SCIENCE & TECHNICAL ADVISORY | RŌPŪ TOHUTOHU I TE PŪTAIAO ME TE HANGARAU

MINISTRY OF HEALTH
MANATŪ HAUORA

Kōrero Pūtaiao (Science Chat)

About vaccines: efficacy, effectiveness, transmission and immunity

This article first appeared in CSU 26 Covid-19 Science Updates 26 March 2021. Covid-19 Science Updates are prepared by the Science and Technical Advisory Team within the Ministry of Health.

Covid-19 Science Updates context and disclaimer: Covid-19 Science Updates contain topical talking points, science advice and research and are intended as a high-level overview. The topics in them are assembled 'at pace' often under urgency and may be based on reports that are not peer-reviewed. Both the content and 'our thinking' components of Covid-19 Science Updates represent science commentary at a single point in time – information may or may not align with Ministry of Health positions or priorities.

Introduction

Following approval of the Pfizer/BioNTech vaccination by Medsafe, the New Zealand COVID-19 Immunisation Programme began in February with the immunisation of border workers and their household contacts. The question of whether or not vaccination may reduce transmission of virus versus purely protection against COVID-19-related diease has been of high public interest for some time. A recent opinion piece in the BMJ[1] discusses vaccine efficacy measures, highlighting what vaccine efficacy actually tells us and what we can infer from it.

Vaccine efficacy compares the rates of disease between vaccinated and unvaccinated people as assessed in controlled clinical trials, conducted as part of vaccine development and approval. Vaccine effectiveness also compares the rates of disease between vaccinated and unvaccinated people but differs in that it is measured in real-world scenarios once the vaccine is approved for use and rolled out in the general population. This report briefly discusses both vaccine efficacy and vaccine effectiveness, as well as measures of transmissibility, in the context of population immunity.

Vaccine efficacy

Hospitalisation and death due to COVID-19 are key clinical outcomes that we seek to prevent through vaccination. However, vaccine efficacy for these outcomes is difficult to assess directly in clinical trials, largely because these outcomes occur less frequently than mild-to-moderate disease, particularly among the trial populations who were generally following public health control measures. For example, in the Pfizer/BioNTech Phase III clinical trial there were only 10 cases of severe COVID-19 disease. Although severe disease is a clinical outcome of great interest, a vaccine trial would need to be much larger and/or require longer follow-up to have enough statistical power to measure efficacy against severe disease. The approach taken by vaccine developers is therefore one that balances clinical relevance with feasibility.

When we look at the efficacy for a COVID-19 vaccine as reported from phase III trials then, what we are seeing is the reported effect of a vaccine on a 'meaningful clinical outcome'. This is usually laboratory confirmed symptomatic disease - both mild and moderate symptoms and can be used to infer the efficacy of the vaccine against severe disease. Furthermore, the real-world data we have on COVID-19 vaccines supports this being the case.

Vaccine efficacy for preventing SARS-CoV-2 infection (symptomatic and asymptomatic) is another outcome of interest, as we are keen to know the potential impact of the vaccine in slowing transmission of the virus. This is hard to reliably measure in the context of vaccine trials, however, and was not the original outcome of interest. Measuring the impact of vaccination on transmissibility in a clinical trial would require frequent PCR screening, viral culture, and/or serology testing for each of the tens of thousands of trial participants, and therefore delay vaccine development.

Vaccine effectiveness

In contrast to vaccine efficacy, vaccine effectiveness is measured once the vaccine is approved for use in the general population and rolled out. It refers to the ability of the vaccine to prevent outcomes of interest in the 'real world'. In this real-world evaluation, the characteristics of those vaccinated, such as their age, comorbidities, and their prior exposure to the disease allows the benefits of vaccination in specific subgroups of the population to be determined. We can also gain an understanding of the impact of vaccination on transmissibility.

Recent real-world data from Israel where the Pfizer/BioNTech vaccine is in wide use has provided us with the first evidence for the effectiveness of the vaccine against COVID-19. An observational study published in the New England Journal of Medicine estimated the vaccine effectiveness (7 days after the second dose) as 94% against symptomatic infection and provided valuable insights into effectiveness against severe COVID-19 disease.[2] Of note, the study recorded a total of 229 cases of severe disease – 55 in the vaccinated group and 174 cases amongst those unvaccinated. In addition, the study estimated the effectiveness of the Pfizer/BioNTech vaccine against viral infection was 92%. Data from another observational study in Israel,[3] found that those vaccinated with the Pfizer/BioNTech vaccine who contracted COVID-19 infections had lower viral loads than those people with COVID-19 who had not been vaccinated. This real-world data provides further optimism about the benefits of vaccination with the Pfizer/BioNtech vaccine in terms of reducing both transmission and disease severity.

Achieving population immunity

Population ('herd') immunity is a theoretical concept defined as achieved when enough people have been infected with a disease or have been vaccinated, such that the infectious disease stops spreading. Population immunity helps protect people in the population who are not vaccinated including those at risk of more severe disease who are not able to be vaccinated (people with certain conditions or with weakened immune systems) and those who may choose not to receive the vaccine.

While clearly desirable, it is too early to determine the exact proportion of a population that needs to be vaccinated to confer or approximate population immunity. The efficacy of the vaccine and its duration of protection are important factors, and evidence of the duration of protection from vaccination and infection are still emerging.

Another key factor affecting population-level immunity is the transmissibility of the disease and whether or not vaccines prevent transmission. For SARS-CoV-2 we know, for example, that the emergence of new variants may change the equation for estimating population-level protection if they have increased transmissibility, or immune escape from vaccines. It is also likely that the rate of transmission is higher in more densely populated areas and in groups of people with a typically greater number of contacts with others, such as people who reside in multigenerational households.

SCIENCE & TECHNICAL ADVISORY | RŌPŪ TOHUTOHU I TE PŪTAIAO ME TE HANGARAU

MINISTRY OF HEALTH | MANATŪ HAUORA

Concluding comments

Communicating the potential population-level benefits of vaccination, along with known individual protection will be important to encourage participation in the vaccination programme. Population immunity will be limited if there are large pockets of the community that choose to be unvaccinated. How the act of being vaccinated may change human behaviour and increase interactions, especially if travel resumes, needs to also to be considered. The many factors that influence population-level immunity make creating targets difficult, which is why it is important to vaccinate as many people as possible; emphasising the benefits of individual protection and the likely impact on transmission.

References

1. Dean, N. & Madewell, Z. *Understanding the spectrum of vaccine efficacy measures.* BMJ Opinion. March 5, 2021. https://blogs.bmj.com/bmj/2021/03/05/understanding-the-spectrum-of-vaccine-efficacy-measures/?utm_source=twitter&utm_medium=social&utm_term=hootsuite&utm_content=sme&utm_campaign=usage
2. Dagan, N., Barda, N., Kepten, E., et al. *BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting.* N Engl J Med. February 24, 2021. DOI: 10.1056/NEJMoa2101765 https://www.nejm.org/doi/full/10.1056/NEJMoa2101765
3. Levine-Tiefenbrun M., Yelin I., Katz R., et al. *Decreased SARS-CoV-2 viral load following vaccination.* medRxiv. February 8, 2021. doi: https://doi.org/10.1101/2021.02.06.21251283 https://www.medrxiv.org/content/10.1101/2021.02.06.21251283v1