COMMISSIONE MEDICO SCIENTIFICA INDIPENDENTE

24 July 2023
Dr Katherine O'Brien
Director Immunization, Vaccines and Biologicals
World Health Organization
Geneva

Request for an open discussion about the questionable perseverance in advocating repeated anti-COVID-19 vaccinations

Dear Dr Katherine O'Brien,

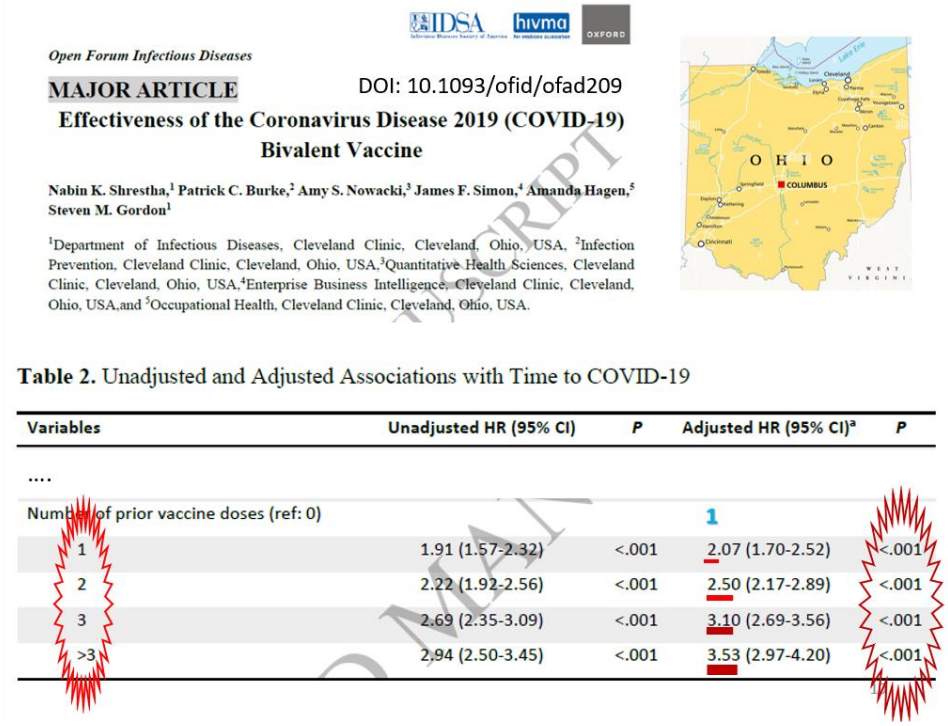
thank you for your answer to our last letter expressing our concerns about the limited effectiveness of COVID-19 vaccination and the safety profile of COVID-19 vaccines. I hope this correspondence will usher in a new phase of constructive scientific debate.

You stated "*the World Health Organization (WHO) reviews on a continuous basis the effectiveness and safety of the COVID-19 vaccines that have received Emergency use status by WHO"*, and provid "*a connection to the WHO's living systematic review and analysis of safety and effectiveness: https://view-hub.org/vaccine/covid/effectiveness-studies (with the analysis of 482 effectiveness and 375 safety studies).*"
You further highlight that "*This information is reviewed by WHO's Strategic Advisory Group of Experts on Immunization (SAGE) and its COVID-19 Working Group to develop and update vaccination policies. WHO applies the highest standards of evidence-based medicine in the development of its policies…*"

Indeed, our intent with these letters was not to open a discussion on the management of the pandemic from its origins, but to question the usefulness of current institutional vaccination recommendations. We are aware of the fact that vaccine effectiveness (VE) evolves quickly over time, with a rapid waning, also admitted by the WHO ("We acknowledge that the current vaccines show modest and short-term effectiveness against infection from the currently circulating SARS COV-2 strains"). Therefore, we are less interested in disputes on the interpretation of studies whose implications would no longer be current. Studies to be carefully reviewed should:
• be **recent**, and concern the latest variants (in principle, only studies on XBB variant would make sense, given that the bivalent booster maintains a modest residual protection against the BA.4/5 variants, but it no longer provides any against XBB, by now dominant (https://doi.org/10.1093/ofid/ofad209)
• still have a **long follow-up**, given that protection from infection and - to a lesser extent - from COVID-19 - declines rapidly over time, and follow-ups of just a few months would not give useful answers
• also present **another fundamental** (and often violated) **requirement in the declaration of vaccination status**, which we will discuss later.
So let's look at the last ten studies proposed by your meta-analysis:

1) Nielsen KF. *Nielsen KF, Moustsen-Helms IR, Schelde AB,et al. Vaccine effectiveness against SARS-CoV-2 reinfection during periods of Alpha, Delta, or Omicron dominance: A Danish nationwide study. PLoS Med. 2022 Nov 22;19(11):e1004037. doi: 10.1371/journal.pmed.1004037.*

This nationwide cohort study showed that among previously infected individuals who have completed a primary vaccination series, vaccines are still effective against SARS-CoV-2 reinfection during Omicron, but VE wanes to 14% at about six months. Then there is a slight increase in protection, around 30% (but no longer statistically significant) at the end of the year. The frequent phenomenon of a slight increase in protection after a nadir could be due to further reinfections, which temporarily reinforce the protection in a part of the subjects. The phenomenon is compatible with the results of the study from Shrestha et al. that we cited in our previous Letter (*Shrestha NK, Burke PC, Nowacki AS, et al. Effectiveness of the Coronavirus Disease 2019 (COVID-19) Bivalent Vaccine, Open Forum Infectious Diseases, 2023;ofad209, https://doi.org/10.1093/ofid/ofad209*), reproduced here again (**Figure 1**), that is: the number of vaccine doses received is directly proportional to the risk of contracting new infections (at least in the medium term).



Open Forum Infectious Diseases

MAJOR ARTICLE DOI: 10.1093/ofid/ofad209

Effectiveness of the Coronavirus Disease 2019 (COVID-19) Bivalent Vaccine

Nabin K. Shrestha,[1] Patrick C. Burke,[2] Amy S. Nowacki,[3] James F. Simon,[4] Amanda Hagen,[5] Steven M. Gordon[1]

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Table 2. Unadjusted and Adjusted Associations with Time to COVID-19

Variables	Unadjusted HR (95% CI)	*P*	Adjusted HR (95% CI)[a]	*P*
....				
Number of prior vaccine doses (ref: 0)			1	
1	1.91 (1.57-2.32)	<.001	2.07 (1.70-2.52)	<.001
2	2.22 (1.92-2.56)	<.001	2.50 (2.17-2.89)	<.001
3	2.69 (2.35-3.09)	<.001	3.10 (2.69-3.56)	<.001
>3	2.94 (2.50-3.45)	<.001	3.53 (2.97-4.20)	<.001

Figure 1. Data from Shrestha NK, et al. Effectiveness of the Coronavirus Disease 2019 (COVID-19) Bivalent Vaccine, Open Forum Infectious Diseases, 2023;ofad209 (*https://doi.org/10.1093/ofid/ofad209*).

Other studies describe a similar phenomenon (eg. *Eythorsson E, Runolfsdottir HL, Ingvarsson RF, et al. Rate of SARS-CoV-2 Reinfection During an Omicron Wave in Iceland. JAMA Netw Open. 2022 Aug 1;5(8):e2225320. doi: 10.1001/jamanetworkopen.2022.25320*). This was also evident in the UKHSA weekly data till week 14 of 2022, when they declared that they would no longer communicate such data (*https://www.gov.uk/government/publications/covid-19-vaccine-weekly-surveillance-reports*).

The same happened with the Italian data (**Figure 2-3**). Unfortunately, the Italian Health Institute of Health (Istituto Superiore di Sanità) (*https://www.epicentro.iss.it/coronavirus/aggiornamenti*), who also declared that those published up to 18 January 2022, on the basis of which we had produced the graphs on the Italian trend in incident infections by vaccination status (see below an example), would no longer be made public.

