COVID-19 Evidence Update

11 March 2021

Real world impact of vaccines and implications for COVID-19 control

To be read in conjunction with

Symptoms, Vaccination and Infectiousness (17 February 2021)

Executive Summary

This review covers the available evidence on the real-world effectiveness of SARS-CoV-2 vaccines, and the likely impact of vaccine roll-out on population protection and implications for COVID-19 restrictions.

Context: At the time of writing 312 million doses of vaccines had been administered worldwide (90m doses in the USA, 40m in the EU, 20m in the UK). Per capita vaccination rates are highest in Israel (over 100 doses per 100 people; the UAE, UK (35 doses per 100) and the USA (27 doses per 100).

State of the evidence: Evidence is emerging rapidly on the real-world impact of vaccine on symptomatic COVID-19, severe disease, hospitalisation and death, which complements the evidence of efficacy in clinical trials. Some data are published in very high-quality journal (The Lancet, NEJM, JAMA), and much is still in pre-print.

Real-world data from Pfizer/BioNTech (BNT162b2) and Oxford AstraZeneca (ChAdOx1) vaccine rollouts:

- Results from Israel indicate that vaccine effectiveness is consistent with clinical trials, although the exact rates vary due to timing of the study and methods used to assess effectiveness.
- In one study, vaccine effectiveness 7+ days after the second dose was 92% for positive PCR test, 94% for symptomatic COVID-19, 87% for hospitalisation, and 92% for severe disease [1].
- The divergence between vaccinated and unvaccinated groups in COVID-19 outcomes was not observed until approximately 12 days post-1st dose of vaccine, possibly due to the high level of infection in the community.
- Infections were still observed following vaccination but they had **significantly reduced viral loads** compared to matched unvaccinated controls, indicating that **viral shedding and contagiousness may be reduced** as well as severity of disease [7].
- Real-world data from the UK is also consistent with clinical trials and real-world data from Israel.
- Rollout of the Pfizer BioNTech and Oxford AstraZeneca vaccines in Scotland has led to a substantial fall in COVID-19 cases requiring hospital admission 28-34 days post-vaccination, by 85% and 94% respectively [13].
- A commentary published in JAMA reports that there is rapidly increasing evidence that fully vaccinated people likely pose **little risk of transmission to unvaccinated people** with the Pfizer/BioNTech or Moderna vaccines between 86% and 92% **effective against symptomatic and asymptomatic** SARS-CoV-2 infection [14].

Potential for sterilising immunity (i.e. prevent infection): Research is ongoing using animal models for a vaccine that can elicit sterilising immunity.

Simulation modelling of vaccine rollout

- UK and USA: Suggest that high efficacy vaccines with significant uptake will reduce the total number of infections, but it will be necessary to maintain non-pharmaceutical interventions for the foreseeable future due to the existing level of infection in the community.
- Modelling for Australia has not been done (published) and will be required to inform relaxing of COVID-19 controls because Australia's exposure to SARS-Cov-2 has been far less than most other countries

Conclusions: While data are limited, real world effectiveness of vaccines is in line with efficacy data in clinical trials. Evidence continues to grow that the vaccines may also reduce transmission.

Implications for SA: It is likely that widespread vaccination will enable staged relaxing of other COVID-19 control measures while maintaining effective control of case numbers. After frontline border, quarantine, aged and disability care residents and staff (Phase 1a) and their families and Australia's other most vulnerable populations (Phase 1b) are vaccinated, domestic COVID-19 controls could be eased. This is with the retention of international border controls and international quarantine to prevent introduction of new cases.

