plan for delaying second vaccine is not tenable
- Monte Carlo methods for estimation of cumulative incidence by day, from days 0 to 24

Hunter, Brainard study results and conclusions

- Highest number of new cases post vaccination on Day 8
- Lowest number of new cases on Day 21, mirroring results of Phase 3 trials
- Vaccine effectiveness estimated to be 91% on Day 21, leveling out after that (improvement over Phase 3 trials)
- Second dose of Pfizer vaccine can be delayed based on re-analysis of Israel data

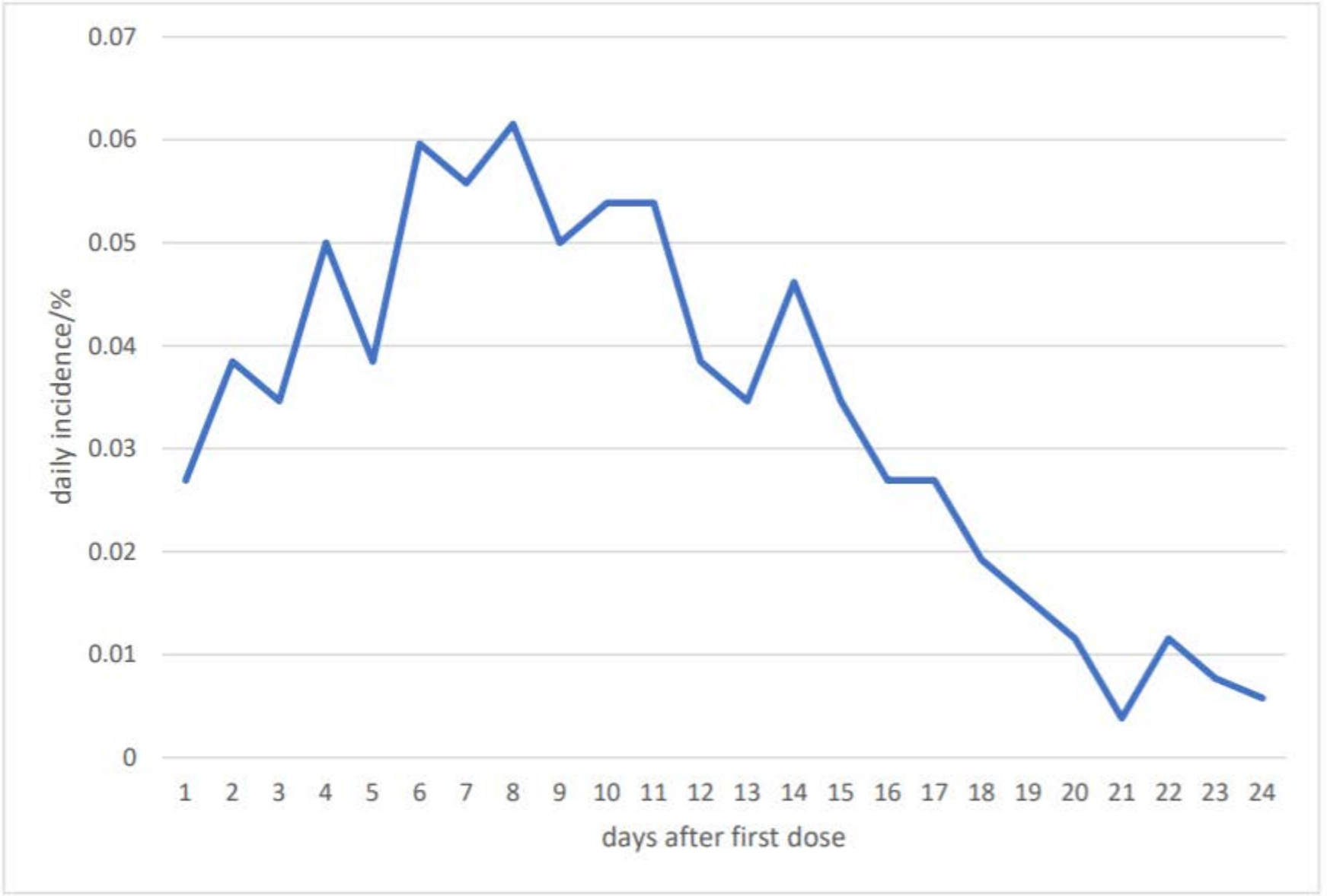


Figure 2. Daily incidence of new infections by days from first dose

Figure 3. Estimated vaccine effectiveness on each day from day 13 to 24 after a single dose with upper and lower 90% credible intervals.