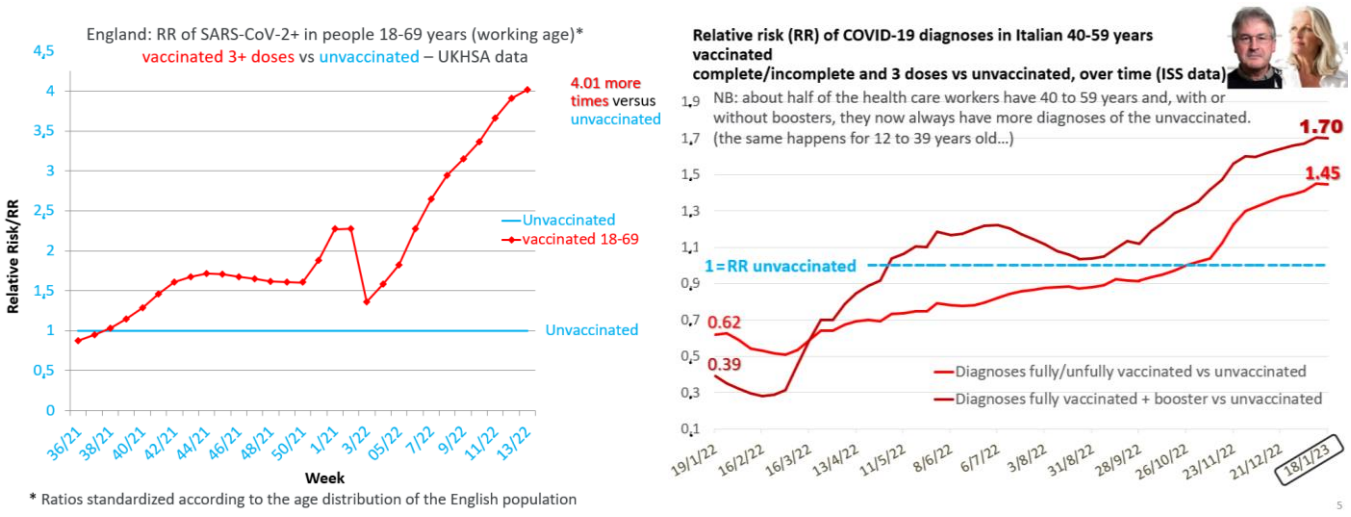


Figure 2-3. Italian data from Istituto Superiore di Sanità (https://www.epicentro.iss.it/coronavirus/aggiornamenti).

Returning to the study from Nielsen et al., no advantage in protection against severe COVID-19 of the vaccinated individuals versus the unvaccinated was documented: "*Due to too few events, it was not possible to estimate VE for hospitalization and death* (*Nielsen, PLOS Med, 2022*))". In any case, it would be not appropriate to compare an infection in vaccinated subjects to one infection in unvaccinated subjects. Indeed, the former have received an additional (temporary) help from vaccination; a correct comparison about incident infections should be made normalizing the

follow-up between previously infected and vaccinated subjects vs subjects previously infected and with a "natural booster" (received from a second infection, usually pauci- or asymptomatic).

2) Wang *Xiaofeng Wang and others, Impact of Vaccination, Prior Infection, and Therapy on Omicron Infection and Mortality, The Journal of Infectious Diseases, Volume 227, Issue 8, 15 April 2023, Pages 970–976, https://doi.org/10.1093/infdis/jiac460*

The study shows that "*Vaccination and prior infection were less effective against Omicron… infection but provided strong protection against ICU admission and death. Boosting greatly increased vaccine effectiveness against Omicron infection and severe outcomes,* ***although effectiveness rapidly over time****.".*
However, the comparison with unvaccinated subjects was misleading for two reasons: first, for the same reason we already explained in the previous point; second, because "*the median times between prior and current infections being… 369 days in the Omicron-predominant period* [about double than the median time after a booster]*, and the immunity acquired via SARS-CoV-2 infection wanes over time*.". Indeed, when the timing of primary infection or vaccination were normalized (as in: *Chemaitelly H, Ayoub HH, AlMukdad S, et al. Protection from previous natural infection compared with mRNA vaccination against SARS-CoV-2 infection and severe COVID-19 in Qatar: a retrospective cohort study. Lancet Microbe. 2022 Dec;3(12):e944-e955. doi: 10.1016/S2666-5247(22)00287-7*), the overall adjusted hazard ratio (HR) for SARS-CoV-2 infection was more favorable after previous natural infection than after BNT162b2 or mRNA-1273 vaccination; and the overall adjusted HR for severe, critical, or fatal COVID-19 cases was much more favorable.

3) Fabiani *Fabiani M, Mateo-Urdiales A, Sacco C, et al. Relative effectiveness of a 2nd booster dose of COVID-19 mRNA vaccine up to four months post administration in individuals aged 80 years or more in Italy: A retrospective matched cohort study. Vaccine. 2023 Jan 4;41(1):76-84. doi: 10.1016/j.vaccine.2022.11.013.*

This large retrospective cohort study, based on the analysis of 831,555 matched pairs of the population aged ≥80 years in Italy, "*found that a 2nd booster dose of mRNA vaccine, 14–118 days post administration, was moderately* (we would argue: very modestly) *effective in preventing SARS-CoV-2 infection compared to a 1st booster dose administered at least 120 days earlier [14.3 %, 95 % CI: 2.2–20.2]. RVE decreased from 28.5 % (24.7–32.1) in the time-interval 14–28 days to* ***7.6 %*** *(****-14.1*** *to 18.3) in the time-interval 56–118 days. However, RVE against severe COVID-19 was higher (34.0 %, 23.4–42.7), decreasing from 43.2 % (30.6–54.9) to 27.2 % (8.3–42.9) over the same time span*."
This study allows to obtain important information, because "*The few studies focusing on the general elderly population were all conducted in Israel, during predominance of the Omicron BA.1 and BA.2 subvariants, and were based on a relatively short follow-up time, ranging from 2 to 10 weeks after the administration of the second booster vaccine dose [7–10*]."
The Authors conclude with some caution "*The cost-benefit of a 3rd booster dose of adapted bivalent COVID-19 vaccine for the elderly people who received the 2nd booster dose at least four months earlier should be carefully evaluated*.". However, they do not avoid a misconduct in data illustration, as you can see in the reported **Figure 4**:

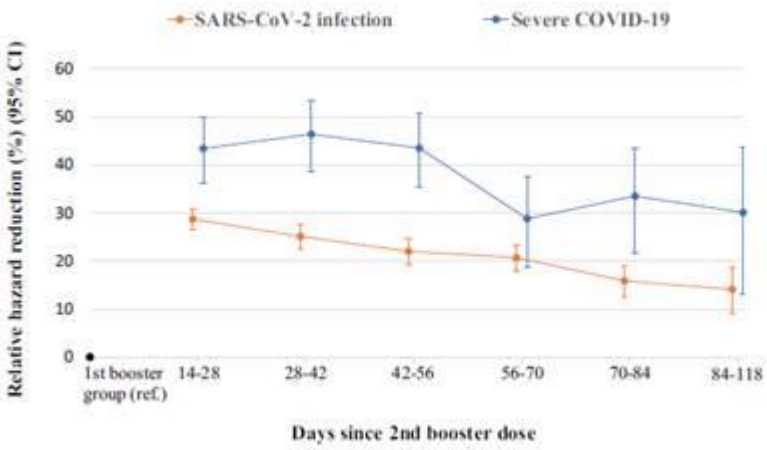


Fig. 4. Relative hazard reduction of SARS-CoV-2 infection and severe COVID-19 at different time intervals after the administration of a second booster vaccine dose (sensitivity analysis).

