What vaccination coverage is required before public health measures can be relaxed in Australia?

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Word count: 1,500

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Keywords/attributes: COVID-19; infectious disease; epidemiology; vaccination; public health

Abstract

In July 2021, the Australian Government announced a national plan to transition its response to the coronavirus disease 2019 (COVID-19) pandemic from the current goal of suppression of community transmission, to managing COVID-19 like other common respiratory pathogens. We modelled the likely morbidity and mortality expected to eventually result from prematurely relaxing lockdowns and/or fully reopening Australia's international border at various levels of vaccination coverage. We find substantial morbidity and mortality is likely to occur with the Government's target of vaccinating 80% of Australians aged ≥16 years, and that vaccinating more than 90% of the total population is highly desirable.

Summary Box

What is known about the subject?

- The Australian Government plans to transition its response to the COVID-19 pandemic to a post-vaccination phase where COVID-19 would be managed similar to other infectious disease. Public health outcomes of vaccination levels from 50% to 100% of the adult population are compared under the final phase of this plan (or from premature relaxation of public health measures).

What are the new findings?

- Symptomatic cases, morbidity, and mortality are modelled with and without: vaccinating children; achieving 95% vaccination in those aged ≥60 years; and giving an mRNA vaccine booster to persons who previously received the ChAdOx1-S vaccine.
- 114,000 hospitalisations and 25,000 deaths are projected to occur with the Australian Government's Phase C vaccination target of 80% of Australians aged ≥16 years, assuming this target is maintained for Phase D (the final post-vaccination phase).
- 18,000 hospitalisations and 5,000 deaths are projected if 90% vaccination coverage is achieved in children, adolescents, and adults (with 95% coverage in those aged ≥60 years), an mRNA vaccine booster is given to persons who previously received the ChAdOx1-S vaccine, and future booster doses are used in the entire population as required, to mitigate waning immunity.

What are the recommendations for policy and practice?

- It is important to (a) start from transparent 'maximum tolerable' levels of morbidity and mortality, including long COVID cases, determined by policymakers, not vaccination coverage; (b) identify minimum vaccination levels for the total population and vulnerable groups required to achieve these public health goals, noting that

vaccination levels and relaxation criteria should be fully informed by comprehensive risk analyses, accounting for scientific uncertainty in key parameters; and (c) fully evaluate public health and economic trade-offs at different vaccination rates.

Introduction

In July 2021, the Australian Government announced a national plan to transition Australia's response to the coronavirus disease COVID-19 pandemic to a post-vaccination phase with a vaccination target of 80% of persons aged ≥16 years for the penultimate Phase C.[1] When the final Phase D is reached, COVID-19 would be managed like other common respiratory pathogens, akin to 'living with the virus like the flu', and the international border would reopen.

Australians can receive one of two COVID-19 vaccines. Those aged between 16-59 years can receive the Pfizer (Comirnaty) vaccine, to mitigate a rare thrombosis with thrombocytopenia syndrome associated with the AstraZeneca (ChAdOx1-S) vaccine, and limited supplies of Comirnaty.[2] Those aged ≥60 years can receive the ChAdOx1-S vaccine. A small proportion of people aged <60 years previously received ChAdOx1-S, and those living in areas affected by an outbreak can also receive ChAdOx1-S.[3] The Government expects sufficient supplies of Comirnaty to be available for all before the end of 2021, supplemented by 10 million doses of the Moderna (Spikevax) vaccine.[4 5] While all these vaccines offer high protection against severe disease, they differ in effectiveness.[6]

We calculated the morbidity and mortality likely to eventually result from managing COVID-19 at different levels of vaccination coverage based on a susceptible-infectious-recovered (SIR) model which assumes homogeneous mixing, detailed in Supplementary Material. We also evaluated the effects of including children and adolescents in the vaccination rollout, noting this age cohort may play a greater role in transmission than with the original strain. Further, we assessed the outcomes of providing a booster dose of an mRNA vaccine to those fully vaccinated with ChAdOx1-S.

Key assumptions

All Australians will eventually be exposed, from either border reopening or an uncontrolled outbreak, to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Depending on public health measures, this may take a few months or a few years. We assumed infections in the unvaccinated population would continue until herd immunity is reached by a combination of vaccination and infection-acquired immunity, and that such infections would be with a variant at least as transmissible as the Delta variant (B.1.617.2), with an estimated basic reproduction number (R_0) of 6.[7]

We assumed Australia would maintain its current vaccination strategy, such that older Australians primarily receive ChAdOx1-S, while most younger people receive an mRNA vaccine. We call this the AZ-mRNA strategy. We compared this to an alternative where those who received two doses of ChAdOx1-S are subsequently given a single booster dose of an mRNA vaccine. We call this the mRNA strategy, and assume those receiving the booster have at least the same protection as if they received two doses of an mRNA vaccine. Assumed vaccine effectiveness is based on observed data.[8]

We considered different age distributions of vaccination uptake. In the "95% 60+" scenarios we assumed 95% of Australians aged ≥60 years are vaccinated, but the proportion vaccinated is lower in those aged <60 years. In the "equal" scenarios, we assumed the proportion vaccinated is the same in all age groups. Further, we examined scenarios where children and adolescents aged ≤15 years are vaccinated at the same proportion as young adults, or remain unvaccinated. For the "95% 60+" scenarios, adults aged <60 years have vaccination levels lower than the overall adult average.

Cumulative projections

We found herd immunity is achieved if ≥95% of the entire population is vaccinated. Using infection fatality rates (IFR) for the original strain,[9] we estimated that if 70% (or 80%) of adult Australians (excluding children <16 years) were fully vaccinated, but with a 95% vaccination level for those aged ≥60 years, the AZ-mRNA strategy would eventually result in some 6.9 million (or 5.5 million) symptomatic COVID-19 cases (Figure 1A), 154,000 (or 114,000) hospitalisations (Figure 1B), and 29,000 (or 25,000) fatalities (Figure 1C).

Morbidity and mortality were improved by higher levels of adult vaccination coverage and if children and adolescents were vaccinated in the same proportion as adults aged <60 years. When children are vaccinated, fatalities are reduced to 19,000 at 80% adult vaccination coverage and to 10,000 at 90% adult vaccination coverage. For 80% adult vaccination coverage, with children also vaccinated, adopting the mRNA strategy, rather than the AZ-mRNA strategy, prevented 6,000 fatalities (30%) and 13,000 hospitalisations (17%) (Figure 1D).

High mortality occurs among vulnerable vaccinated people unless a very high proportion of the entire population is vaccinated. As shown in Figure 2, under the AZ-mRNA strategy, approximately 14,000 deaths are expected among vaccinated persons aged ≥60 years even if 70% of the overall adult population is vaccinated (with 95% coverage in those ≥60 years). Ensuring that 95% of those aged ≥60 years are fully vaccinated avoids, in total, about 43,000 fatalities under the AZ-mRNA vaccination strategy at a 70% adult vaccination level (Figure 1C). Switching to the mRNA strategy would approximately halve mortality among vaccinated persons aged ≥60 years (Figure 2). Vaccinating both children and adolescents

would prevent 10,000 fatalities among vaccinated persons aged ≥60 years, even after 100% of the adult population is vaccinated (Figure 2).

Findings in context

The Grattan Institute has modelled the effects of vaccinating at least 80% of the entire Australian population by the end of 2021.[10] They find premature relaxation of restrictions – even at 70% coverage – would likely result in rapid, widespread community transmission that would overwhelm health systems. Similarly, Burnet Institute modelling suggested that if restrictions are dropped before herd immunity is reached, thousands of fatalities are likely to occur, 45% of which can be expected within the vaccinated population.[11]

The Doherty Institute estimated that if 80% of those aged ≥16 years are vaccinated (64% of the total population) there could be between 10,000-16,000 hospital admissions and 1,300 to 2,300 deaths over 180 days from a seeding event of the virus.[12] Their findings of relatively low morbidity and mortality arise, in part, from: their 180 days modelling time horizon; a low assumed proportion of symptomatic infections (<30% for those aged <30 years and <50% for all those <60 years of age); assumed low transmission among children; baseline Public Health Service Measures (PHSM) that reduce the reproduction number from 6.32 to 3.6; and their assumption that Test, Trace, Isolate and Quarantine (TTIQ) remains partially effective even at very high new daily cases.