Suggested citation: Miller C, Dono J, Wesselingh S. (2021) Real world impact of vaccines and implications for COVID-19 control. SAHMRI, Adelaide, South Australia. https://www.sahmri.org/covid19/

Excerpt from
Symptoms, Vaccination and Infectiousness (17 Feb 2021)

Executive Summary

This review covers the available evidence on:

1. *Whether the degree of symptoms experienced by a COVID-19 case correlates to their degree of infectiousness and likelihood of spreading COVID-19 to others including their close contacts*
2. *The likely impact of COVID-19 vaccination on transmission potential in the community (i.e. 'sterilising immunity'), and whether the reduction in illness severity and symptoms is likely to impact on disease transmission risk.*

***State of the evidence**:*

- *There are multiple high quality systematic reviews investigating secondary attack rates (SAR) of SARS-CoV-2 and the predictors of infectiousness, including symptom status and severity of disease. Several studies report on specific symptoms (e.g. dry cough, fever) individually, but most studies differentiate cases based on presence/absence of any symptom (asymptomatic, pre-symptomatic, symptomatic – mild/moderate/severe).*
- *There are systematic reviews which report on viral RNA shedding, viral load and viable virus shedding (capable of transmission). Several of these studies also report on symptom status of cases.*
- *There are no peer-reviewed studies reporting on the impact of vaccination on transmission. There is one pre-print publication for each of Pfizer and Oxford-AstraZenica vaccines reporting early indications of predictors of infectiousness. Israel has a very high community vaccination rates and provides first real-world evidence of the impact of widespread vaccination.*

Overview:

- *Systematic reviews [a1-5] indicate that secondary attack rates (transmission) are significantly higher:*
  - *For symptomatic cases than asymptomatic cases (e.g. 18.0% vs 0.7% in households);*
  - *As severity of COVID-19 increases;*
  - *Increased age (older adults vs other adults and adults vs children)*
  - *With household contact, especially spouses, and with prolonged close contact. Risk of transmissions with household and family contacts are magnitudes of risk higher than with other close contacts (e.g. 3 x times higher).*
  - *In indoor environments (e.g. 18.7 x higher [a10]))*
- *Expectoration (expelling sputum) was associated with 4 times the odds of secondary infection in one study [a18].*
- *Studies [a13, a21] of cultivable (infectious or transmissible) virus indicate:*
  - *Risk of transmission is only present early and for a limited number of days post symptom onset (up to 9 days), duration may be extended with severity of illness and age.*
  - *However, viral shedding and positive PCR tests may persist.*
  - *There is a strong relationship between Ct value and ability to recover infectious (transmissible) virus.*

- *One pre-print study [a28] (Oxford-AstraZenica) reports on the **substantial impact of the vaccine on reduced PCR positivity in trial participants, indicating the vaccine may impact on transmission by reducing the number of infected people in the population.***
- *One pre-print study [a31] reports on Ct rates of positive qPCR test in real world setting (Pfizer, Israel), pre- and (early) post-population vaccination roll out. **Authors estimate vaccination is reducing viral load by 1.6 – 20 times with substantial potential to impact on transmission.***

Conclusion: Presence of symptoms and severity correlate with infectiousness/transmission of COVID-19. Early data suggest that vaccination will reduce severity and viral load; indicating potential to reduce transmission.

SUMMARY OF KEY EVIDENCE

Effectiveness of vaccines on preventing disease in real-world settings

Israel real world data

[1] Dagan, N., et al., *BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting.* **N Engl J Med**, 2021 DOI: 10.1056/NEJMoa2101765 [Feb 24].

- Israel; BNT162b2 (Pfizer/BioNTech) vaccine; Health services data, matched control study (n=596,618 in each group [vaccinated: unvaccinated])
- Vaccine effectiveness estimated **14-20 days after first dose**: positive PCR test=46%; symptomatic COVID-19=57%; hospitalisation=74%; severe disease=62%; death=72%
- Vaccine effectiveness estimated **21-27 days after first dose** (gradual shifting between first and second doses): positive PCR test=60%; symptomatic COVID-19=66%; hospitalisation=78%; severe disease=80%; death=84%
- Vaccine effectiveness estimated **7+ days after second dose**: positive PCR test=92%; symptomatic COVID-19=94%; hospitalisation=87%; severe disease=92%
- Effectiveness was slightly lower in persons with multiple co-existing conditions
- Estimated effectiveness for the asymptomatic proxy was 29% (14-20 days after 1st dose), 52% (21-27 days after 1st dose) and 90% (7+ days after second dose)
- **Key points: findings were consistent with randomised trial; the cumulative incidence of symptomatic COVID-19 began to diverge between the two groups around day 12 after the first dose (Note: high background transmission likely influenced results in first 12 days)**

[2] Amit, S., et al., *Early rate reductions of SARS-CoV-2 infection and COVID-19 in BNT162b2 vaccine recipients.* **The Lancet**, 2021. 397: p. 875-877 DOI: 10.1016/s0140-6736(21)00448-7 [Mar 6].