Indeed, they present six time frames, the first five of 14 days each, the latter, albeit with the same length in the graph, is of 34 days, clearly much longer, without any explanation. This expedient may serve to mask the final arrival point of the curve, which could have reached zero, or even below the level of the comparison group. Indeed, the same Authors already used the same expedient, in the case of Italian 5-11 year old children [*Sacco C, Del Manso M, Mateo-Urdiales A, et al. Effectiveness of BNT162b2 vaccine against SARS-CoV-2 infection and severe COVID-19 in children aged 5–11 years in Italy: a retrospective analysis of January–April, 2022". Lancet 2022. doi: 10.1016/S0140-6736(22)01185-0*], in which the graph (reproduced below. **Figure 5** in our numbering) showed a modest residual protection of 21.2% in the vaccinated children, while on the same date

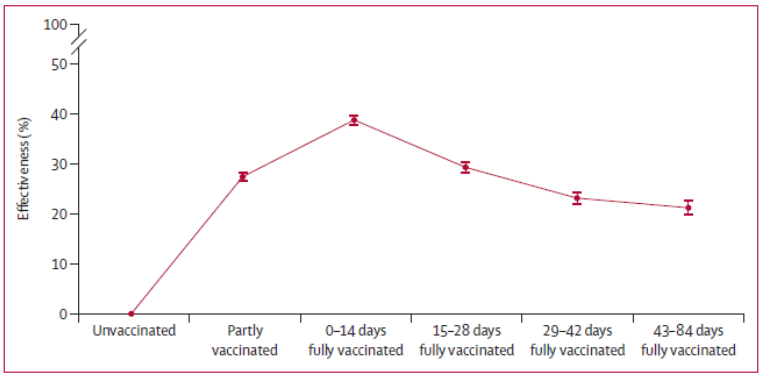


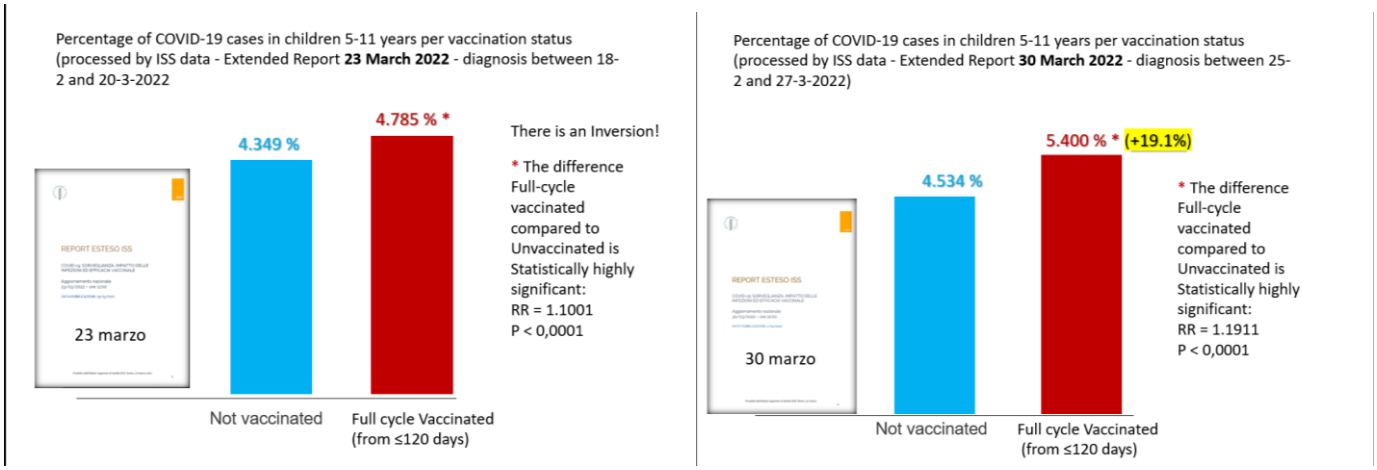
Figure 3: **Effectiveness of BNT162b2 vaccine against laboratory-confirmed SARS-CoV-2 infection**

Figure 5 in our numbering.

the official Bulletins of the Istituto Superiore di Sanità (ISS), the Institute to which the authors belong, showed a 21.6% ***below*** the level of unvaccinated children).

Indeed, the authors concluded "*vaccination against COVID-19 in 5–11 year children was "moderately effective" in preventing infection, … decreasing to 21.2% at 43-84 days*". However, these claims are misleading.

In fact, at about 84 days (April, 6) the same ISS Bulletins allow us to calculate that the VE against infection was actually around 21.6, but ***below***, not ***above***, the level for the unvaccinated individuals. You can easily check what we say: already in the March, 23 Bulletin *https://www.epicentro.iss.it/coronavirus/bollettino/Bollettino-sorveglianza-integrata-COVID-19_23-marzo-2022.pdf* the previously positive VE had become significantly negative, and the situation worsened according to data reported in the next two Bulletins, https://www.epicentro.iss.it/coronavirus/bollettino/Bollettino-sorveglianza-integrata-COVID-19_6-aprile-2022.pdf // https://www.epicentro.iss.it/coronavirus/bollettino/Bollettino-sorveglianza-integrata-COVID-19_30-marzo-2022.pdf (see Table 4A), remaining so until July 6, 2022. The comparison between the information reported in the two mentioned weeks is illustrated below (**Figure 6**).



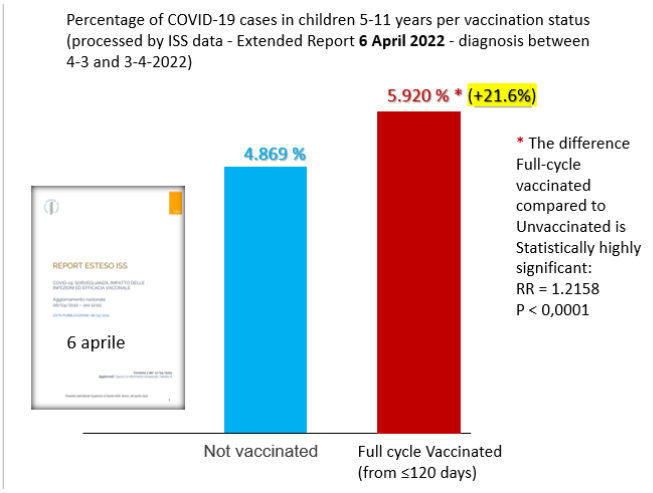


Figure 6. Graphs calculated by the data of the specified Bulletins of the Istituto Superiore di Sanità.

After a few months, the VE versus unvaccinated returned negative in October, and remained negative since then until January 18, 2023. At that point, the Italian ISS, which we solicited for an open discussion, instead announced that it would no longer publish the Tables that provided access to the data allowing to calculate those trends.

4) Chemaitelly *Hiam Chemaitelly, Houssein H. Ayoub, Patrick Tang, et al. Long-term COVID-19 booster effectiveness by infection history and clinical vulnerability and immune imprinting medRxiv 2022.11.14.22282103;*
doi: https://doi.org/10.1101/2022.11.14.22282103
This fundamental study, already cited in our previous letter with the two following examples (**Figure 7**), shows that after six months the VE of Pfizer and Moderna mRNA vaccines turns negative.

