Efficacy, "protection" and vaccination to prevent COVID-19

The public appears to have a poor understanding of "protection" as encompassed by the term "efficacy" in regard to vaccination against COVID-19. In mid-2021 I polled 24 individuals drawn from family, friends, neighbours, my accountant, librarians, recent medical graduates, University students and one random stranger. The question was:

"What do you think 95 percent vaccine protection against COVD-19 means"? Answers included:

"Vaccination prevents COVID 95 times out of 100".
"If I get COVID, it will be 95 percent less severe".
"I'm protected 95 percent of the time".
"Vaccinated people have only a 1/20 chance of getting COVID".
"The vaccine lowers the viral load by 95 percent".
"I don't know what it means".

None are correct − a plaint to science communication and investigative journalism. This may explain what prompted the WHO to advise, "An efficacy of 80% does not mean that 20% of the vaccinated group will become ill". The WHO declined to tell us what efficacy does mean. What the WHO did say is, "If a vaccine has high efficacy, a lot fewer people in the group who received the vaccine got sick than the people in the group who received the placebo" [1]. The WHO is either confused or obfuscating. It is not "a lot fewer people". It is less than 1 percent people.

Nonetheless, the common thread seems to be that something worthwhile stands behind a number as high as 95 percent. And as such, "protection" signifies a welcome and markedly reduced risk of acquiring COVID-19 in a vaccinated individual. Likewise, one should worry when vaccine-induced immunity wanes over time [2].

What people desire (but may not express) is, "How less likely am I to get COVID-19 if I am vaccinated? This is called the absolute risk reduction (ARR). Efficacy does not measure ARR and cannot be calculated from it. This is because efficacy is computed from a comparison of the fraction of vaccinated who get COVID-19 relative to the fraction of unvaccinated who get COVID-19. In other words, efficacy is contingent on getting COVID-19.

The original Pfizer-BioNTech BNT162b2 Comirnaty randomised placebo controlled trial (RCT) was published in the NEJM on December 31st 2020 [3]. 36,523 participants were split almost equally into a vaccinated and a saline, unvaccinated, control group. At 60 days there were 170 cases of symptomatic, PCR-confirmed COVID-19. 8/18,198 (0.04 percent) occured in those vaccinated and 162/18,325 (0.88 percent) in those given saline. Compared to the saline group, 5 percent (0.04/0.88, 1/20th) of the vaccinated group got COVID-19.

Since humans are more favourably disposed towards success than failure, efficacy (protection) is expressed as 95 percent rather than 5 percent. The analogous situation is framing a surgical procedure with a 5 percent mortality rate as a 95 percent survival rate. It is believed patients are less likely to reject an operation when presented with the latter.

Assuming, as we must, that vaccination and control groups were at similar risk of acquiring SARS-CoV-2 and getting COVID-19, casting efficacy as "protection" loses sight of the fact that

neither vaccine nor saline "protected" the 18,163 of the 18,325 in the placebo group who did not get symptomatic COVID-19. The remedy for assessing the absolute risk reduction of acquiring COVID-19 is to count bodies and deduct, rather than computing proportions of those who succumbed to COVID-19.

In the Pfizer trial, 99.96 percent of those vaccinated did not get COVID-19.
In the Pfizer trial, 99.12 percent of those saline-ated did not get COVID-19.

The difference between the two is the absolute risk reduction. In this case, 0.84 percent.

This is 113 times smaller than the 95 percent "protection" statistic. It also implies that 119 people had to be vaccinated in order to prevent one case of COVID-19. (0.84 percent = 1/119). This statistic is called the number needed to treat (NNT).

	COVID	No COVID	Totals	No COVID	
Given vaccine	8	18190	18198	99.96%	
Given saline	162	18163	18325	99.12%	
Totals	170	36353	36523	0.84%	<--- ARR

Note: Virus transmission and asymptomatic infections were not outcome measures in the Pfizer trial.

In the 2015 U.S. *Communicating Risks and Benefits: An Evidence-Based User's Guide*, the FDA state, "**Provide absolute risks, not just relative risks**. Patients are unduly influenced when risk information is presented using a relative risk approach; this can result in suboptimal decisions" (FDA emphasis). Presumably "suboptimal" cautions physicians against denying patients data necessary for making personal choices for or against vaccination [4].