- Israel; BNT162b2 (Pfizer/BioNTech) vaccine; Health services data; retrospective cohort of 9109 vaccine-eligible Health Care Workers, comparing vaccinated versus unvaccinated.
- Overall, there were 170 SARS-CoV-2 infections among HCWs in the period between 19 Dec 2020, and 24 Jan 2021, of which 99 (58%) HCWs reported symptoms and were designated as COVID-19 cases. Of the 170 HCWs who became infected, 89 (52%) were unvaccinated, 78 (46%) tested positive after the first dose, and three (2%) tested positive after the second dose.
- For all COVID-19 positive cases: Adjusted rate reductions of SARS-CoV-2 infections (vaccinated compared to unvaccinated) were 30% (95% CI 2–50) and 75% (72–84) for days 1–14 and days 15–28 after the first dose, respectively
- For all symptomatic COVID-19 cases: Adjusted rate reductions of COVID-19 disease were 47% (95% CI 17–66) and 85% (71–92) for days 1–14 and days 15–28 after the first dose, respectively.

[3] Abu Jabal, K., et al., *Impact of age, ethnicity, sex and prior infection status on immunogenicity following a single dose of the BNT162b2 mRNA COVID-19 vaccine: real-world evidence from healthcare workers, Israel, December 2020 to January 2021.* **Euro Surveill**, 2021. 26 DOI: 10.2807/1560-7917.ES.2021.26.6.2100096 [Feb]

- Israel; BNT162b2 (Pfizer/BioNTech) vaccine; n=514
- A single dose of the BNT162b2 mRNA COVID19 vaccine was immunogenic in the vast majority (92%) of our study cohort 21 days post vaccination, a result compatible with trial data

[4] Chodick, G., et al. *The Effectiveness of the First Dose of BNT162b2 Vaccine in Reducing SARS-COV-2 Infection 13-24 Days After Immunisation: Real-World Evidence.* medRxiv, 2021. 160: p. 106-111 DOI: 10.1101/2021.01.27.21250612 [Jan]. **(preprint)**

- Israel, BNT162b2 (Pfizer/BioNTech) vaccine; Health services data, retrospective cohort study
- Estimate the short-term effectiveness of the first dose of the BNT162b2 vaccine. The cumulative incidence of SARS-CoV-2 infection was 0·57% (n=2484) during days 1-12 and 0·27% (n=614) in days 13-24. This equates to an effectiveness rate of 51% 13-24 days after the first dose (compared to the first 12 days).
- The decrement in incidence was evident from day 18 after first dose.

[5] Hunter, P.R., et al., *Estimating the effectiveness of the Pfizer COVID-19 BNT162b2 vaccine after a single dose. A reanalysis of a study of 'real-world' vaccination outcomes from Israel."* medRxiv, 2021 DOI: 10.1101/2021.02.01.21250957 **(preprint)**

- Re-analysis of data from Chodick paper
- At day 14 there was no apparent effect of the vaccine but from then on until day 21 the effectiveness reached 91% (90% credible intervals: 83 to 98%). After then the effectiveness levelled off, and case numbers became quite low.