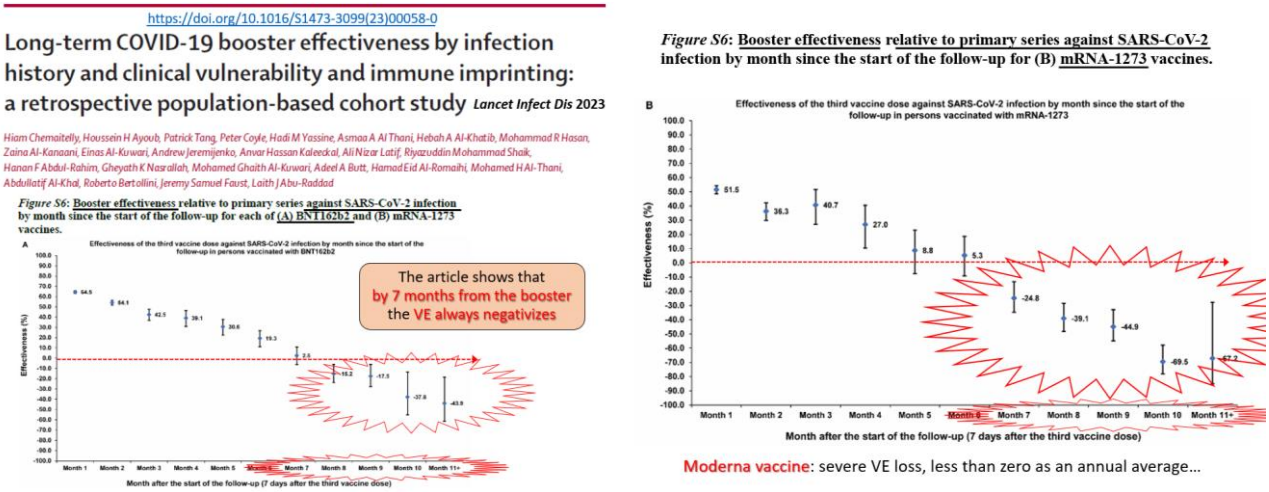
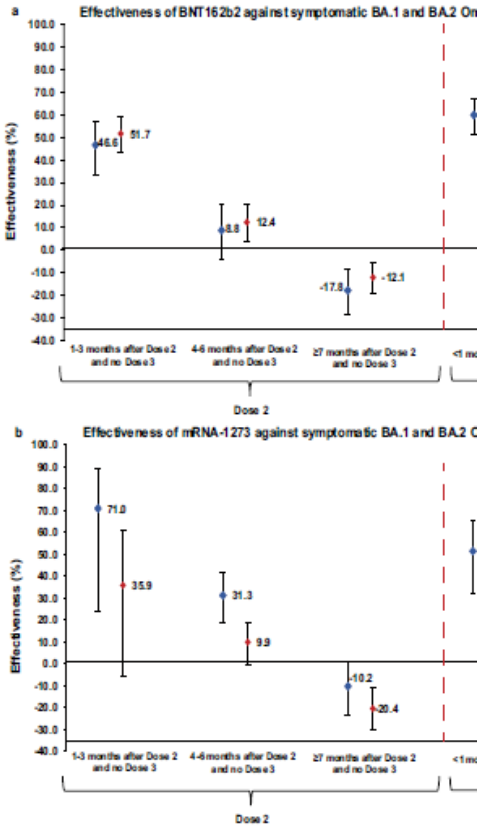


Figure 7 (in our numbering). Booster effectiveness relative to primary series against SARS-CoV-2 infection by month of follow-up for Pfizer and Moderna vaccines in Qatar (*Chemaitelly, Lancet Infect Dis 2003*)

Note that the same Authors have already given evidence (*Chemaitelly, H., Ayoub, H.H., AlMukdad, S. et al. Duration of mRNA vaccine protection against SARS-CoV-2 Omicron BA.1 and BA.2 subvariants in Qatar. Nat Commun **13**, 3082 (2022). https://doi.org/10.1038/s41467-022-30895-3*) that VE against the even less evasive BA.1 and BA.2 Omicron variants negativized by 7 months **after dose 2** (see below, **Figure 8,** from the cited reference). This means that the **further negativization** ≥7 months **after dose 3 makes an already bad VE even worse**.



Effectiveness of mRNA vaccines against symptomatic SARS-CoV-2 BA.1 and BA.2 Omicron **Figure 8** in our numbering (*Chemaitelly, Nat Commun, 2022*).

5) Canetti *Canetti M, Barda N, Gilboa M, et al. Six-Month Follow-up after a Fourth BNT162b2 Vaccine Dose. N Engl J Med. 2022 Dec 1;387(22):2092-2094. doi: 10.1056/NEJMc2211283.* (Note that we do not comment the previous reference – Jorgensen et al – not having content relevant to our discussion)

In this prospective cohort study of Israeli health care workers, time-specific VE of Pfizer vaccine (comparing infection rates among participants not yet infected since vaccination) waned with time, decreasing from 52% (95% CI, 45 to 58) during the first 5 weeks after vaccination to **–2%** (**–27%** to 17%) at 15 to 26 weeks (about 3.5-6.0 months). Again, the time of the last time frame is much longer than that of the previous ones, and it is likely that at about 6 months the VE was worse than -2%.

6) Grewal *Ramandip Grewal, Lena Nguyen, Sarah A Buchan, et al. Effectiveness of mRNA COVID-19 vaccine booster doses against Omicron severe outcomes medRxiv 2022.10.31.22281766; doi: https://doi.org/10.1101/2022.10.31.22281766*

This test-negative study concerns Omicron-associated hospitalization or death among community-dwelling adults aged ≥50 years, and suggests that 1 or 2 booster doses of monovalent mRNA COVID-19 vaccines initially restored strong protection against severe outcomes, but VE subsequently declined over time, particularly so during a period of BA.4/BA.5 predominance.

7) Tartof *Tartof SY, Slezak JM, Puzniak L, et al. BNT162b2 vaccine effectiveness against SARS-CoV-2 omicron BA.4 and BA.5. Lancet Infect Dis. 2022 Dec;22(12):1663-1665. doi: 10.1016/S1473-3099(22)00692-2.*

This test-negative study determined the VE of Pfizer–BioNTech against BA.4/5 among subjects aged 18 years or older, members of the health insurance provider Kaiser Permanente (Southern California), diagnosed with an acute respiratory infection and tested for SARS-CoV-2.
Between May 9th and Aug 26th, 2022, 24% of patients who had a healthcare encounter were unvaccinated, 25% had received two doses and 52% three doses, 3029 of which, aged 50 years and older, had received a fourth dose. The following Table (**Figure 9**) shows the adjusted effectiveness (the highlights are ours):

	Hospital	Emergency department	Urgent care	Outpatient
Two doses of BNT162b2				
<6 months since second dose	NC	30 (−86 to 74)	50 (10 to 72)	30 (4 to 49)
≥6 months since second dose	−4 (−118 to 50)	44 (20 to 61)	7 (−11 to 22)	19 (9 to 29)
Overall	−4 (−116 to 50)	44 (19 to 61)	11 (−7 to 25)	21 (11 to 30)
Three doses of BNT162b2				
<3 months since third dose	NC	71 (18 to 90)	59 (35 to 74)	55 (41 to 65)
3–5 months since third dose	72 (13 to 91)	36 (−3 to 60)	28 (10 to 42)	23 (11 to 33)
<6 months since third dose	73 (25 to 91)	43 (10 to 63)	34 (18 to 46)	29 (19 to 37)
≥6 months since third dose	38 (−31 to 71)	37 (8 to 57)	11 (−7 to 26)	6 (−7 to 17)
Overall	50 (−1 to 76)	39 (14 to 57)	20 (5 to 33)	17 (7 to 26)
Four doses of BNT162b2†				
<3 months since fourth dose	66 (20 to 85)	65 (35 to 82)	35 (10 to 54)	28 (10 to 43)
≥3 months since fourth dose	33 (−112 to 79)	78 (50 to 91)	20 (−23 to 48)	11 (−18 to 34)
Overall	60 (11 to 82)	69 (44 to 83)	32 (7 to 50)	25 (7 to 39)

Data are vaccine effectiveness, with 95% CIs in parentheses. NC=not calculated (ie, fewer than five total cases). *Adjusted for week of COVID-19 health-care encounter, age, sex, race or ethnicity, previous SARS-CoV-2 infection, BMI, Charlson score, and history of previous influenza and pneumococcal vaccination, and nirmatrelvir plus ritonavir receipt. †Analysis done among individuals aged ≥50 years (for whom a fourth dose was recommended at the time of the study).