Projected morbidity and mortality would have been much higher if we had used preliminary estimates of the virulence of the Delta variant.[13] Our reported results are likely a lower cumulative bound of public health outcomes because they: ignore possible overshoot of herd immunity in an uncontrolled outbreak; assume immunity wanes relatively slowly; are based

on age-dependent hospitalisation and fatality rates for the original strain; assume 95% of those aged ≥60 years are fully vaccinated *prior* to relaxation of public health measures and the international border reopening; and only consider the acute phase of infection, noting that people hospitalised during the first wave in the United Kingdom were subsequently 4 times more likely to be readmitted to hospital and 8 times more likely to die than a matched control group.[14] Our results also do not include indirect deaths resulting from healthcare disruption or morbidity from long COVID. If only 5% of symptomatic cases develop long COVID (which can also occur in vaccine breakthrough infections)[15] some 270,000 Australians could be affected assuming only 80% of those aged ≥16 years are vaccinated with the AZ-mRNA strategy.

Key parameters, especially Delta variant hospitalisation and fatality rates and vaccine effectiveness, are subject to considerable uncertainty. Thus, our projections may change as parameter estimates are updated.

Conclusions

Under its National Plan, Australia plans to transition to Phase C, with reduced public health measures and recourse to lockdown only in exceptional circumstances, after achieving 80% vaccination coverage for those aged ≥16 years. Our results suggest that transitioning to Phase D at the *same level* of vaccination coverage accompanied by a cessation of public health measures could lead to approximately 50,000 fatalities – multiples of the annual fatalities from influenza in Australia – and 270,000 cases of long COVID. These health impacts could be reduced to approximately 5,000 fatalities and 40,000 cases of long COVID if four key vaccination criteria were attained prior to Phase D:

1. Children and adolescents are vaccinated.

2. Vaccine coverage among adults aged ≥60, and other vulnerable groups (including Indigenous Australians), is ≥95%.
3. Persons vaccinated with ChAdOx1-S are given an mRNA booster; and
4. Vaccination coverage for the entire population is ≥90%.

A robust vaccination and transition strategy should also:

1. Start from transparent 'maximum tolerable' levels of morbidity and mortality, including long COVID cases, determined by policymakers, not vaccination coverage;
2. Identify minimum vaccination levels for the total population and vulnerable groups required to achieve these public health goals, noting that vaccination levels and relaxation criteria should be fully informed by comprehensive risk analyses, accounting for scientific uncertainty in key parameters; and
3. Fully evaluate public health and economic trade-offs at different vaccination rates.

The consequences of significantly relaxing public health measures prematurely could prove to be irreversible and unacceptable and prevent Australia from obtaining a safe and affordable path to a 'post-COVID-19' era.

Contributors

Each author contributed equally to the manuscript.

Funding

The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests

The authors have no competing interests or relevant disclosures.

Patient consent for publication

Not required.

Data availability statement

Data are available at a public, open access repository at: https://osf.io/6j4rd/

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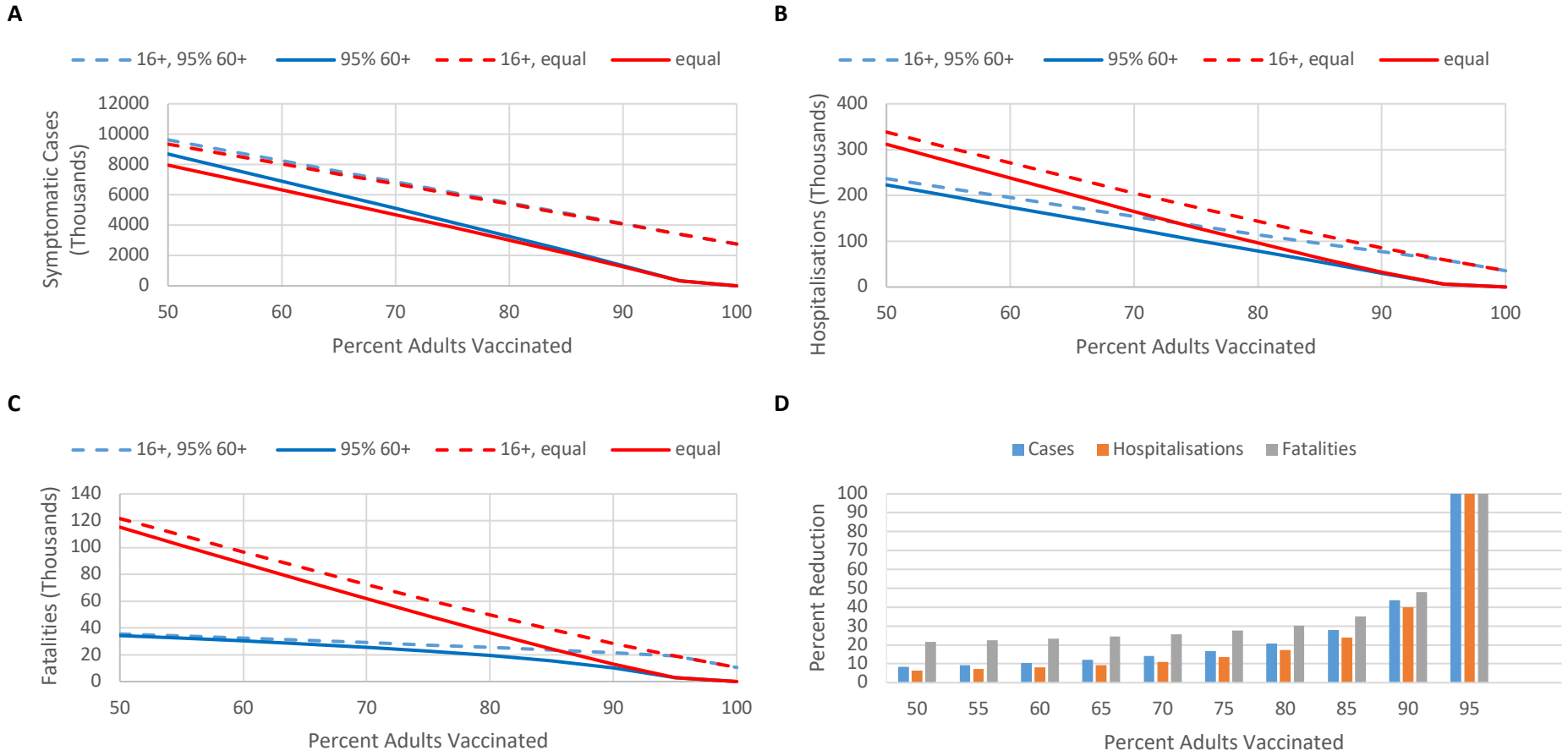
Figures

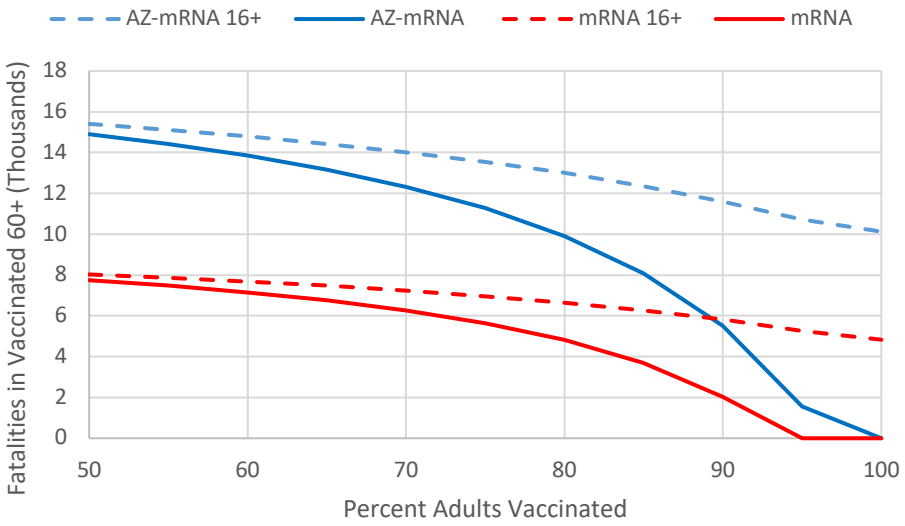
Figure 1. Projected symptomatic cases (A), hospitalisations (B), and fatalities (C) under Australia's AZ-mRNA vaccination strategy, and proportion of outcomes that could be prevented with the mRNA vaccination strategy (D), at various vaccination levels.