Back to the case presentation—asymptomatic household transmission

- Family of four living in Southern California
- 23 year old son, h/o liking to party, contacted by a friend who was symptomatic and tested SARS-CoV-2 positive on PCR
- 23 year old family index case, who was completely asymptomatic, tested positive by PCR
- 55 year old mom, no significant med hx, soon tested positive after a day of cough, fever, malaise
- 72 year old high-risk dad and 15 year old daughter tested multiple times and remained negative

Transmission

23 yr old male, partied with PCR+ friend

Goes home to family

+, asymptomatic

Mom
55 yrs
+

Sister
15 yrs
-

Dad
72 yrs
-

Family follow-up two weeks later….

- Dad remained healthy, vaccinated, no side effects from vaccine
- Mom also vaccinated at same time (despite recency of Covid), with symptoms of fatigue, fever (temp 102), malaise, swollen nodes and simply does not want to go thru this again

Sadaat et al, Single dose vaccination in HCWs, Methods

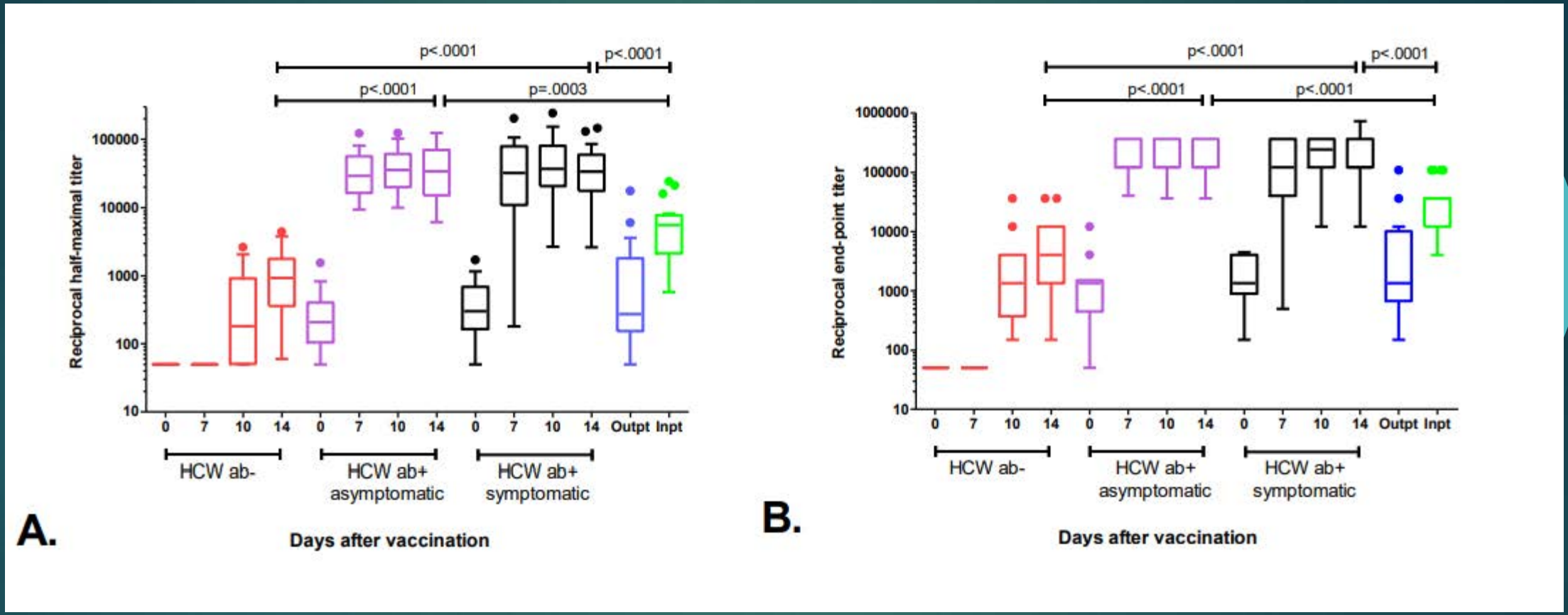
- U of Maryland convenience sample (small)
- Enrolled HCWs with no hx of Covid, asymptomatic Covid, and symptomatic Covid—all given vaccine (either Pfizer or Moderna)
- Measured IgG antibody titers at different time points among these three groups post vaccination, and live virus neutralization at two time points
- Data for inpatients and outpatients (ab titers) who were NOT vaccinated post Covid were also included, from blood draws a month to two months post infection
- Simple comparisons made among groups, presented graphically