Table: **Adjusted effectiveness* of BNT162b2 vaccine against omicron (B.1.1.529) subvariants BA.4 and BA.5, by highest level of care and number and timing of receipt of BNT162b2 doses**

Figure 9 (*Tartof, Lancet Infect Dis, 2022*)

The results suggest that two doses of BNT162b2 offered little protection against all BA.4/5 outcomes measured, including hospital admission.
A booster (third or fourth dose) provided protection against BA.4/5, which probably wanes after 3 months against milder outcomes like outpatient, or in urgent care encounters, and after more than three months also against BA.4/5-related hospitalisation.

8) Surie *Surie D, Bonnell L, Adams K, et al. Effectiveness of Monovalent mRNA Vaccines Against COVID-19–Associated Hospitalization Among Immunocompetent Adults During BA.1/BA.2 and BA.4/BA.5 Predominant Periods of SARS-CoV-2 Omicron Variant in the United States — IVY Network, 18 States, December 26, 2021–August 31, 2022. MMWR Morb Mortal Wkly Rep 2022;71:1327–1334. DOI:* http://dx.doi.org/10.15585/mmwr.mm7142a3 . (Note that we do not comment the previous reference – Embi et al – not having content relevant to our discussion)

In this study among immunocompetent adults, monovalent mRNA vaccines–associated hospitalization during the BA.4/BA.5 predominant period showed a VE waning to 29 (3-48)% at >120 days interval from last vaccine dose and illness onset.

9) Consonni *Dario Consonni, Andrea Lombardi, Davide Mangioni, et al. Immunogenicity and effectiveness of BNT162b2 COVID-19 vaccine in a cohort of healthcare workers in Milan (Lombardy Region, Northern Italy). Epidemiologia&Prevenzione, 2022* https://epiprev.it/6048

This cohort study in Milan (Lombardy Region, Northern Italy) included 4,771 health care workers in a "negative cohort", without history of SARS-CoV-2 infection or elevated serum antibody before the vaccination campaign. VE (see the **Figure 10**) was high in the four months following the second dose and declined afterwards. VE raised after the third dose and then declined to low values during the Omicron period. The VE against infection collapsed to **1%** at about 120 days after the third dose, when the follow-up was interrupted.

VACCINATION STATUS	NUMBER OF INFECTIONS	PERSON-YEARS	RATE (PER 1,000 PY)	VE (%)*	95%CI
NEGATIVE COHORT	1,401	4,432.1	316		
Unvaccinated	98	544.5	180	Reference	
Vaccinated with 1 dose					
0-13 days	16	165.6	97	0	0-37
14+ days	7	195.7	36	64	17-84
Vaccinated with 2 doses					
7-119 days	46	1,228.9	37	70	54-80
120+ days	97	1,585.5	61	16	0-43
Vaccinated with 3 doses					
7-29 days	61	184.3	331	57	35-71
30-44 days	149	108.5	1,373	44	21-60
45-59 days	176	91.9	1,916	48	27-62
60-74 days	158	75.8	2,083	41	17-58
75-89 days	96	63.6	1,509	38	11-57
90-119 days	157	101.5	1,547	24	0-47
120+ days	340	86.3	3,939	1	0-32

Figure 10. VE by month of follow-up and vaccination status in Health care workers without previous infection (*Consonni, E&P 2022*).

10) Laake *Ida Laake and others, Effectiveness of mRNA Booster Vaccination Against Mild, Moderate, and Severe COVID-19 Caused by the Omicron Variant in a Large, Population-Based, Norwegian Cohort, The Journal of Infectious Diseases, Volume 226, Issue 11, 1 December 2022, Pages 1924–1933, https://doi.org/10.1093/infdis/jiac419*

In this large Norwegian cohort (85,801 participants), VE at >120 days from booster vaccination with mRNA vaccine against Omicron infection was 12.2 (-2.6 to 24.8), against mild COVID-19 was **-25.6** (-57.3 to -3), against moderate COVID-19 27.1 (8.6-41.8), while it could not be determined for severe COVID-9, due to shorter follow-up.
The article reports that "*in a recent surveillance report from the United Kingdom, VE estimates for mRNA booster vaccination against Omicron infection compared to unvaccinated individuals…,* ***declined to almost no effect 20 weeks after vaccination*** *[16].*".

In short, the most recent publications you mention, despite a follow-up of a few months, show how the efficacy against the infection is reduced to zero and sometimes it even becomes negative with respect to the unvaccinated. Even the protection against ***severe*** COVID declines rather rapidly, and the only strategy opposed so far is to anticipate the administration of subsequent boosters.
Even "updated" vaccines do not seem to keep up with the continuous generation of new immunoevasive variants, as also a publication of a few days ago substantially confirms (*Fabiani M, Mateo-Urdiales A, Sacco C, et al. Relative effectiveness of a 2nd booster dose of COVID-19 mRNA vaccine up to four months post administration in individuals aged 80 years or more in Italy: A retrospective matched cohort study. Vaccine. 2023 Jan 4;41(1):76-84. doi: 10.1016/j.vaccine.2022.11.013*). After finding that "*the protection induced by the first booster dose has likely waned after 120 days*" and that protection with a second monovalent booster is no longer statistically significant at 60-118 days, the authors seem content to state that with a *new* bivalent booster (original/BA.4-5) the protection at 60-118 days was 34.7% (19.7-46.9), waning by only 5% points in the elderly ≥80 years.
However, these already unexciting results must be further downsized, considering both the pertinent observations of the Editorial by Madhi and Feikin (*Shabir A Madhi, Daniel R Feikin. Are bivalent vaccines better than ancestral-virus monovalent vaccines in protecting against severe omicron COVID-19? Lancet Infect Dis 2023;Published Online July 18, 2023 https://doi.org/10.1016/ S1473-3099(23)00425-5*); and for the misleading way in which data are presented, which affects many studies. Indeed, reiterating the trick of displaying the ***average*** protection between 60 and 118 days, can try to avoid a worse impression if the residual protection were displayed ***close to the end*** of the 120 days... And, above all, for the **fundamental bias** that we explain below.
The articles of Wilson Sy (*https://www.academia.edu/83924771/Mortality_risk_of_COVID_19_injections_evidence_from_New_South_Wales_and_England; https://www.academia.edu/85597731/Data_reporting_flaw_in_plain_sight_distorting_COVID_19_mortality_statistics; https://www.opastpublishers.com/open-access-articles/australian-covid19-pandemic-a-bradford-hill-analysis-of-iatrogenic-excess-mortality.pdf; https://www.researchgate.net/publication/371342838_Simpson's_Paradox_in_the_correlations_between_excess_mortality_and_COVID-19_injections_a_case_study_of_iatrogenic_pandemic_for_elderly_Australians*), and of the professors Norman Fenton and Martin Neil (Mathematician and Bayesian statistician at Queen Mary University of London, respectively) have documented a shocking **statistical illusion** (*Probability and Risk: Is vaccine efficacy a statistical illusion?; Probability and Risk: The impact of misclassifying deaths in evaluating vaccine safety: the same statistical illusion; The illusion of vaccine efficacy revisited (substack.com)*).