Note: Blue lines denote a scenario where 95% of those aged ≥60 years are vaccinated, but younger age groups are vaccinated at a lower level (stepped scenario). Red lines denote an equal scenario with vaccination coverage uniform across age groups. Dashed lines show effects of

excluding children and adolescents (aged ≤15 years) from vaccination coverage. A stepped scenario, *including* children and adolescents aged ≤15 years, is shown in panel D.

Figure 2. Projected mortality in vaccinated persons aged ≥60 years at various levels of overall vaccination coverage



Note: Figure depicts a stepped scenario where 95% of persons aged ≥60 years are vaccinated, but vaccination coverage varies in other age groups. Blue lines denote the AZ-mRNA strategy. Red lines show the mRNA strategy. Dashed lines show the effect of *excluding* children and adolescents (aged ≤15 years) from vaccination coverage.

Supplementary Material

Methods

Under the assumption of homogeneous mixing, the reproduction number R is given by R0.S/N, where R0 is the initial reproduction number at 100% susceptibles, S represents remaining susceptibles, and N is the total population size. Herd immunity is reached when R equals 1, or S equals N/R0.

We assume that Australia returns to a pre-pandemic state, removing all international border controls and public health social distancing measures, after a fraction FV of the population has been vaccinated. We further assume that current measures to restrict COVID-19 outbreaks continue to be successful prior to opening, so the number of susceptibles removed by infection prior to that point is a negligible fraction of the total population. If VE^I is the average vaccine effectiveness against infection, the number of susceptibles remaining in the population after vaccination is $N.(1 – FV.VE^I)$, comprising $N.(1 - FV)$ unvaccinated, and $N.FV.(1 - VE^I)$ susceptible vaccinated.

If $N.(1-FV.VE^I)$ is less than N/R0, herd immunity has been achieved through vaccination. If not, then once border controls and public health measures are removed, we contend that sufficient new infections must eventually occur to reach or exceed herd immunity. If border controls and public health measures are removed abruptly before herd immunity is reached, there will be an uncontrolled outbreak. In an active outbreak, herd immunity marks the point where active cases stop growing, but further infections occur even as active cases decline, and the outbreak will overshoot herd immunity, leaving a number of remaining susceptibles $S < N/R0$. If sufficient control measures are retained to "flatten the curve", then infections will stop when S approximately equals N/R0. Thus, the number of infections required to reach herd immunity represents a conservative lower bound for the number of infections which must follow a return to pre-pandemic conditions.

If vaccinated infectives transmit the virus at the same rate as unvaccinated infectives, then herd immunity is reached when $N.(1 - FV.VE^I – 1/R0)$ have been infected. This represents a fraction FSI of the $N.(1 – FV.VE^I)$ susceptibles present post-vaccination, given by $FSI = 1 – 1/(R0.(1-FV.VE^I))$. We note there is evidence that, in the case of COVID-19, vaccinated infectives may be less effective at transmitting the virus than unvaccinated infectives.[1] If OR^T is the odds ratio for transmission by vaccinated infectives, it is possible to show that the fraction of initial susceptibles that need to be infected to reach herd immunity is given by:

$$FSI = 1 – 1/(R0.(1-FV.VE^T)), \quad (1)$$

where VE^T, the vaccine efficacy against transmission, is given by $1 – VE^T = OR^T.(1 – VE^I)$. The (minimum) number of infections post-vaccination is then $FSI.N.(1 – FV.\ VE^I)$.

In order to calculate the corresponding numbers of hospitalisations and deaths, it is necessary to resolve age classes, because hospitalisation and fatality rates from COVID-19 are highly age-dependent, and Australia's vaccination strategy discriminates according to age. We allow the fraction vaccinated FV_j to vary by age group j. If there are N_j individuals in age group j, FSI is calculated using the population total $FV = \Sigma\ FV_j.N_j / N$. Given our assumption of homogeneous mixing, all age groups are equally exposed, and the same proportion FSI of susceptibles is infected in each age group. Thus, the number of infected cases in age group j is:

$$NC_j = FSI.N_j.(1-FV_j.VE^I) \quad (2)$$

If a fraction FSY of infected cases are symptomatic, the number of symptomatic cases in age group j is:

$$NS_j = FSY.FSI.N_j.(1-FV_j.VE^S) \quad (3)$$

where VE^S is vaccine effectiveness against symptoms.

If CHR_j is the case hospitalisation rate for age class j (i.e., the fraction of symptomatic cases hospitalised), the number hospitalised in age class j will be:

$$NH_j = FSY.FSI.N_j.(1-FV_j.VE^H).CHR_j \quad (4)$$

where VE^H is vaccine effectiveness against hospitalisation.

If IFR_j is the infection fatality rate (*not* the case fatality rate) for age class j, and VE^D the vaccine effectiveness against death by COVID-19, the number of fatalities in age class j will be:

$$NF_j = FSI.N_j.(1-FV_j.VE^D).IFR_j. \quad (5)$$

These formulae apply for a vaccination strategy using a single vaccine. Australia is currently using two vaccines, AstraZeneca (ChAdOx1-S) and Pfizer (Comirnaty), with different effectiveness, and these vaccines are differentially available to different age classes. The effective population-wide effectiveness against transmission used to calculate FSI was calculated as the average of the effectiveness of the vaccines against transmission weighted by the numbers receiving them.

We define FV_{jk} as the fraction of individuals in age class j who receive vaccine k. The numbers of infected cases, symptomatic cases, hospitalisations and fatalities for age class j are then:

$$NC_j = FSI.N_j.(1-\Sigma_k FV_{jk}.VE^I_k); \quad (6)$$

$$NS_j = FSY.FSI.N_j.(1-\Sigma_k FV_{jk}.VE^S_k); \quad (7)$$

$$NH_j = FSY.FSI.N_j.(1-\Sigma_k FV_{jk}.VE^H_k).CHR_j; \quad (8)$$

$$NF_j = FSI.N_j.(1-\Sigma_k FV_{jk}.VE^D_k).IFR_j. \quad (9)$$

Sources of input data and parameters

Demographics.

The age distribution of Australians in 2019 was obtained from the Australian Bureau of Statistics (ABS). In our analysis, we have aggregated these into the age classes shown in Supplementary Table 1. The precise role of young children in transmitting SARS-CoV-2 is unclear, with some arguing they transmit at lower rates to adults, and others arguing there is no clinically meaningful difference.[2] However, there is increasing evidence that children play an important role in transmission of the Delta variant of SARS-CoV-2.[3-5] We have included children aged 0 to 11 in our analysis, and assumed they are as susceptible to infection and as likely to transmit as adolescents and adults.

Supplementary Table 1. Australian population numbers by age class.

Age class	0-11	12-15	16-29	30-39	40-49	50-59	60-69	70-79	80+
Number (,000s)	3826	1207	4879	3673	3274	3080	2613	1792	1021

Reproduction number and fraction symptomatic.

Our calculations focus on the Delta variant, which is now the dominant variant in most nations, including Australia. The reproduction number R0 for the Delta variant is estimated to be around 5.5 to 6.5.[6] We have used an intermediate value of 6.

We have set the proportion of adult and adolescent infected cases displaying symptoms, FSY, to 0.8.[7] We do assume a smaller fraction, 0.5, of infected cases among children display symptoms.[2]

Case hospitalisation rates and infection fatality rates.

Case hospitalisation rates by age class for the original strain and Alpha variant were reported by Nyberg et al.[8] Public Health England reported that hospitalisation rates for the Delta variant in England and Scotland were, respectively, 2.26 and 1.85 times those for Alpha.[9] We have applied a factor of 2 to Nyberg et al.'s estimates for Alpha to obtain case hospitalisation rates by age class for Delta (Supplementary Table 2). Nyberg et al.'s estimates of CHR for Alpha are approximately 1.5 times their estimates for the original strain of SARS-CoV-2, so our estimates for Delta are approximately 3 times our estimates for the original strain.