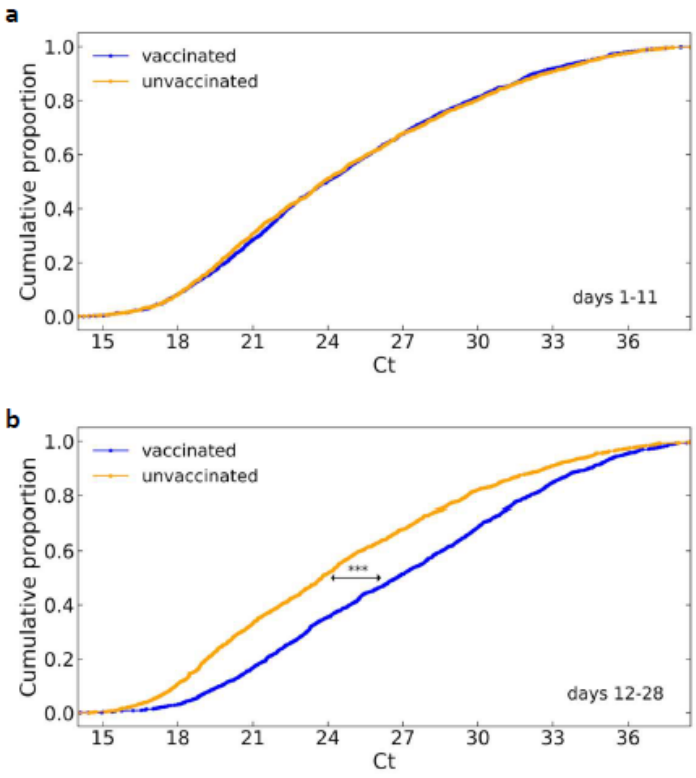
[6] Aran, D., *Estimating real-world COVID-19 vaccine effectiveness in Israel using aggregated counts.* medRxiv, 2021 DOI: 10.1101/2021.02.05.21251139 [23-Feb-2021]. **(preprint)**

- Under an assumption of no effectiveness on the first two weeks after the 1st dose, the authors observe very low effectiveness on the third week. After the 2nd dose, on weeks 1 and 2 we find 73-85% effectiveness in reducing positive cases, hospitalizations, and severe cases, which increase to 89-97% effectiveness 14 days after the 2nd dose.
- The authors note they cannot differentiate between the possibility that the 1st dose is effective but only after three weeks, or that the vaccine is only protective following the 2nd dose of the vaccine.

Studies measuring differences in PCR and antibody tests based on vaccination status

[7] Levine-Tiefenbrun, M., et al., *Decreased SARS-CoV-2 viral load following vaccination.* medRxiv, 2021 DOI: 10.1101/2021.02.06.21251283 [8-Feb-2021]. **(preprint)**

- Israel, BNT162b2 (Pfizer/BioNTech)
- Retrospectively collected and analyzed the RT-qPCR test measurements of the 3 viral genes for positive post-vaccination tests performed at MHS central laboratory between 23 December 2020 and 25 January 2021 (n=2,897 patients). Used matched unvaccinated controls.
- Our results show that infections occurring 12 days or longer following vaccination have significantly reduced viral loads, potentially affecting viral shedding and contagiousness as well as severity of the disease.



[8] Petter, E., et al., *Initial real world evidence for lower viral load of individuals who have been vaccinated by BNT162b2.* medRxiv, 2021 DOI: 10.1101/2021.02.08.21251329 [8-Feb-2021]. **(preprint)**

- Israel, BNT162b2 (Pfizer/BioNTech)
- Looking for signs of transmission reduction by vaccines, the authors sought to analyze the Ct value of positive qPCR tests collected between 1 December to 1 February 1st 2021, used age and date to infer vaccination as health information was not available.
- Estimate suggests that vaccination reduces the viral load by 1.6x to 20x in individuals who are positive for SARS-CoV-2. This estimate might improve after more individuals receive the second dose.

[9] Grupel, D., et al., *Kinetics of SARS-CoV-2 anti-s IgG after BNT162b2 vaccination.* medRxiv, 2021 DOI: 10.1101/2021.03.03.21252844 [5-Mar-2021]. **(preprint)**

- In our cohort of Israeli healthcare workers (n=116), a robust antibody response (anti-s IgG) is demonstrated, starting roughly two weeks after the first dose of BNT162b2 and peaking around day 30 (approximately 10 days after the second dose).
- Decline is slow after peaking, though data was limited to six weeks.