Results

- HCW with prior Covid-19 showed secondary antibody responses to vaccine with IgG spike binding titers increasing by 7 days and peaking at 10 and 14 days post inoculation
- At all time points tested, HCW with prior Covid-19 showed statistically significantly higher antibody titers compared to HCW with no history of SARS-CoV-2 infection
- Live virus neutralization also was significantly better in HCW with Covid-19, compared to HCW withoutCovid-19

to them to antibody responses of HCW who were IgG negative to SARS-CoV-2 spike protein. HCW with prior COVID-19 showed clear secondary antibody responses to vaccination with IgG spike binding titers rapidly increasing by 7 days and peaking by days 10 and 14 post-vaccination. At all time points tested, HCW with prior COVID-19 infection showed statistically significant higher antibody titers of binding and functional antibody compared to HCW without prior COVID-19 infection ($p<.0001$for each of the time points tested). In times of

		Group 1 (n=17)	Group 2 (n=16)	Group 3 (n=26)	Inpatient (n=19)	Outpatient (n=19)
Age (years)	Median	38	40	38	41	32
	Range	29-55	25-72	23-59	28-48	18 - 81
Gender [n (%)]	Male	5 (29)	4 (25)	3 (12)	16 (84)	8 (42)
	Female	12 (71)	12 (75)	23 (88)	3 (16)	11 (58)
Race/Ethnicity [n (%)]	African American	2 (12)	5 (31)	5 (19)	4 (22)	2 (11)
	Caucasian	12 (71)	9 (56)	18 (69)	1 (6)	13 (68)
	Asian	3 (18)	2 (13)	3 (14)	0 (0)	2 (11)
	Hispanic or Latino	0 (0)	0 (0)	0 (0)	13 (72)	2 (11)
Vaccine [n (%)]	Pfizer-BioNTech	10 (59)	6 (37)	13 (50)	N/A	N/A
	Moderna	7 (41)	10 (63)	13 (50)	N/A	N/A


p<.0001
p<.0001
p<.0001
p=.0003
Reciprocal half-maximal titer
100000
10000
1000
100
10
0 7 10 14 0 7 10 14 0 7 10 14 Outpt Inpt
HCW ab-
HCW ab+ asymptomatic
HCW ab+ symptomatic
A.
Days after vaccination
p<.0001
p<.0001
p<.0001
p<.0001
Reciprocal end-point titer
1000000
100000
10000
1000
100
10
0 7 10 14 0 7 10 14 0 7 10 14 Outpt Inpt
HCW ab-
HCW ab+ asymptomatic
HCW ab+ symptomatic
B.
Days after vaccination

Limitations of HCW study

- Small numbers of participants
- Not randomly selected
- Not all received same vaccine
- No follow-up on changes in antibody titers that might have occurred after second dose among participants in all study groups

Summary points

- We need more directed studies, and further analyses, to be able to provide more definitive recommendations about delay of second dose/s of currently available vaccine
- Conducting a study of one dose vs. two doses would require careful IRB scrutiny, given design of original vaccine efficacy studies
- For persons with history of Covid-19, delay (or even not accepting) second dose may be acceptable, tho definitive study still missing

Take home test

- How would you design and implement a study (trial or other design) to determine if single dose vaccine (of the two available in the US now), provides adequate protection in a real world (not Phase 3) study?

(Strategies you may consider: randomize by state or by country…it is ok to think out of the box on this 'test').

References

- Sadaat et al. Single dose vaccination in HCW's previously infected with SARS-CoV-2. https://www.medrxiv.org/content/10.1101/2021.01.30.21250843v1
- "Estimating the effectiveness of the Pfizer COVID-19 BNT162b2 vaccine after a single dose. A reanalysis of a study of 'real-world' vaccination outcomes from Israel," Hunter and Brainard. Preprint available at *medRxiv*. https://www.medrxiv.org/content/10.1101/2021.02.01.21250957v1

- Thanks to Grazia Ori, MPH for graphics