In 2010 [redacted] and his colleagues warned of dangers communicating information solely in terms of relative risk. One example they gave was a 1995 caution issued by the *UK Committee on Safety of Medicines*. It was stated, "that third generation oral contraceptive pills increased the risk of potentially life threatening thrombosis twofold. The news provoked great anxiety, and many women stopped taking the pill, which led to unwanted pregnancies and abortions—some 13 000 additional abortions in the next year in England and Wales—and an extra £46m (€55m; $71m) in costs for the NHS". However, the twofold relative risk increase was an absolute increase from 1/7000 with the second generation pill to 2/7000 with the third generation pill [5]. [redacted] regards this a moral issue and concluded, "The problem of misleading reporting has not gone away". In 2021 it had still "not gone away". Only then the moral issues included, *inter alia*, whether to decline vaccination or lose one's livelihood.

Saline placebos

One assumes that vaccine scientists and manufacturers conduct RCTs to prove that the active ingredient is responsible for the observed effects. RCTs are experiments. All experiments require a control / placebo to mitigate known and unknown confounding factors. To put it another way, without a valid control it is impossible to ascertain whether or not the outcome of interest is a pure effect of the entity under test. The Pfizer entity is an mRNA that codes for the SARS-CoV-2 spike protein. In this regard, perhaps too little attention has been given to the choice and dosing of placebos in the Pfizer (and other) COVID-19 vaccine trials.

1. Normal saline is arguably an adequate control for addressing local problems. That is, effects wrought by injury to skin, subcutaneous tissue, blood vessels, muscle, introduced microorganisms, the transient passage of a metallic foreign body and local vaccine reactogenicity.
2. A few cubic millimetres of an injected, salt / water mixture is not expected to mirror the diverse systemic, ongoing immunogenic events of a vaccine mixture. (Although Pfizer thought otherwise: '[redacted].
3. Attributing vaccine efficacy to the mRNA component of a COVID-19 vaccine requires a placebo whose composition is identical to the vaccine minus the mRNA. Compare COVID-19 vaccinations with, for example, the trial of measles vaccination conducted in 1975 by [redacted] and colleagues: [redacted]
4. [redacted] [7]. Controlling for this possibility requires substituting the vaccine lipid nanoparticle / simian adenovirus vector nucleic acid with unrelated nucleic acid species which itself, and its product, are judged harmless.
5. In regard to mRNA vaccines, "..[redacted] [8]. What is understood is that vaccine lipids and mRNA themselves are foreign and thus potential antigens. Unless individual constituents of the lipid nanoparticles remain invisible to the adaptive immune system, there is a theoretical possibility that vaccines induce antibodies reactive against mRNA. Such may impair the PCR testing required to diagnose COVID-19 in symptomatic participants. If so, the number of COVID-19 cases in both vaccinated and unvaccinated groups may be underestimated.

If one were conducting a two month RCT to evaluate a drug treatment for hypertension, the placebo would be given every day for the duration of the study. Given the duration of COVID-19 vaccine RCTs is typically 60 days, for 59/60 days these experiments were uncontrolled (58/60 if one includes the 300 fewer individuals who received a second injection in the Pfizer study). The use of an ephemeral, non-immunogenic control is not a fair test of the active ingredient's ability to reduce the relative and absolute risks of symptomatic COVID-19.

Compared to measles vaccination, with an NNT of 1-2 persons, there seems little basis for the third word of the COVID-19 vaccination mantra, "safe and effective". "Safe" is not addressed in this essay.

[redacted]

12th January 2024

References

1. https://www.who.int/news-room/feature-stories/detail/vaccine-efficacy-effectiveness-and-protection
2. https://www.bmj.com/content/374/bmj.n2113.long
3. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7745181/pdf/NEJMoa2034577.pdf
4. Fischhoff B. *et al*. *Communicating risks and benefits: An evidence based user's guide*. Government Printing Office, 2012 https://www.fda.gov/media/81597/download
5. Gigerenzer *et al*. Misleading communication of risk. Editors should enforce transparent reporting in abstracts. BMJ. 2010: 341; 791-792 BMJ 2010;341:c4830 doi: 10.1136/bmj.c48306.
6. Bloom JL, Schiff GM, Graubarth H, et al. Evaluation of a trivalent measles, mumps, rubella vaccine in children. *The Journal of Pediatrics* 1975; 87: 85-72.
7. Kobiyama K, Ishii KJ. Making innate sense of mRNA vaccine adjuvanticity. *Nature Immunology* 2022;23(4):474-76.
8. Li C, Lee A, Grigoryan L, Arunachalam PS, Scott MK, Trisal M, et al. Mechanisms of innate and adaptive immunity to the Pfizer-BioNTech BNT162b2 vaccine. *Nature Immunology* 2022;23(4):543-55.