In fact, many countries have theorized (e.g. CDC USA *https://www.cdc.gov/coronavirus/2019-ncov/php/hdbreakthrough.html#report , accesso 15-8-2022*) or applied (Australia, England *https://www.academia.edu/83924771/Mortality_risk_of_COVID_19_injections_evidence_from_New_South_Wales_and_England*) or admitted in response to an FOI (Sweden …) a systematic shift of the results of the vaccination injections in the 14 (or 21) days following each injection, transferred to the previous vaccination status. That is, what happens in the 14 days after the 1st injection was imputed to the group of unvaccinated individuals, and what happens in the first 14 days after the 2nd, 3rd, 4th injection, respectively, was (back)attributed to the subjects who were single, double or triple dosed…). This shift causes a **statistical illusion** that **can show a fictitious VE also with the administration of an inert vaccine**, or can even show a positive VE (at least in the first few months) with a vaccine burdened by a *negative VE*, as shown in the examples below (**Figure 11**).

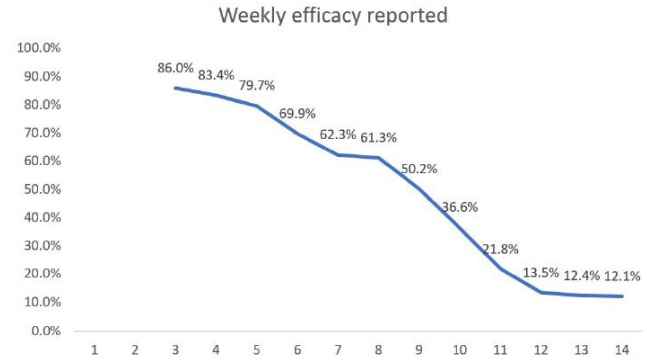


Fig. 11.A Example simulated with the 14 day rule or

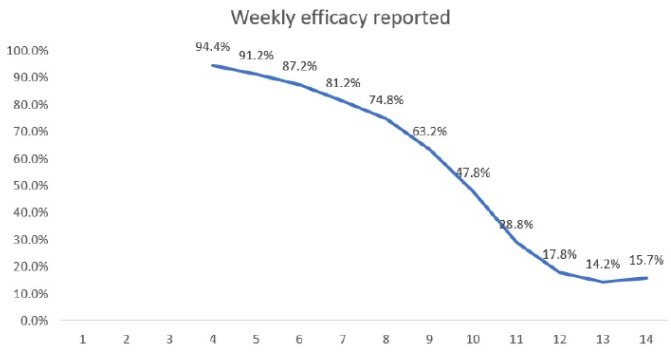


Fig. 11.B with the 21 day rule…

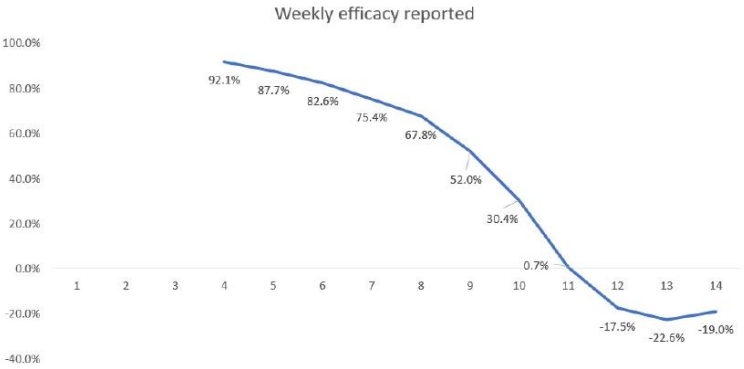
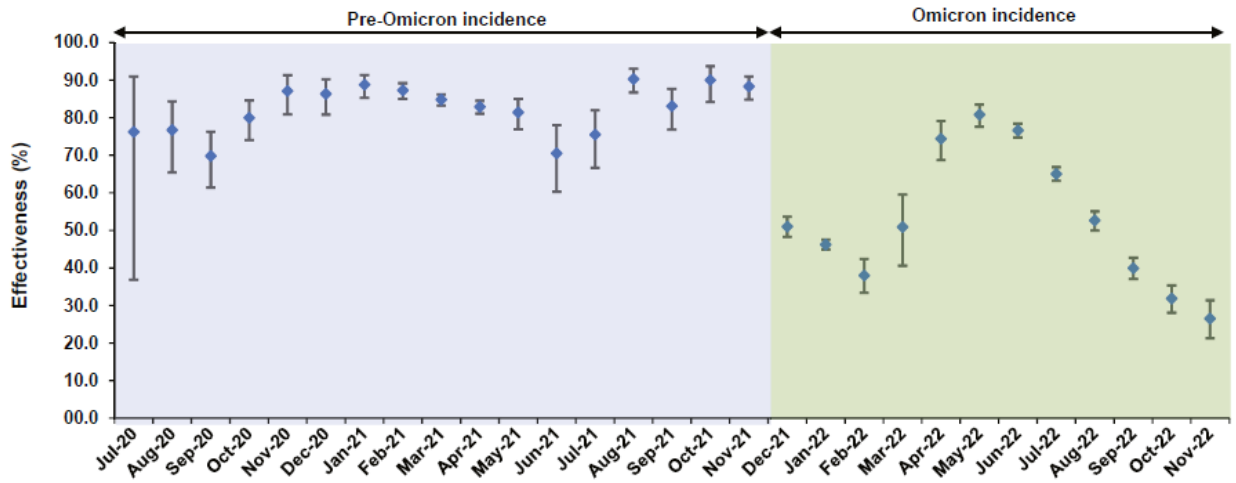


Fig. 11.C … and example simulated with a vaccine having indeed a negative VE (i.e. worse than the placebo), but which may still appear to be effective in the first few months...

Please note: using the excel sheets provided by professors Fenton and Neil for possible checks, the simulations give the same results even by varying as desired the numbers of people at the start of any rollout, the infection rates, and/or the speed of the vaccination campaign.
Consequently, it will not be possible to quantify the extent of vaccine effectiveness or safety with certainty, even in the first few months after any dose, if the Institutions continue to provide data on health events using the methods described above, or if the studies continue to calculate them likewise.
Unfortunately, reading even the above cited ten studies, taken from the meta-analysis indicated by the WHO, we can find some direct or indirect confirmations of the fact that this bias (of the 7, or 14, or... days of shift) continues to take place.

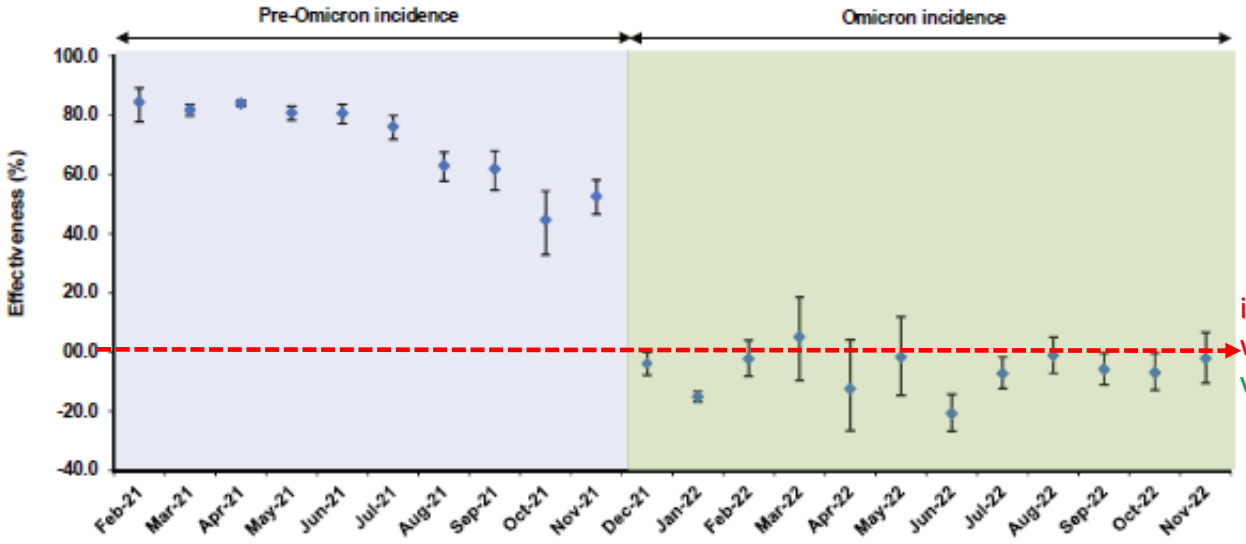
Another blow to the current narrative comes from research just published in the Lancet (*Suelen H. Qassim, Hiam Chemaitelly, Houssein H. Ayoub, et al. Population immunity of natural infection, primary-series vaccination, and booster vaccination in Qatar during the COVID-19 pandemic: an observational study; eClinicalMedicine 2023;62: 102102* https://doi.org/10.1016/j.eclinm.2023.102102), to estimate the population immunity of previous SARS-CoV-2 infection or of COVID-19 vaccination, respectively against reinfection or against breakthrough infection (**Figure 12**, **A**, **B** and **C**). After Omicron emergence, effectiveness dropped in the three groups, mostly in subjects vaccinated with three doses (in line with what has been shown for some time, even in comparisons of proxies such as viral loads. Eg *Woodbridge Y, Amit S, Huppert A, Kopelman NM. Viral load dynamics of SARS-CoV-2 Delta and Omicron variants following multiple vaccine doses and previous infection. Nat Commun. 2022 Nov 7;13(1):6706. doi: 10.1038/s41467-022-33096-0*).