Based on a meta-analysis of data from many nations, Levin et al.[10] derived an equation relating infection fatality rate to age for the original strain: $\log_{10}(\text{IFR}) = -3.27 + 0.0524*\text{age}$. We have applied this equation to each year class, and then calculated population-weighted average IFR for each age class.

Based on Canadian data, Fisman and Tuite estimated that the fatality rate for Delta is 2.32 times the fatality rate for the original strain.[11] We have used this to scale up the age-dependent estimates from Levin et al.[10] The Levin et al. equation yields extremely high fatality rates for those aged over 80 years, especially when multiplied by the factor of 2.32 from Fisman and Tuite.[11] To avoid unreasonably high values, we have capped fatality rates in individual year classes at 30% when calculating the age class averages given in Supplementary Table 2.

Supplementary Table 2. CHR and IFR (percent) by age class.

Age class	0-11	12-15	16-29	30-39	40-49	50-59	60-69	70-79	80+
CHR Original	1.0	0.7	1.5	2.6	3.4	4.9	7.1	12.5	16.2
CHR Alpha	0.9	0.7	1.9	3.4	5.0	7.2	10.6	16.9	21.7
CHR Delta	1.8	1.4	3.8	6.8	10.0	14.4	21.2	33.8	43.4
IFR Original	0.001	0.003	0.009	0.036	0.123	0.408	1.334	4.257	17.009
IFR Delta	0.003	0.006	0.022	0.084	0.286	0.947	3.095	9.876	27.169

Given that there is still substantial uncertainty about the hospitalisation and fatality rates for the Delta variant, we have calculated outcomes using both the estimates for the original strain (as a likely lower bound, denoted CHR Original and IFR Original) and the larger estimates for the Delta variant (denoted CHR Delta and IFR Delta).

Vaccine effectiveness.

The estimates used for effectiveness against infection, symptoms, hospitalisation and death, and the odds ratio for transmission, for the ChAdOx1-S and Comirnaty vaccines and the Delta variant, are listed in Supplementary Table 3, along with the sources. We know of no published estimates of vaccine effectiveness against fatalities for the Delta variant. For the Comirnaty vaccine and the Alpha variant, Hass et al. reported vaccine effectiveness against hospitalisations and fatalities of 97.2% and 96.7% respectively, based on the mass vaccination program in Israel.[12] These estimates were statistically indistinguishable. We have, therefore, set the vaccine effectiveness against fatalities equal to the vaccine effectiveness against hospitalisation for the Delta variant.

There have been reports from Israel and elsewhere that vaccine effectiveness against Delta may wane substantially in the 6 months following infection.[13] The estimates in Supplementary Table 2 may then be over-optimistic, unless booster shots are used to maintain immunity. The estimates cited are for 2 doses of either vaccine, except with regard to the odds of transmission in breakthrough infections (OR^T), where only data for persons who received a single dose were available in the literature.[1]

It is possible that transmission may be reduced to a greater extent in breakthrough cases occurring in fully vaccinated persons. However, emerging evidence suggests that in contrast to ancestral strains, viral load may not be reduced in the initial stage of disease in vaccine breakthrough infections caused by the Delta variant of SARS-CoV-2,[14,15] although the duration of viral shedding may still be reduced.[16] If this preliminary evidence is confirmed, the estimate of the degree to which transmission is reduced (which is primarily based on the Alpha variant)[1] may instead be too large.

Supplementary Table 3. Estimates used in this study for vaccine effectiveness against the Delta variant

	ChAdOx1-S	**Comirnaty**	**Source**
VE^I (infection)	0.60	0.79	Sheikh et al.[17]
OR^T (transmission)	0.52	0.54	Harris et al.[1]
VE^S (symptomatic disease)	0.67	0.88	Stowe et al.[18]
VE^H (hospitalisation)	0.92	0.96	Stowe et al.[18]
VE^D (death)	0.92	0.96	= VE^H (See text).

Vaccine effectiveness is lower for ChAdOx1-S than Comirnaty. We assume that a single booster dose of an mRNA vaccine, administered after two standard doses of the ChAdOx1-S vaccine, can lift antibodies to levels matching or exceeding those produced by two doses of the Comirnaty vaccine. Evidence suggests a heterologous 2-dose combination of the ChAdOx1-S and Comirnaty vaccines might be superior to homologous dosing of the Comirnaty vaccine.[19] Thus, we assume that a 2-dose homologous series of the ChAdOx1-S vaccine followed by a mRNA booster dose would provide

protection that is at least on par with a homologous series of the Comirnaty vaccine. In addition to standard homologous scenarios reflecting the current rollout of the ChAdOx1-S and Comirnaty vaccines in Australia, we consider alternative scenarios in which all those who received ChAdOx1-S are assumed to receive an mRNA booster, and thereby enjoy vaccine effectiveness equivalent to that produced by 2 doses of Comirnaty.

Vaccination Scenarios

Age distribution.

We consider a range of levels of vaccination uptake among adult Australians (aged 16 years and older), from 50% to 100%. For each level, we consider 4 different age distributions of the vaccine, which involve two binary choices.

1. Percentage vaccine uptake is assumed to be equal across all adult age groups, or vaccine uptake is assumed to be 95% in the 60+ age groups. In the latter case, vaccination levels in younger adults are reduced so that the population average across all individuals aged ≥16 years matches the designated level. These choices are denoted in Figures as "equal" or "95% 60+", respectively.
2. Children and adolescents younger than 16 years may be unvaccinated, or vaccinated at the same rates as young adults. The former scenarios are denoted in Figures as "16+". Note that, in "95% 60+" scenarios, when children are also vaccinated, the average vaccination rate for the whole population is lower than for the adult population.

Vaccination Type.

Under our standard scenarios, 90% of vaccinated adults aged ≥60 years are assumed to receive the ChAdOx1-S vaccine, and 10% the Comirnaty vaccine, while 90% of adults under 60 are assumed to receive the Comirnaty vaccine, and 10% the ChAdOx1-S vaccine. In scenarios where children under 16 are vaccinated, they are all assumed to receive the Comirnaty vaccine. These standard scenarios for vaccine allocation are denoted by "AZ-mRNA" in Figures.

We also consider alternative "mRNA" scenarios, in which everyone who is vaccinated is treated as if they had received the equivalent of two doses of the Comirnaty vaccine. We assume that when the Moderna (Spikevax) vaccine becomes available in Australia, eligibility will initially be the same as the Comirnaty vaccine. i.e., the Spikevax vaccine will be offered to those aged under 60 years. We also consider the Comirnaty and Spikevax vaccines to be similarly effective, based on their biological similarity and the results of clinical trials.[20,21]

Supplementary Results

If children are not vaccinated, the total infections required to reach herd immunity decline from almost 14 million for 50% of adults vaccinated, to around 5 million with 100% of adults vaccinated (Supplementary Figure 1A). Total symptomatic cases decline from just over 9 million to just under 3 million (Supplementary Figure 1B). The age distribution of vaccination uptake within adults ("95 60+" vs "equal") makes little difference to total infections, or total symptomatic cases, because adult susceptibility to infection and symptoms is assumed to be independent of age. (The small predicted differences are due to a change in the overall population ratio of Comirnaty vaccinations to ChAdOx1-S vaccinations.)

Vaccinating children produces a marked reduction in infections and symptomatic cases at all vaccination levels. This is partly due to a direct reduction in the number of children infected, but the reduction is larger at high adult vaccination levels. If children are not vaccinated, the proportion of susceptibles infected, FSI, is larger. Herd immunity is not attained with the "AZ-mRNA" vaccine combination even when 100% of adults are vaccinated. There are consequently many more infections among vaccinated adults when children are not vaccinated.