Modelling study estimating impact on transmission

[10] Lipsitch, M., et al., *Interpreting vaccine efficacy trial results for infection and transmission.* medRxiv, 2021 DOI: 10.1101/2021.02.25.21252415 [Feb 28]. **(preprint)**

- The impact of a vaccine on transmission is a composite of its effect on becoming infected (because someone not infected cannot transmit) and its effect on the infectiousness of those who get infected despite vaccination: these components have been called the vaccine efficacy for susceptibility to infection and vaccine efficacy for infectiousness [7].

- Here we describe the results of simulations of randomized trials that are designed to clarify what information is gained by swabbing individuals for viral infection, how this relates to other measures of vaccine efficacy, and what information is present in measures combining different reasons for sampling (no symptoms vs. symptoms). This approach estimates these vaccines' effects on viral positivity, a prevalence measure which under reasonable assumptions forms a lower bound on efficacy against transmission.
- Our main findings are as follows: first, that a single cross-sectional comparison of PCR positivity odds between individuals in vaccine vs. control groups provides a relatively accurate estimate, subject to sampling error, of vaccine effectiveness against viral positivity, which is a composite of effects in reducing susceptibility to infection and in reducing duration.
- Applying this approach to published data from the RCT of the Moderna vaccine, we estimate that one dose of vaccine reduces the potential for transmission by at least 61%.
- **This study supports the use of PCR positive tests as an indicator for assessing transmission following vaccination**

UK real world data

[11] Bernal, J.L., et al., *Early effectiveness of COVID-19 vaccination with BNT162b2 mRNA vaccine and ChAdOx1 adenovirus vector vaccine on symptomatic disease, hospitalisations and mortality in older adults in England.* medRxiv, 2021 DOI: 10.1101/2021.03.01.21252652 (**preprint**)

- UK; BNT162b2 (Pfizer/BioNTech) & ChAdOx1 (Astrazeneca) vaccines; Test negative case control design, community setting among adults aged 70 years and over
- A **single dose** of the **BNT162b2** vaccine is approximately 60-70% effective at preventing symptomatic disease in adults aged 70 years and older in England and 2 doses are approximately 85-90% effective. Those vaccinated who went on to become a symptomatic case had a 44% lower risk of hospitalisation and a 51% lower risk of death compared to unvaccinated cases.
- The effect of a **single dose of the ChAdOx1** vaccine against symptomatic disease was approximately 60-75% and there was again an additional protective effect against hospitalisation, though it is too early to assess the effect and mortality.

[12] Hall, V., et al., *Effectiveness of BNT162b2 mRNA Vaccine Against Infection and COVID-19 Vaccine Coverage in Healthcare Workers in England, Multicentre Prospective Cohort Study (the SIREN Study).* **SSRN**, 2021 [22-Feb-2021].

- UK; BNT162b2; prospective cohort study in Health Care Workers (HCW), n=23,324. Regular (2-wk intervals) PCR testing and monthly antibody testing, of HCW, not just symptomatic cases
- A **single dose of BNT162b2** vaccine demonstrated vaccine effectiveness of 72% (95% CI 58-86) 21 days after first dose and 86% (95% CI 76-97) seven days after two doses in the antibody negative cohort.
- Following the first dose, there was a significant protection from infection increasing from day 10 onwards, and plateauing after 21 days
- In the **vaccinated group**, 21 days after the **first dose**, there were **71 new infections** (incidence density 8 per 10,000 person-days of follow-up) and **9 new infections** seven days after the **second dose** (incidence density of 4 per 10,000 person days of follow-up); **32 (40%) had classic COVID-19 symptoms, 13 (16%) had other symptoms, 10 (13%) were asymptomatic and 25 (31%) did not complete the symptom status questionnaire for the time period.**

[13] Vasileiou, E., et al., *Effectiveness of first dose of COVID-19 vaccines against hospital admissions in Scotland: national prospective cohort study of 5.4 million people.* SSRN, 2021 [19-Feb-2021]. **(preprint)**

- A prospective cohort study using a database comprising of linked vaccination, primary care, RT-PCR testing, hospitalisation and mortality records for 5.4 million people in Scotland.

- The first dose of the BNT162b2 vaccine was associated with a vaccine effect of 85% (CI 76-91) for COVID-19 related hospitalisation at 28-34 days post-vaccination.
- The vaccine effect at the same time interval for the ChAdOx1 vaccine was 94% (CI 73-99).