A Effectiveness of previous infection against reinfection

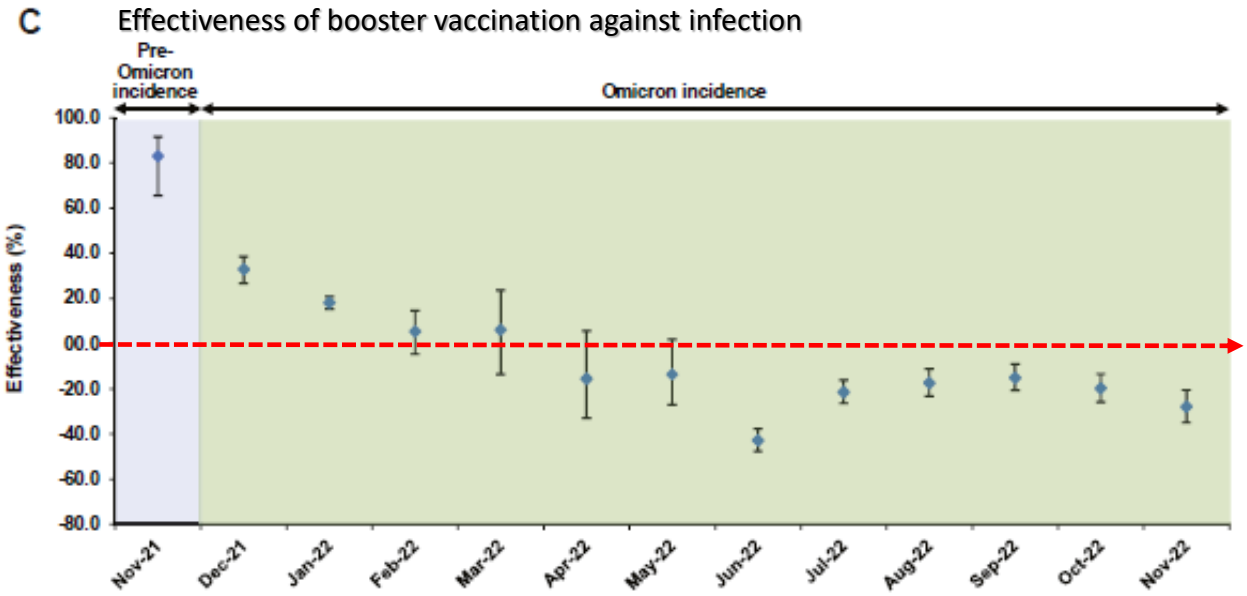


~30%

B Effectiveness of primary-series vaccination against infection



in tendency worse than previously infected



from June 2022 significantly worse than previously infected

Interestingly, the authors note that in general "*effectiveness declined over time after a wave, but rebounded to a higher level after a new wave, reflecting the recent increase in the number of individuals who were infected and protected against reinfection*."

As for the **effectiveness against severe, critical, or fatal COVID-19**, there is **no waning of protection by previous infection**, while "***there was an indication of some decline in VE of primary-series vaccination and booster vaccinations over time***" (**Fig. 13**, *Qassim, eClinMed 2023*, reproduced as Table S5).

Population immunity of natural infection, primary-series vaccination, and booster vaccination in Qatar during the COVID-19 pandemic: an observational study

Suelen H. Qassim,[a,b,c,*] Hiam Chemaitelly,[a,b,c] Houssein H. Ayoub,[d] Peter Coyle,[e,f,g] Patrick Tang,[h] Hadi M. Yassine,[f,i] Asmaa A. Al Thani,[f,j] Hebah A. Al-Khatib,[f,i] Mohammad R. Hasan,[h] Zaina Al-Kanaani,[e] Einas Al-Kuwari,[e] Andrew Jeremijenko,[e] Anvar Hassan Kaleeckal,[e] Ali Nizar Latif,[e] Riyazuddin Mohammad Shaik,[e] Hanan F. Abdul-Rahim,[i] Gheyath K. Nasrallah,[f,i] Mohamed Ghaith Al-Kuwari,[k] Adeel A. Butt,[a,e,l] Hamad Eid Al-Romaihi,[m] Mohamed H. Al-Thani,[m] Abdullatif Al-Khal,[e] Roberto Bertollini,[m] and Laith J. Abu-Raddad[a,b,c,n,**]

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Fig. 13 in our numbering

Table S5: **Effectiveness against severe, critical, or fatal COVID-19 of A) previous SARS-CoV-2 infection, B) primary-series (two-dose) mRNA vaccination, and C) booster (third-dose) mRNA vaccination, in Qatar, between July of 2020 and November of 2022.**

A) Effectiveness of previous SARS-CoV-2 infection	
Calendar month	**Effectiveness in % (95% CI)‡**
Jul-Dec, 2020	97.6 (82.8 to 99.7)
Jan-Jun, 2021	97.6 (95.5 to 98.7)
Jul-Dec, 2021	96.8 (87.0 to 99.2)
Jan-Jun, 2022	94.1 (83.9 to 97.8)
Jul-Nov, 2022	91.1 (60.5 to 98.0)

B) Effectiveness of primary-series (two-dose) mRNA vaccination	
Calendar month	**Effectiveness in % (95% CI)‡**
Feb-Apr, 2021	95.4 (93.6 to 96.7)
May-Jul, 2021	96.9 (94.8 to 98.1)
Aug-Oct, 2021	91.4 (86.6 to 94.5)
Nov, 2021-Jan, 2022	82.3 (76.6 to 86.6)
Feb-Apr, 2022	81.4 (48.5 to 93.3)
May-Jul, 2022	83.8 (14.1 to 96.9)
Aug-Nov, 2022	**53.1** (**-41.3** to 87.1)

C) Effectiveness of booster (third-dose) mRNA vaccination	
Calendar month	**Effectiveness in % (95% CI)‡**
Nov, 2021-Jan, 2022	95.0 (90.5 to 97.4)
Feb-Apr, 2022	96.2 (69.6 to 99.5)
May-Jul, 2022	**43.6** (**-51.4** to 84.5)
Aug-Nov, 2022	90.4 (9.6 to 99.0)

Therefore, "*although population immunity against infection waned rapidly, population immunity against severe COVID-19 was durable over the study duration and showed slow waning even with introduction of Omicron. This* ***slow waning appeared also to affect only vaccine immunity***."