The age distribution of vaccine uptake among adults has a large effect on total hospitalisations (Supplementary Figure 1C), and an even larger effect on fatalities (Supplementary Figure 1D). Vaccinating 95% of adults aged ≥60 years dramatically reduces the total numbers of hospitalisations and deaths, especially at low average adult vaccination levels. This is because of the greater vulnerability of unvaccinated adults aged ≥60 years, who suffer much larger case hospitalisation rates and infection fatality rates (Supplementary Table 2). In scenarios where children remain unvaccinated, as adult vaccination rates increase from 50% to 100%, fatalities decrease from 350,000 to 40,000 under the "equal" strategy, and from 240,000 to 40,000 under the "95% 60+" strategy. The differences between the "95% 60+" and "equal" strategies diminish as the percent of adults vaccinated increases, and when the average adult vaccination level reaches 95%, the two strategies are identical.

Children experience very low case hospitalisation rates and infection fatality rates, so numbers of hospitalisations and fatalities are reduced only modestly, relative to adults, when children are vaccinated. However, an estimated 12,000 hospitalisations in children and adolescents are prevented when vaccination levels reach 75% in children. Further, even when adult vaccination levels of 95 or 100% are achieved, there are still substantial breakthrough infections among vaccinated adults when children are not vaccinated.

The effect of giving a mRNA vaccine booster dose to adults who have received two doses of ChAdOx1-S is observed in Supplementary Figure 2, which compares the "AZ-mRNA" and "mRNA" scenarios. All scenarios presented in Supplementary Figure 2 assume a "95% 60+" age distribution, with and without vaccinating children. The mRNA booster dose lowers infections, symptomatic cases and hospitalisations by relatively small fractions (Supplementary Figure 2A, B, C). It has a much more substantial effect on fatalities (Supplementary Figure 2D) because these occur primarily in the 60+ age group, 90% of whom are assumed to receive the ChAdOx1-S vaccine under the "AZ-mRNA" strategy. Breakthrough fatalities in the 60+ age group are halved by the higher effectiveness of the mRNA vaccine against hospitalisation and death. Again, when children are not vaccinated, herd immunity is not achieved even at adult vaccination levels of 95% and 100%, and this allows breakthrough infections, hospitalisations and fatalities to occur.

Almost all the results presented here use the estimated age distributions of CHR and IFR for the original strain of SARS-CoV-2 (Supplementary Table 2). The effects of adopting the substantially higher hospitalisation and fatality rates for the Delta variant as proposed by some reports (Supplementary Table 2) are shown in Supplementary Figure 3. The results, under all vaccination scenarios, are that hospitalisations increase by approximately a factor of 3, and fatalities by approximately a factor of 2.

We highlight the importance of high vaccination coverage in younger adults, and of vaccinating children, in preventing breakthrough infections and fatalities among vaccinated but vulnerable older adults. This effect can be observed in Supplementary Figure 4, which shows how the numbers of deaths among vaccinated adults aged ≥60 years change depending on the average adult vaccination level, and the vaccination status of children. All the results in Supplementary Figure 4 assume 95% of adults aged ≥60 years are vaccinated. Results are presented for the "AZ-mRNA" strategy, in which 90% of vaccinated adults aged ≥60 years receive ChAdOx1-S, and for the "mRNA" strategy, in which all vaccinated adults receive a Comirnaty-equivalent vaccine. Results based on IFR for the original strain are shown in Supplementary Figure 4A, and for IFR based on the Delta variant in Supplementary Figure 4B.

There are three important conclusions to be drawn from Supplementary Figure 4. First, the mRNA strategy almost halves fatalities resulting from breakthough infections in vaccinated adults aged ≥60 years, due to the higher effectiveness of the mRNA vaccine against death. Second, vaccinating children substantially lowers fatalities among vaccinated adults aged ≥60 years, especially at higher adult average vaccination rates, because it brings the whole population closer to herd immunity. Third, the fatalities predicted using IFR for the Delta variant are approximately twice those predicted using IFR for the original strain.

The plots in Supplementary Figures 1 to 3 represent totals for the whole population. We calculated infections, symptomatic cases, hospitalisations and fatalities for each age group, and their predicted distributions over age groups. Given that the projected numbers differ across age groups, we plotted the percentages of people in each age group experiencing these outcomes, for a subset of adult vaccination levels from 50 to 95%, for the "95% 60+" scenario, with children under 16 unvaccinated (Supplementary Figure 5), and vaccinated (Supplementary Figure 6), using the "AZ-mRNA" vaccination strategy.

When children and adolescents are unvaccinated, infection rates fall into one of three patterns (Supplementary Figure 5A). For adults aged 16 to 69, infection rates fall steeply from 56% for 50% of adults vaccinated down to 13% for 95% of adults vaccinated. This is because the vaccination rate in this age group increases rapidly. For children and adolescents, who remain unvaccinated, there is a much weaker decline in the percent infected, from 74% for 50% of adults vaccinated, to 52% for 95% of adults vaccinated. Given the number of susceptible children remains unchanged, this decline reflects a decrease in FSI, the fraction of susceptibles infected to reach herd immunity, as more adults are vaccinated. In these scenarios, the vaccination coverage among adults aged ≥60 remains constant, at 95%. There is the same weak decline in the proportion of adults aged ≥60 infected, from 30% for 50% of adults vaccinated, to 21% for 95% of adults vaccinated. Given only 5% of these older adults are unvaccinated, most of these infections are breakthrough infections among the vaccinated.

It might seem surprising that a level of adult vaccination as high as 95% yields relatively little protection for vaccinated older adults. This is because, with children and adolescents (about 20% of the total population) unvaccinated, vaccinating 95% of adults does not get the population close to herd immunity. When children and adolescents are vaccinated at the same level as adults aged 16 to

59, there is a much more impressive decline in infection rates among adults aged ≥60 as vaccination coverage increases, falling to 3% at 95% coverage (Supplementary Figure 6A).

Symptomatic cases (Supplementary Figures 5B and 6B) show essentially the same patterns as infections, except that only 50% of infected children aged 0 to 9 years are assumed to be symptomatic, so their case percentages are reduced accordingly. Note that, at 95% adult vaccination coverage, adults aged 16 to 59 and adults aged ≥60 have the same vaccination coverage, but adults aged ≥60 experience higher rates of infection and symptomatic cases. This occurs because, under the "AZ-mRNA" vaccine strategy, 90% of vaccinated adults aged ≥60 receive the ChAdOx1-S vaccine, which has substantially lower effectiveness against infection, symptoms, hospitalisation and fatalities than the Comirnaty vaccine (Supplementary Table 3).

The age distribution of hospitalisations reflects the strong increase in case hospitalisation rates with age (Supplementary Table 2). Even when they are unvaccinated, only 0.3 to 0.4% of children and adolescents are hospitalised at adult vaccination rates of 50%, compared to 2% of adults aged 50 to 59 (Supplementary Figure 5C). We observe the percentage of adults aged 16 to 59 hospitalised declines rapidly with increasing vaccination coverage and, at adult vaccination rates of 90 or 95%, adults aged 50 to 59 are hospitalised at rates lower than those for children and adolescents. Even though they are 95% vaccinated, hospitalisation rates of adults aged ≥80 are around 1% and decline only weakly as more young adults are vaccinated. As already noted, when children and adolescents are vaccinated the population is much closer to herd immunity at vaccination rates of 90 and 95%, and hospitalisation rates in children and adolescents, and in adults aged ≥60, are greatly reduced (Supplementary Figure 6C).

Infection fatality rates are much more strongly age dependent than case hospitalisation rates (Supplementary Table 2). Fatalities occur predominantly among adults aged ≥70, despite their 95% vaccination rates (Supplementary Figure 5D). Fatality rates among children, adolescents and adults aged 16 to 29 are lower than 1 in 50,000 at 80% adult vaccination coverage, though this still represents over 100 fatalities. The importance of vaccinating children and adolescents to protect vulnerable groups in the population, particularly the elderly, is evident in a comparison of Supplementary Figures 5D and 6D. Fatality rates among those aged ≥80 remain above 1% when children and adolescents are unvaccinated but fall to below 0.2% when the entire population has 95% coverage.

