Australian Nursing & Midwifery Federation

ANMF COVID-19 RESOURCE

The effectiveness and safety of the Moderna COVID-19 vaccine

***ALERT* Evidence regarding COVID-19 is continually evolving. This resource will be updated regularly to reflect new emerging evidence but may not always include the very latest evidence in real-time.**

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Key points

- *Any vaccine used in Australia must be approved by the Therapeutic Goods Administration (TGA).*
- *The Moderna Australia Spikevax (elasomeran) mRNA vaccine has provisional TGA approval in Australia.*
- *The vaccine uses the same mRNA technology as the Pfizer (Comirnaty) vaccine already administered in Australia and contains synthetic mRNA for specific spike proteins not complete or viable viruses.*
- *All TGA provisionally-approved COVID-19 vaccines are effective for reducing the severity of COVID-19 infections, risk of hospitalisation, reducing risk of transmission to others, and protecting against death.*
- *Moderna appears to be more effective against the Delta variant than Pfizer, but both vaccines are still effective.*
- *The vaccines cannot cause COVID-19 infection or change human DNA.*
- *Vaccination symptoms are local or systemic reactions to foreign particles, not a 'mild' form of COVID-19.*
- *Vaccinated people must still follow official guidance and recommendations regarding infection prevention and control (i.e. hand hygiene, respiratory etiquette, physical distance).*

Introduction

The Australian Government has secured 25 million doses of *Moderna* Australia's COVID-19 vaccine *Spikevax (elasomeran)* also called the mRNA-1273 vaccine following provisional approval by the Australian Therapeutic Goods Administration (TGA). The *Moderna* vaccine will shore up and diversify Australia's supply and also afford opportunity for potential booster shots. of the addition of the *Moderna* vaccine means that there are now four COVID-19 vaccines with TGA provisional approval (these include *Pfizer/BioNtech*, *Oxford/AstraZeneca* and *Janssen-Cilag (Johnson & Johnson* which is provisionally approved but not yet included in Australia's COVID-19 vaccination program). It is important to understand that the provisional approval process is extremely rigorous and that greater scrutiny and detail is demanded from drug companies to comply with the TGA's strict requirements.[1] All COVID-19 vaccines in Australia have been deemed safe and effective and the benefits of receiving any one of the vaccines significantly outweigh the risks, particularly now that uncontrolled community transmission is again a real threat.[1] Only vaccines that are approved as safe and effective by the TGA and granted provisional registration will be available in Australia. Safety and effectiveness is determined through analysis of ongoing clinical trials, international collaboration, and advice from the Advisory Committee on Vaccines (ACV). The TGA will continue to monitor the safety, quality, and efficacy of all vaccines before and following provisional approval.[2,3]

Evidence indicates that the COVID-19 vaccines provisionally approved for use in Australia are effective in reducing the severity of illness and likelihood of hospitalisation by over 80 percent and also substantially reduce mortality.[4] The vaccines are also very effective for preventing a person from transmitting the virus to others. There is emerging evidence showing significant reductions in household transmission for *Pfizer* and *AstraZeneca* (40-50% reduced transmission among household members after one dose of either,[5] and 81% following two doses of *Pfizer*),[6] and *Moderna* (41.9% reduced transmission among household members).[7] Because 100 percent of transmissions are not prevented, all current official public health and social restriction recommendations should continue to be observed regardless of vaccine status.

How efficacious/effective is the Moderna vaccine?

A trial enrolled 30,420 participants and administered either the vaccine or a placebo with 15,210 in each group. Vaccine efficacy was 94.1 percent (95% Confidence Interval, 89.3 to 96.8%; P<0.001). Efficacy was similar across secondary analyses, including; assessment at 14 days following first dose; analyses that included participants who had evidence of SARS-CoV-2 infection at baseline (11 people in the vaccine group and 185 in the placebo group), and analyses for participants aged 65 years or older.[8] Severe COVID-19 illness and one fatality occurred among 30 participants in the placebo group. This suggests that the vaccine provided 100 percent protection against severe COVID-19 disease, COVID-19-related death, and showed no evidence of vaccine-associated enhanced disease (VAED).[9]

The United States Centers for Disease Control and Prevention (CDC) highlight that the level of certainty for the benefits of the *Moderna* COVID-19 vaccine was 'high certainty' for the prevention of symptomatic COVID-19 and that evidence was 'moderate certainty' for the estimate of prevention of COVID-19–associated hospitalisation.[10] Because data on COVID-19–associated hospitalisations and deaths are still limited, evidence was of 'very low certainty' for the estimates of prevention of asymptomatic SARS-CoV-2 infection and all-cause death, but the prevention of symptomatic infection can reasonably be expected to also prevent associated hospitalisations and deaths.[10]

While not able to determine protection against asymptomatic infection and unable to account for whether people in the vaccine group did not refer themselves for testing, in a Phase 1 trial, at 119 days following vaccination and 90 days following the second dose among 34 adult participants, the vaccine was found to produce high levels of binding and neutralising antibodies three months after vaccination.[11] The same study reported finding no serious adverse events nor trial halting phenomena.