We believe that these signals and the precautionary principle should stop the drive to vaccinate and re-vaccinate those who do not have strong personal health reasons, starting with all those who have overcome one or more natural infections.

Your answer went on like this:

"*Reading your concern about diminished vaccine effectiveness, please refer to WHO's updated Roadmap for prioritizing uses of COVID-19 vaccines (30 March 2023)…*
In more detail, the updated Roadmap is focusing on the adequate vaccination of populations at highest risk, which are first and foremost older adults, people with certain comorbidities, immunocompromised individuals, but also pregnant women. The spacing of repeat booster vaccination has been extended for most of these groups in light of the combined vaccine and infection induced immunity status (so called hybrid immunity). In population groups at lower risk of severe disease, vaccination recommendations have been further relaxed."

Indeed, when we question the WHO "**perseverance in advocating repeated anti-COVID-19 vaccinations**", we look exactly to your "Roadmap (30 March 2023)". We struggle to consider *relaxed* the following recommendations:
«continuing vaccination with available vaccines in view of a "baseline" scenario:
• longer interval [one year? six months?] for additional boosters (in addition to the 1st booster…) to priority groups
• boosters beyond the 1st booster are no longer routinely recommended for medium-risk groups
• additional booster in pregnancy within the second half of the second semester, if the last dose was administered >6 months before
• additional booster (2nd booster) for healthcare professionals 12 months after the last dose
• primary series + booster for healthy young adults
• for healthy children and adolescents consider primary series, based on context, cost…».
The WHO Recommendations (intended to become **binding** if amendments to the International Regulations are approved in 2024) are already strengthened against various targets by the Ecdc and Ema Recommendations for the autumn 2023 vaccination campaign. Eg:
• for children under 5 years of age, with no history of vaccination or previous infection with Sars-CoV-2, is recommended a primary series consisting of 2 or 3 doses (depending on the specific vaccine) just adapted ...

Alternatively to your recommendations, we consider with interest the Swiss recommendations from the CFV (Federal Vaccination Commission) with the FOPH (Federal Office of Public Health). In spring/summer 2023 no vaccination against COVID-19 is recommended in Switzerland, not even for people at particular risk (PPR). However, they can receive the vaccination after an individual check with their doctor.
If a new wave of SARS-CoV-2 should come, a vaccination would be recommended… to PPR.
Anyone who wants to be vaccinated without a recommendation must bear the costs.
On the subject of responsibility, the usual rules apply. In case of damage, the following can be required to answer:
1) the manufacturer, if the vaccine is defective;
2) who performed the vaccination or the hospital, according to the rules on the mandate ("physician's responsibility"), based on the code of obligations. The rules on patient information also apply. It is mandatory to inform about the type of vaccination and its risks. Taking into account the accessible information: from the manufacturer, any recommendations from Health authorities and professional associations, as well as the results of scientific and technical studies. The information must include both frequent and rare risks, if known and potentially serious. Furthermore, the patient should be reminded that not all the risks are currently known (e.g. any long-term damage);

3) in a subsidiary way the Confederation, for mandated vaccinations... But the decision to getting vaccinate or not depends entirely on the individual, along with the person administering the vaccine.

Finally, you stated:

«*Our expert group has also investigated the possible negative effect of so-called immunological imprinting of the current vaccines, which is claimed by one of the papers you quote. While such effects can be observed in the laboratory, the clinical relevance has not been established, and methodological explanations have been found for the observations on negative vaccine effectiveness that you quote. The recommendation that future vaccines should be based on an updated viral strain acknowledges the considerations.*
We would like to state again that the current vaccines continue to be highly effective against the prevention of severe disease and death, even for the currently circulating virus strains.»

Your last statement seems to be partially contradicted by the same documentation you sent us, and that we have analyzed and commented accordingly. And this even without having to recognize the **fundamental bias** we mentioned above (that is the "7, 14 or 21 days shift" to previous vaccination status).
For the rest, there is a great controversy on the extent of adverse reactions and adverse events following these vaccinations, documented by the official sources of active surveillance.
To deal with it in an evidence-based manner, in addition to activating a real active surveillance, we think it is necessary to reform the data collection and communication systems, and **to accept an open scientific debate on them**.

We are not disputing the fact that immunization does not start from the moment of inoculation of a vaccine, and that it actually requires 1 to 3 weeks to establish an adequate response. But in these weeks the consequences of the injection may differ from those of drinking a glass of water. The interest of those who receive the injection, but also of those who decide health policies for the good of the community, is to know in a transparent way all the consequences of that inoculation, for better or for worse, and from that moment on (also the possible long-term consequences, favorable or not).

A request is therefore that the institutions continue - if they believe - to present the data **also** in the current way (however, making explicit the adjustments they implement because deemed appropriate). But that, in parallel, they also make raw data immediately available, without adjustments, including **all health events** (infections of any nature, other events of health interest, hospitalizations, deaths) **from the instant following each inoculation**. What has been observed must be **associated with the different vaccination statuses of 1, 2, 3, 4… doses**, coinciding with the precise moment of each corresponding inoculation. In this way, independent researchers will be able to verify the path, the soundness of institutional scientific communication, and to discuss as needed the interpretations on which it is based. The time limits for such detections should be reasonably extended; but, above all, the events of health significance occurring in the following months and years should also report the personal vaccination status in the patient history, expressed unequivocally as inoculation with 1, 2, 3, 4... doses of vaccine, as it seems logical to do for products that have been tested in a formally valid way (randomised controlled trials) only for a few months, and of which any long-term effects are not known, even non-specific ones.

Another basic request is to avoid all forms of censorship and to accept comments and suggestions also from critical voices and different positions (provided of course they make explicit reference to the scientific method and to the discussion of the available evidence). This scientific debate should take place even in institutional settings, without imposing dogmas or prejudicial exclusion areas, allowing the normal scientific dialectic to improve the interpretations of the data and to correct possible serious errors in the public health strategies adopted.

You concluded "*The virus continuous to evolve as does the population immunity. We will continue to monitor the virological, epidemiological and immunological situation and will adapt our recommendations as needed … the disease will stay with us and we need to protect the most vulnerable populations*".

Indeed, our position is similar in principle, although the strategies we deem evidence-based differ, as differ assumptions and forecasts consistent with most evidence grounded indications.
For example, the cited last Qatar study (*Qassim et al. eClinicalMedicine 2023; https://doi.org/10.1016/j.eclinm.2023.102102*) states: "*finding suggests that SARS-CoV-2 epidemiology may exhibit a similar pattern to that of common-cold coronaviruses. Long-term immune protection against severe COVID-19 could contribute to a benign pattern of infection that is perhaps not dissimilar to that of common-cold coronaviruses. Some of the vaccine effectiveness measures post Omicron introduction, particularly for booster vaccination, were negative in value, perhaps suggesting negative immune imprinting. This effect was pronounced during the BA.4/BA.5 wave. This finding supports similar recent findings in this same population.*[10,52]"
This hypothesis seems reasonably fitting with the most recent available evidence, does not exclude the commitment to protect the most vulnerable, but it seems consistent with the position currently taken by Swiss healthcare.
In any case similar choices, destined to affect the epidemiological and health situation and the economic and social development of the whole world, would deserve a public debate, and the request to "**Trust the scientific evidence**", not to "Trust ***the Science***", or to be delegated to a group of "experts".

Kind regards

24-07-2023

The Italian **independent Medical-Scientific Commission** (**CMSi**):

Dr. Alberto Donzelli, Prof. Marco Cosentino, Prof. Vanni Frajese, Dr. Patrizia Gentilini,
Prof. Eduardo Missoni, Dr. Panagis Polykretis, Dr. Sandro Sanvenero, Dr. Eugenio Serravalle

and

Norman Fenton, Professor Emeritus of Risk, Queen Mary University of London.