Commentary on real world impact on asymptomatic infection and transmission

[14] Christie A, et al. CDC Interim Recommendations for Fully Vaccinated People: An Important First Step. **JAMA**. Published online March 10, 2021. doi:10.1001/jama.2021.4367

- Reports on US Centers for Disease Control and Prevention (US CDC) advice to vaccinated people as well as early transmission data from Israel, UK and USA.
- CDC has released its initial public health recommendations for fully vaccinated people (individuals who are at least 2 weeks out from having received their second Pfizer-BioNTech or Moderna vaccine dose, or from their Janssen single-dose vaccine).
- Preliminary but rapidly increasing evidence suggests that fully vaccinated people likely pose little risk of transmission to unvaccinated people.
- Studies from the **US, UK, and Israel found that 2 doses of Pfizer-BioNTech or Moderna** vaccines were **86% to 92% effective against asymptomatic and symptomatic** SARS-CoV-2 infection.
- More specifically, studies from **Israel** demonstrated that the **Pfizer-BioNTech** COVID-19 vaccine was **90% effective against asymptomatic infection**, and vaccinated people who developed COVID-19 had a **substantially lower viral load** than unvaccinated people.
- Viral load has been identified as a key driver of transmission and **this observation may indicate reduced transmissibility.** Collectively, these findings demonstrate that vaccination has the potential to substantially reduce the COVID-19 disease burden in the US.

The potential for a vaccine to achieve protective/sterilising immunity

Review

[15] Kim, D.S., et al., *Will SARS-CoV-2 Infection Elicit Long-Lasting Protective or Sterilising Immunity? Implications for Vaccine Strategies (2020).* **Front Immunol**, 2020. 11: p. 571481 DOI: 10.3389/fimmu.2020.571481

- Emerging evidence from recent SARS-CoV-2 reports, combined with literature from nearly two decades of SARSCoV research, provide good reason to believe that it should be possible to generate protective immunity against SARS-CoV-2 in humans, either following natural infection or with a vaccine.
- Whether natural infection will induce a humoral and cell-mediated immune response that provides long-lasting protection against reinfection, and how this compares with the immune response generated by vaccination, and whether the inflammatory response will impair the proper formation of a memory compartment currently remains unknown.

Commentary

[16] Peiris, M., et al., *What can we expect from first-generation COVID-19 vaccines?* **The Lancet**, 2020. 396: p. 1467-1469 DOI: 10.1016/s0140-6736(20)31976-0

- Given an initial reproduction number of around 2·2,1 which has since been revised to as high as about 4, and taking into account overdispersion of infections, perhaps about **25–50% of the population would have to be immune to the virus to achieve suppression of community transmission**.
- Challenge studies in vaccinated primates showed reductions in pathology, symptoms, and viral load in the lower respiratory tract, but failed to elicit sterilising immunity in the upper airways. Sterilising immunity in the upper airways has been claimed for one vaccine, but peer-reviewed publication of these data are awaited. [From Novavax press release (4 Aug 2020), stating that sterile immunity that prevented viral

replication in the upper and lower respiratory tracts was observed in the Non-Human primates macaques; this information was also cited in the Keech paper).

- These observations suggest that we cannot assume COVID-19 vaccines, even if shown to be effective in reducing severity of disease, will reduce virus transmission to a comparable degree. The notion that COVID-19-vaccine-induced population immunity will allow a return to pre-COVID-19 "normalcy" might be based on illusory assumptions.
- Crucially, it will be important to communicate to policy makers and the general public that first-generation vaccines are only one tool in the overall public health response to COVID-19 and are unlikely to be the ultimate solution that many expect.

The quest for a vaccine that confers sterilising immunity is ongoing, with some studies (pre-prints) suggesting that it has been observed in animals [17-19].