The fatality rates in Supplementary Figures 5D and 6D are percentages of the population in each age class. We have also plotted total fatalities as a percentage of infections; that is, the population wide infection fatality rate or IFR (Supplementary Figure 7). The population wide IFR is low, around 0.2 to 0.3%, when 95% of 60+ adults are vaccinated, and children are unvaccinated, and a little higher when children are vaccinated. Because adults aged ≥60 enjoy 95% vaccination coverage, their infections and fatalities are reduced, while many infections occur among unvaccinated children, adolescents and adults aged <60, who suffer relatively few fatalities. This means that the ratio of total fatalities to total infections is particularly low.

It may seem counter-intuitive that, for the "95% 60+" scenarios, population IFR increases as the vaccination coverage among adults increases. The explanation is that, while fatalities among the vaccinated elderly do decline with increasing adult vaccination levels, infections among younger adults decline even more rapidly as they enjoy higher vaccination coverage, so the ratio of total fatalities to the total number of infections (population wide IFR) increases (Supplementary Figure 5A, 5D). By contrast, for the "equal" scenarios where vaccination rates are constant throughout the adult population, infections are more evenly distributed across age groups, and the population wide

IFR is much higher, around 0.9 to 1% at 50% adult vaccination, declining to around 0.4 to 0.6% at 95% vaccination (Supplementary Figure 7B). The decline in population wide IFR with increasing vaccination coverage for these scenarios occurs because vaccine effectiveness against fatalities is much higher than vaccine effectiveness against infection.

Low population wide infection fatality rates around 0.2% are being observed in the current outbreak of the Delta variant in the UK,[14] where around 95% of adults over 60, and 60% of all adults, have had 2 doses of vaccines. These observations are consistent with the results in Supplementary Figure 7A. However, it is worth noting that population infection fatality rates around 0.2% continue to exceed those of seasonal influenza, and that COVID-19 is associated with greater health loss.[22,23]

Supplementary References

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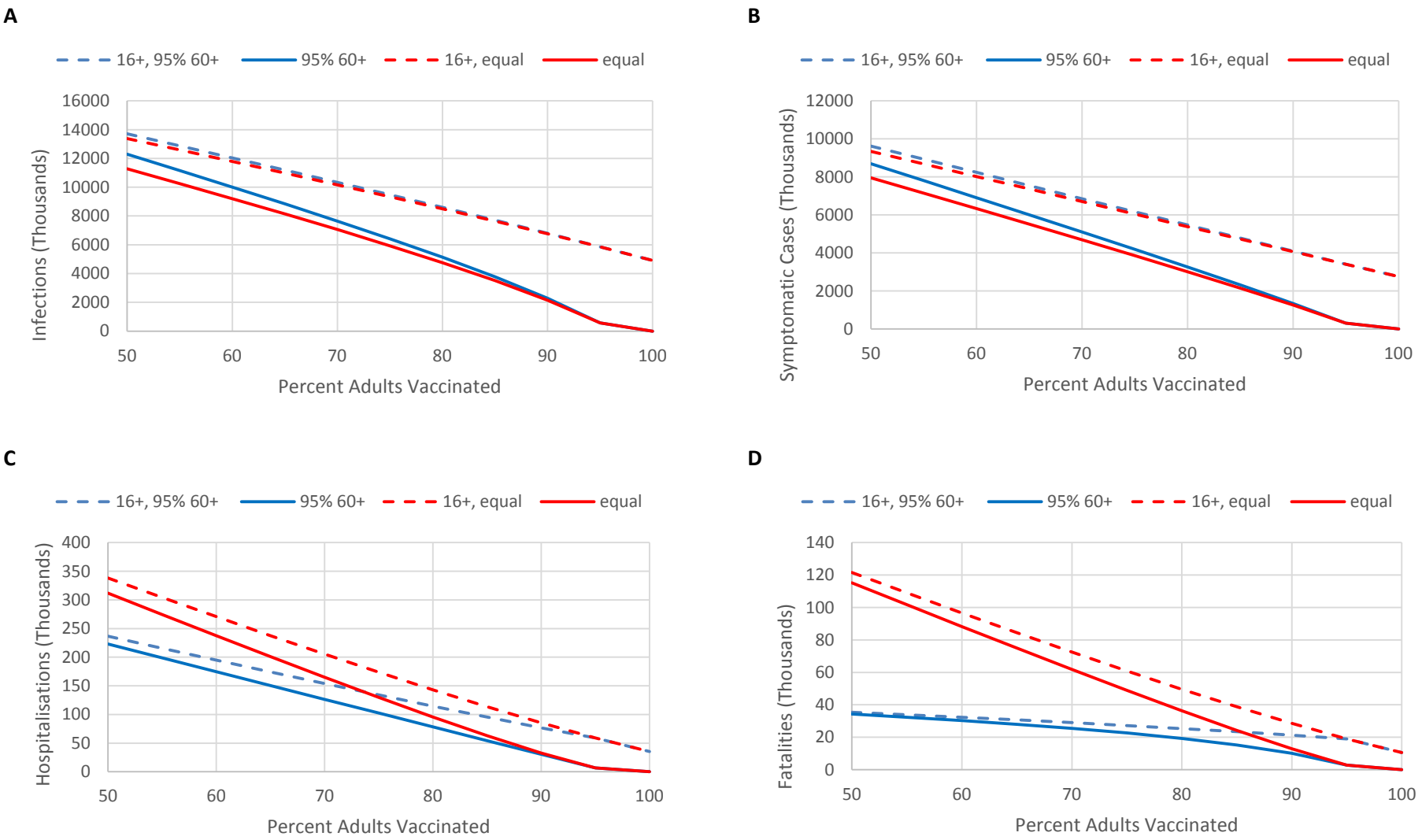
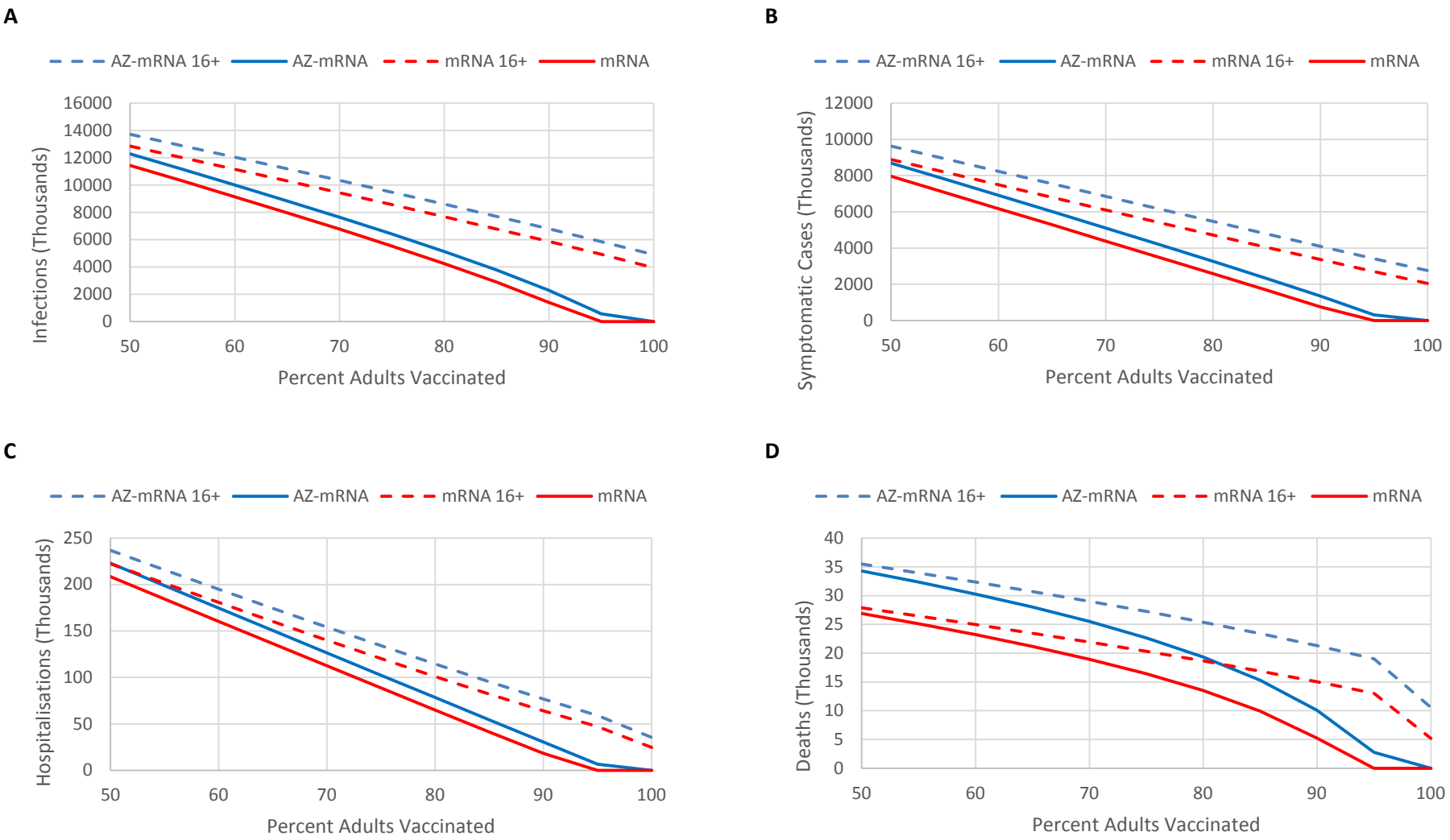
Additional supplementary material can be sourced at https://osf.io/6j4rd/.

