

Understanding announcements about Vaccines. What does 95% “Efficacy” actually mean?

What is the difference between efficacy and effectiveness? 0.11811

Lately, we have started hearing that there are vaccines close to being deployed that can greatly slow the proliferation of COVID-19. The companies that expect to offer these vaccines publish results on their trials as a percentage of “Efficacy”. Typically, when someone says something is 95% effective, we can correctly assume that this means that there is only one part in twenty (ratio of 1:20) of something occurring. The problem is that efficacy is not the same as effectiveness for vaccines.

As an example of effectiveness, in an N95 effectiveness test, no more than five particles out of every one-hundred particles in a potentially infected particle cloud (of size above .3um) should make it through the filter. The 95% is only a testing metric, as almost all masks have some leakage against the face. Your N95 may only be providing on the order of 85% of filtration for you and probably less if you have a beard.

The vaccines coming out soon are being tested within a trial “group”, as in the Phzyzer trial. Efficacy is based on results from a small number of people within the trial group. The testing methodology uses a group of people (volunteers) who are divided in half where one half gets a vaccine and the other half gets a placebo. Based strictly on a small number of people in the group who became infected during the trial timeframe with the disease, what can we tell about the effectiveness of the vaccine? **The efficacy is the ratio of people who only became infected with the disease, with or without taking the vaccine;** not a percentage of people getting ill or not getting ill within the group. Therefore, we can only guess at the effective rate based on historical data and the make-up of the group.

Therefore, published efficacies of vaccines are not ratios used in the same manner as one would use the effectiveness of a vaccine. In the case of the latest Pfizer vaccine candidate, a small sample of the people (170 people) in a group of about 44,000 eventually got the disease. The ratio of the members that got the disease was 95:5 or 162:8 (therefore 8 out of 170 people did not get the disease or 4.7% of the 170; a 95.2% efficacy) of the members who received a placebo compared to the ones who received the vaccine. This is very different than saying of the 44,000 people who took the vaccine, we can only expect that 5% of this population would get the disease, or 2,200 would get the disease and 41,800 would not (or are protected).

There are an incredible amount of unknowns in any trial group. Things like: 1) What about other drug or illness interactions? 2) Was the trial long enough to truly tell what side-effects will occur from the vaccines over an extended period? 3) How does the group makeup match with the general population. 4) Were there different behaviors of the two groups? 5) What about mutated forms of the virus, will the

vaccines still be effective? These factors may all affect the effectiveness of a vaccine against COVID-19 on the general population. ***This is why efficacy is very different than effectiveness.*** There are many questions (some long term) to ask and get answered before the effectiveness of a vaccine can be determined. The efficacy should only be considered only an initial indication of the value of the vaccine.

When you start dealing with hundreds of millions of people, outliers are plentiful and can greatly affect the effectiveness of a vaccine. A recent article in the NY Times*¹ says, *"A 95 percent efficacy is certainly compelling evidence that a vaccine works well. But that number doesn't tell you what your chances are of becoming sick if you get vaccinated."*

The fact that the fractions were so small may suggest that the efficacy percentage itself can easily be wrong. In general, sample sizes need to be large to be accurate. Also, *"..., the most important efficacy endpoint, protection against severe disease and death, is difficult to assess in phase 3 clinical trials."**² As you may be aware, that is exactly where we are now in most of the vaccines about to be distributed to the general population. For example, if just an additional ten percent or seventeen more people became ill who took the vaccine over those who took the placebo, then the efficacy drops to 162:25 or only 87%, and we still do not know the risks of side effects.

As the article*¹ referenced suggests since in most cases, the actual predictability of a drugs' effectiveness in the general population is most often lower. This can be due to many reasons. Were the people in the study always wearing masks in any potentially unsafe situation? As stated in a recent research study*², the behavior of higher-risk patients can easily affect the test results, "For example, older participants could be more likely to avoid social gatherings or use of public transport, reducing their likelihood of exposure to SARS-CoV-2. " and also, "However, given that older participants, especially people with comorbidities, are more likely to socially shield, they might be less likely to be exposed to SARS-CoV-2 and so a mortality efficacy endpoint might still not be met. "

Therefore, in conclusion, efficacy does not equal effectiveness and we may not know how effective the latest vaccines are for years to come. As Pfizer says in their press release*³, *"This release contains forward-looking information about Pfizer's efforts to combat COVID-19, the collaboration between BioNTech and Pfizer to develop a potential COVID-19 vaccine, the BNT162 mRNA vaccine program, and modRNA candidate BNT162b2 (including qualitative assessments of available data, potential benefits, expectations for clinical trials, anticipated timing of regulatory submissions and anticipated manufacturing, distribution and supply), that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. "*

There may also be difficulty in getting the vaccine around the world. In another recent study printed in Health Affairs *⁴, other factors beyond efficacy will affect how well a vaccine performs, *"Yet, these biological factors—including vaccine efficacy as demonstrated through clinical trials—are only some of the many influences whose complex interaction will determine the real-world effectiveness of COVID-19 vaccination and its ability to alter the trajectory of the pandemic. How well a vaccine program "works" will also depend on how quickly it can be manufactured, how efficiently it can be distributed to locations in greatest need, how persuasive health messaging can be in promoting public acceptance, and how consistently the public can adhere to the many complementary prevention strategies (e.g., masks, hand-washing, distancing) to limit the spread of the virus."*

Even with all the weight of the US government behind the distribution of the vaccine across the world, *"...based on current projections, the companies expect to produce globally up to 50 million vaccine doses*

in 2020 and up to 1.3 billion doses by the end of 2021.” The world’s population is 7.8 billion, and if the vaccines need two doses per person, we still have a long way to go to achieve herd immunity.

In conclusion, “On Thursday, Dr. Paltiel and his colleagues published a study in the journal Health Affairs in which they simulated the coming rollout of coronavirus vaccines. They modeled vaccines with efficacy rates ranging from high to low, but also considered how quickly and widely a vaccine could be distributed as the pandemic continues to rage.” “The results, Dr. Paltiel said, were heartbreaking. He and his colleagues found that when it comes to cutting down on infections, hospitalizations and deaths, the deployment mattered just as much as the efficacy. The study left Dr. Paltiel worried that the United States has not done enough to prepare for the massive distribution of the vaccine in the months to come.”

NOTES:

1. “2 Companies Say Their Vaccines Are 95% Effective. What Does That Mean?”
<https://www.nytimes.com/2020/11/20/health/covid-vaccine-95-effective.html?auth=login-google> Nov. 20, 2020, Carl Zimmer
2. “What defines an efficacious COVID-19 vaccine? A review of the challenges assessing the clinical efficacy of vaccines against SARS-CoV-2”. Hodgson, Mansetts, etc. Oct 27,2020
[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30773-8/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30773-8/fulltext)
3. “PFIZER AND BIONTECH CONCLUDE PHASE 3 STUDY OF COVID-19 VACCINE CANDIDATE, MEETING ALL PRIMARY EFFICACY ENDPOINTS “ <https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-conclude-phase-3-study-covid-19-vaccine#:~:text=NEW%20YORK%20%26%20MAINZ%2C%20Germany%2D%2D,the%20study's%20primary%20efficacy%20endpoints>. Nov. 18, 2020
4. Clinical Outcomes Of A COVID-19 Vaccine: Implementation Over Efficacy
<https://www.healthaffairs.org/doi/10.1377/hlthaff.2020.02054>

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