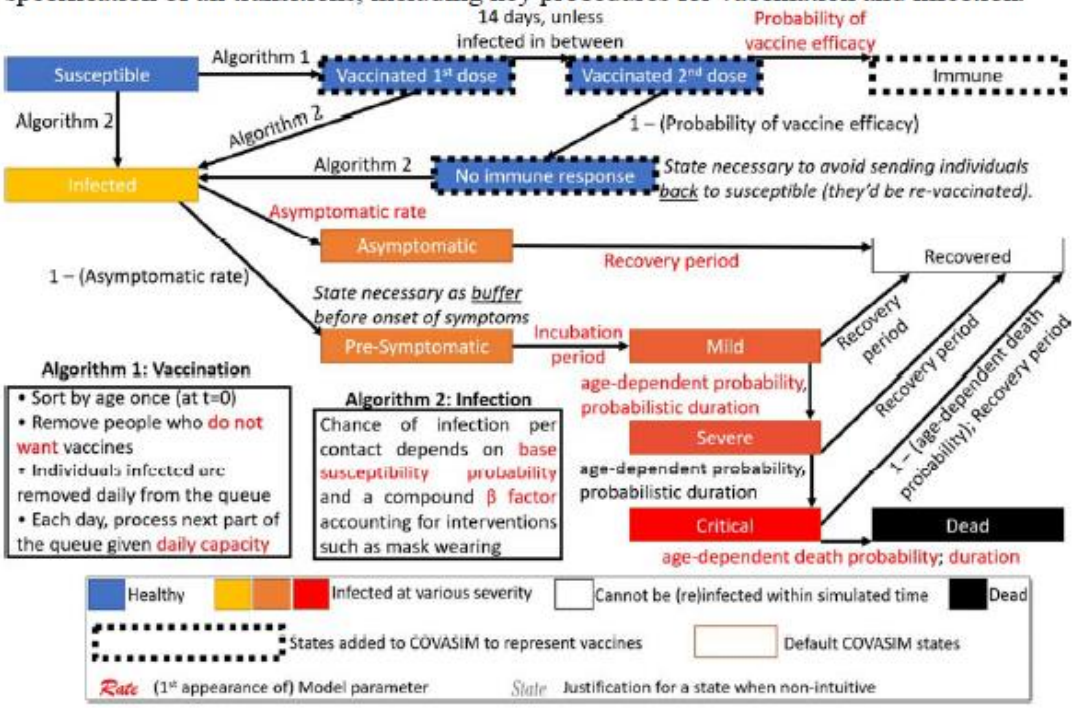
Simulation modelling of vaccine rollout in UK and USA

[Note: potentially less relevant for Australia due to high level of existing infection in UK and USA]

[20] Li, J., et al., *Returning to a normal life via COVID-19 vaccines in the USA: a large-scale agent-based simulation study.* medRxiv, 2021 DOI: 10.1101/2021.01.31.21250872 [3-Feb-2021]. **(pre-print)**

- US; In early 2021, two vaccines were deployed (Pfizer-BioNTech and Moderna) with plans for up to three additional vaccines (AstraZeneca, Janssen, Novavax)
- Used large-scale simulations to identify *when* there will be an inflection point in the dynamics of the disease, and the *level* of cases that will be obtained
- By adding vaccines to a previously validated Agent Based Model (ABM) of COVID-19, we are able to assess how the number and timing of cases depends on key factors such as the population's interest in vaccines and the efficacy of vaccines.
    - We extend the validated COVASIM model with a detailed process of vaccination, accounting for vaccine efficacy, interest in vaccination, and fluctuations in vaccination capacity. Our process models the need for two doses and the possibility of being infected until the second dose is administered.
    - We examine vaccination interventions under two hypotheses for the number of doses available and considering concurrent non-pharmaceutical interventions.

Figure 1. Overview of our modified COVASIM model containing the state diagram and specification of all transitions, including key procedures for vaccination and infection.



- Regarding our approach to vaccine efficacy, we note that individuals can be infected after their first dose, as has been documented on thousands of cases. We thus only apply the probability of vaccine efficacy only after the 2nd dose.

Table 3. Vaccine parameters used in the study. Intermediate values in the interval bounded by the low and high values are automatically explored.