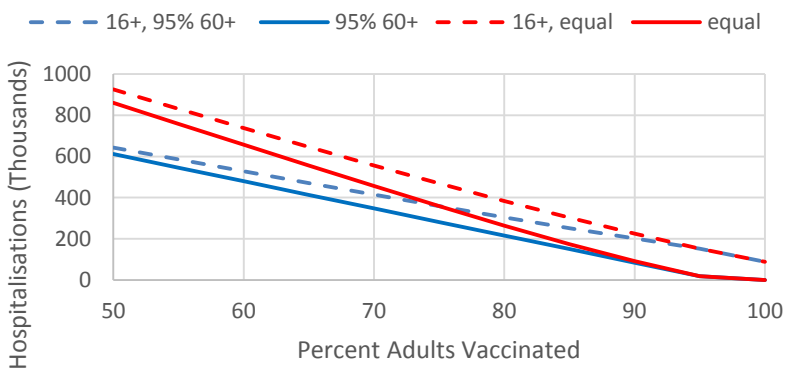


Supplementary Figure 1. Predicted infections (A), symptomatic cases (B), hospitalisations (C) and fatalities (D), all in thousands, vs adult vaccination level, for the "AZ-mRNA" strategy, using CHR and IFR observed for the original strain of SARS-CoV-2.



Supplementary Figure 2. Comparison of predicted infections (A), symptomatic cases (B), hospitalisations (C) and fatalities (D), all in thousands, vs adult vaccination level, for the "AZ-mRNA" and "mRNA" strategies, with 95% of adults aged 60+ vaccinated, with and without children under 16 years vaccinated.

A



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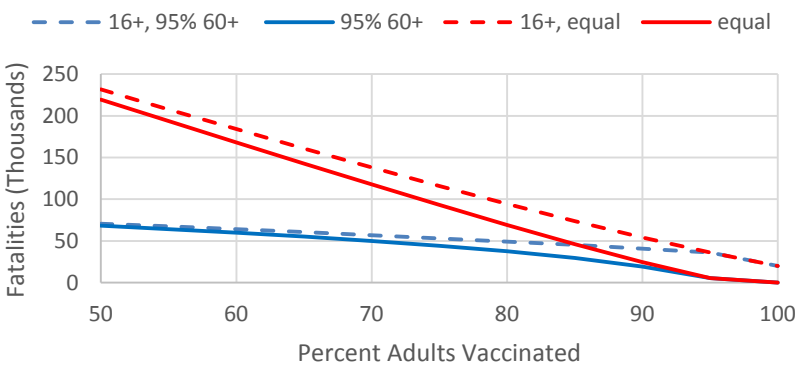
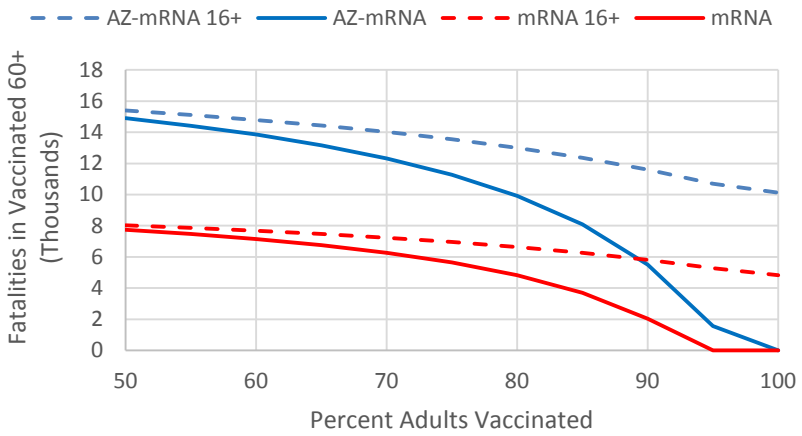


Supplementary Figure 3. Predicted hospitalisations (A) and fatalities (B), all in thousands, vs adult vaccination level, for the "AZ-mRNA" strategy, using CHR and IFR scaled up for the Delta variant.