COVID-19 variants

As commonly occurs with other viruses (e.g. influenza), new variants of the SARS-CoV-2 virus have arisen through natural genetic mutation.[12] Variants that have altered spike proteins (see below) unlike those of the original virus may be less susceptible to current vaccines.[13] The collection of data regarding the vaccines, particularly in the face of variant strains, is ongoing, and in some cases yet to be released.[14-16] The impact of the vaccines on infectiousness/ transmission of SARS-CoV-2 variants between people is still emerging.[17]

In a un-peer reviewed pre-print, a comparison of the *Pfizer* and *Moderna* vaccines found that while both vaccines were effective for protecting against COVID-19 infection and hospitalisation, effectiveness appeared to be lower against the Delta variant compared to the earlier Alpha variant; *Moderna* (76%, 95% CI: 58-87%) and *Pfizer* (42%, 95% CI: 13-62%) among 25,589 vaccinated individuals.[18] When comparing rates of infection between matched individuals fully vaccinated with *Moderna* versus *Pfizer* across Mayo Clinic Health System sites in Minnesota, Wisconsin, Arizona, Florida, and Iowa, *Moderna* conferred a two-fold risk reduction against breakthrough infection compared to *Pfizer* (IRR = 0.50, 95% CI: 0.39-0.64).[18] The same study found that the *Moderna* vaccine was highly effective (real world) against infection (86%, 95% CI: 81-90.6%) and hospitalisation (91.6%, 95% CI: 81-97%) likely to be caused by the Alpha variant.[18] The authors highlighted the need to consider dosing regimens to support ongoing protection against infection and severe disease.

How the Moderna vaccine works

COVID-19 is caused by the SARS-CoV-2 virus and its more recent variants. Viruses need a host cell to reproduce and cause infection. SARS-CoV-2 viruses are coated in 'spike proteins' that bind to 'ACE2 receptor proteins' which are located on the surface of cells within the human body. When the spike protein and receptor proteins bind, the virus can enter the cell and replicate resulting in infection.[19,20]

To reduce illness severity or prevent infection, the body's immune system must recognise the virus. To do this 'B-cells' produce antibodies that bind to SARS-CoV-2 spike proteins. This then prevents the virus from binding to other human cells. Simultaneously, 'T-cells' identify and destroy infected cells and prevent further infection.

The effectiveness of a person's immune response to SARS-CoV-2 depends on the ability of their body to quickly recognise and respond to viral spike proteins and infected cells. Once the immune system is able to do this, the B- and T-cells remain within the body and continue to provide protection against future infection.[21]

Because variants can have differently shaped spike proteins, the antibodies produced by the body based on the original type of SARS-CoV-2 may not bind as effectively to new variants.[22] Research continues into establishing how well existing vaccines work to develop an effective immune response and reduce the severity of illness caused by variants.[12,23] The vaccine development process can be readily modified to accommodate new virus strains in the same manner as for influenza,[24,25] and research into modifications to the *Moderna* vaccine for use against variants is progressing.[23]

The *Moderna* vaccine is given in two 0.5mL doses 28 days apart.[8] There are currently no data on the interchangeability of the vaccine with others, so the second dose should not be substituted with another type of vaccine. Like the *Pfizer/Cominarty* vaccine the *Moderna* COVID-19 vaccine uses synthetic genetic code (messenger RNA/mRNA) to cause the body to make replicas of the SARS-CoV-2 spike protein which are recognised as foreign and cause an immune response.[26] If the body recognises the SARS-CoV-2 spike protein in the future, B- and T-cells can inhibit infection and reproduction of the virus and thus reduce the severity of illness and risk of death.[21]

The *Moderna* vaccine is transported in ten-dose vials frozen at between -25°C and -15°C,[27] and is able to be stored at 2-8°C for up to 30 days. It may be kept for up to one hour at room temperature (15-25°C).[8]

How safe is the Moderna vaccine?

Reactions (reactogenicity) are the immune system's response to the introduction of a foreign body and not a "mild form" of COVID-19. It is not possible for the vaccine to infect a person with COVID-19 or cause changes to human DNA.[22] Severe anaphylactic reactions to the *Moderna* vaccine appears to be very rare (2.5 cases per million doses).[28]

Reactogenicity can include local injection site pain, redness, swelling, and other more systemic symptoms such as fever, muscle soreness, fatigue, or headache.[8] Most reactions are mild (i.e. do not interfere with daily activities) and only last a day or two. Moderate to severe reactions (i.e. headache, fever/chills, fatigue) are very uncommon and usually also resolve in two to three days.[8]

In an un-peer reviewed pre-print, electronic health records for 31,029 vaccinated individuals and 30,933 matched unvaccinated individuals were examined revealing that vaccine-associated adverse effects for both *Pfizer* and *Moderna* were extremely rare and that vaccinated and unvaccinated individuals were seen in the clinic at similar rates within 21 days of the first or second actual or assigned vaccination date (first dose Odds Ratio = 1.14, 95% CI: 1.10-1.18; second dose Odds Ratio = 0.91, 95% CI: 0.86-0.96).[29] Incidence rates of all surveyed adverse effects were similar or lower in vaccinated individuals compared to unvaccinated individuals after either vaccine dose.[29]

Conclusion

All three COVID-19 vaccines approved for administration in Australia are safe and effective and have met the TGA's strict requirements. Each vaccine is being continuously monitored as the roll-out progresses. The *Moderna* vaccine will be the latest in the range of vaccines being administered in Australia, and like the *Pfizer* and *AstraZeneca* vaccines, has shown strong effectiveness for preventing severe illness, hospitalisation, and transmission reduction. While evidence for prevention of death is difficult to establish, it is reasonable that lower risk of severe illness, hospitalisation, and transmission also flow on to reducing risk of death. While the Delta variant appears to be more resistant to all of the vaccines, even one dose does appear to convey protection and with growing community transmission in Australia, the benefits of vaccination outweigh the risks for the vast majority of people in most circumstances. If you are concerned about receiving a vaccination, it is important to discuss this with your treating healthcare professional/s who will be able to provide evidence-based and personalised information and guidance.

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