	Low Value	High Value
Vaccine Compliance	20%	60%
Vaccine Efficacy	88%	99%

- The authors note that even if a small fraction of the population seeks vaccines, and even if vaccines are less effective than announced, the vaccination campaign can reduce the total number of infections. Note that increasing the efficacies of vaccines results in lower infections for all scenarios and vaccine plans.
- The authors note that their model is *built very specifically for the USA.*
- Key findings: the authors demonstrate the **necessity to maintain non-pharmaceutical interventions over the next six months**. As interventions are relaxed (from scenario 1 offering the most control to scenario 6 offering no control), there is an increase in case count such that a return to normalcy is not achieved through vaccination but rather through a very high number of infected individuals. Also, there is an unexpected interplay between vaccination strategies, non-pharmaceutical interventions, and vaccination availabilities.

[21] Moore, S., et al., *Vaccination and Non-Pharmaceutical Interventions: When can the UK relax about COVID-19?* medRxiv, 2021 DOI: 10.1101/2020.12.27.20248896 [26-Jan-2021]. **(pre-print)**

- Used an age-structured mathematical model, matched to a range of epidemiological data in the UK, that also captures the roll-out of a two-dose vaccination programme targeted at specific age groups

- Our predictions highlight the population-level risks of early relaxation leading to a pronounced wave of infection, hospital admissions and deaths. Only vaccines that offer high infection-blocking efficacy with high uptake in the general population allow relaxation of NPIs without a huge surge in deaths.
- While the novel vaccines against SARS-CoV-2 offer a potential exit strategy for this outbreak, this is highly contingent on the infection-blocking (or transmission-blocking) action of the vaccine and the population uptake, both of which need to be carefully monitored as vaccine programmes are rolled out.
- Throughout, we assume 95% uptake in care homes, 85% elsewhere above the age of 50 and 75% below the age of 50 for dose 1, dropping to 75% and 66% for above and below 50 respectively for dose 2. In practice, vaccination is also likely to be highly correlated within households and socio-demographic groups, which will weaken the population-scale impact of any infection blocking 76 by the vaccine.
- We use a 2-dose model to simulate the impact of vaccination in both reducing infection (and hence onward transmission) and in reducing symptomatic disease. We assume that delivery of the second dose is prioritised over new first doses, with a minimum day delay between doses.
- **The role of vaccines in blocking infection, and hence onward transmission, is less clear so we consider a range of infection efficacy from 0% to 85%, which we assume operates by preventing primary infection. We note that the disease efficacy takes into account both infection blocking and the reduction of severe symptoms if infection does occur.**
- Here we have shown that high efficacy vaccines that provide a substantial level of infection blocking offer a means of eventually relaxing controls without suffering a large subsequent wave of hospitalisations and deaths. Our conclusions rely on not only the vaccine characteristics but also upon the uptake in the population.
- Early relaxation of non-pharmaceutical interventions (NPIs), before sufficient immunity has been established is shown to precipitate a large wave of infection with resultant hospital admission and deaths; a similar impact is predicted from any final release of NPIs if herd immunity has not been achieved.

Vaccine impact on those previously exposed to COVID-19

[Note: of lesser relevance for Australia]

[22] Demonbreun, A.R., et al., *Comparison of IgG and neutralizing antibody responses after one or two doses of COVID-19 mRNA vaccine in previously infected and uninfected persons.* medRxiv, 2021 DOI: 10.1101/2021.03.04.21252913 **(pre-print)**

- US; BNT162b2/Pfizer and mRNA-1273/Moderna
- Following the initial phase of vaccine deployment it has been suggested that two doses of currently available mRNA vaccines are not necessary for individuals previously diagnosed with COVID-19, and for those who test seropositive for SARS-CoV-2.
- The authors document strong antibody responses to the first vaccine dose among individuals with confirmed cases of COVID-19, consistent with recent reports. The authors document a pattern of mild and heterogeneous responses to the first dose among individuals previously unexposed to SARS-CoV-2, with more robust responses following the second dose, consistent with clinical trials data. Importantly, **responses in the seropositive group** suggest that immunity following the first vaccine dose is significantly lower than the **convalescent COVID-19 group**. And like the **seronegative group**, two doses are required for the seropositive group to attain a level of protection that is comparable to the COVID-19 group.

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