A



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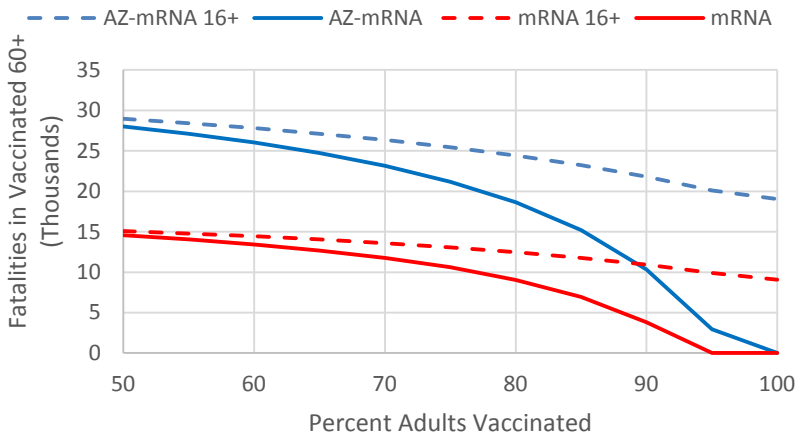
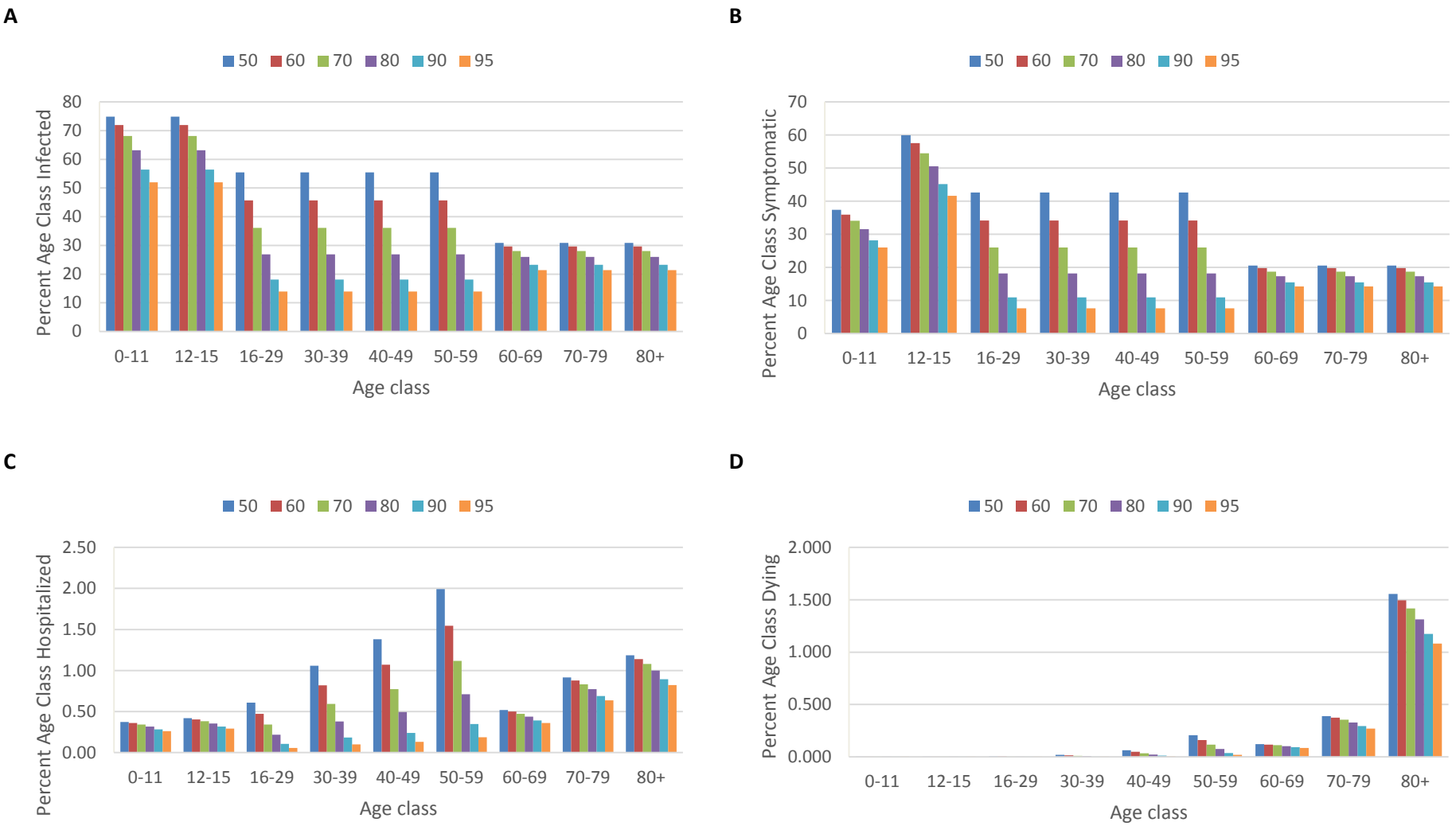
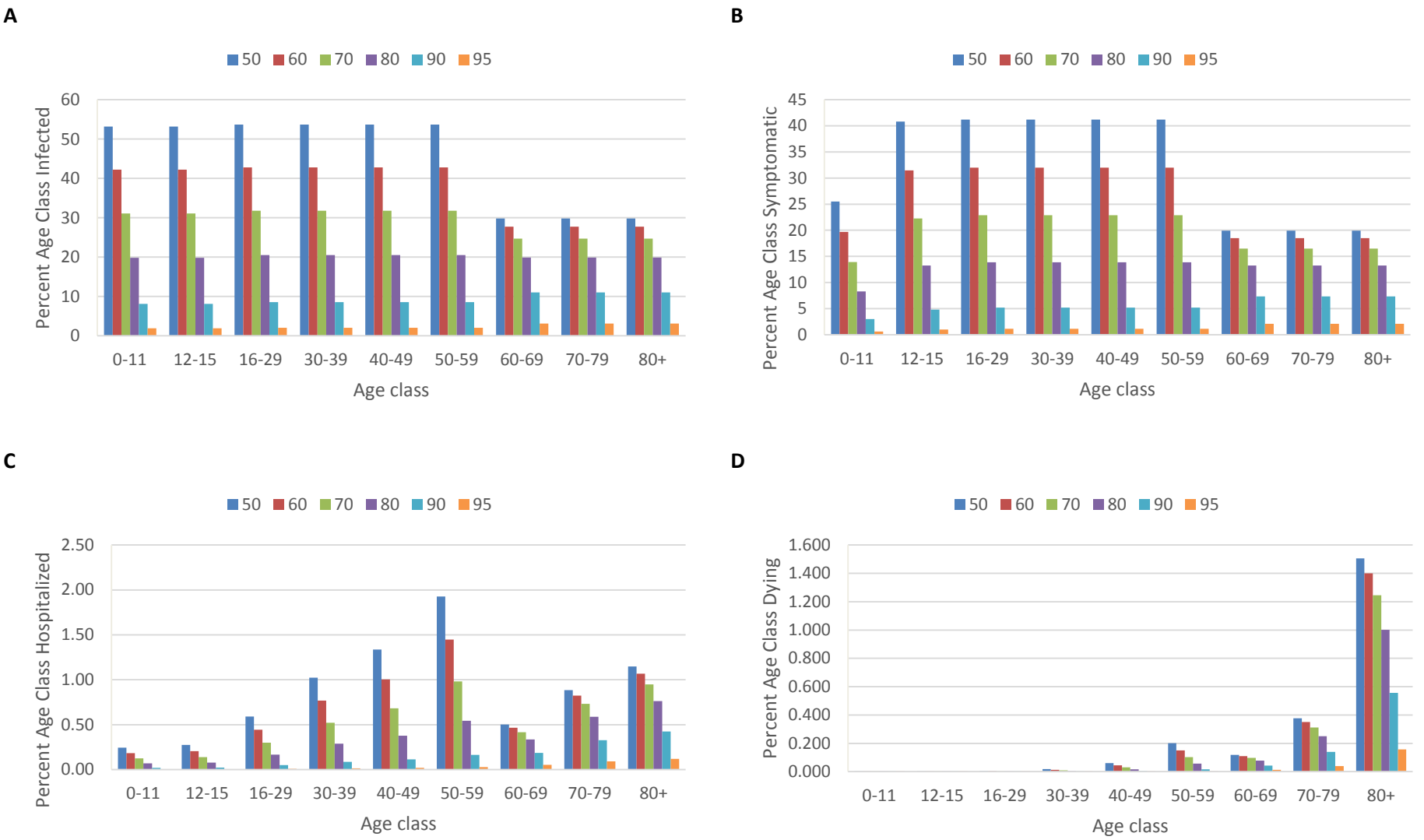


Supplementary Figure 4. Fatalities in thousands of vaccinated adults aged 60 years and over, vs adult vaccination level, for 95% of adults aged 60+ vaccinated, using IFR for the original strain of SARS-CoV-2 (A), and for the Delta variant (B).

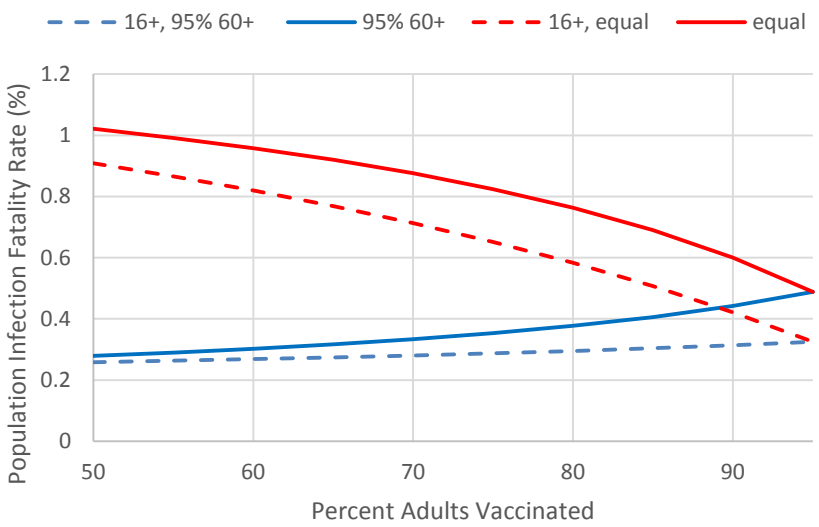


Supplementary Figure 5. Percentage of population in each age class infected (A), symptomatic (B), hospitalised (C) and dying (D), for 50, 60, 70, 80, 90 and 95% of adults vaccinated. Assumes the "AZ-mRNA" vaccination strategy, 95% of adults aged 60+ vaccinated, children under 16 unvaccinated.



Supplementary Figure 6. Percentage of population in each age class infected (A), symptomatic (B), hospitalised (C) and dying (D), for 50, 60, 70, 80, 90 and 95% of adults vaccinated. Assumes the "AZ-mRNA" vaccination strategy, 95% of adults aged 60+ vaccinated, children under 16 vaccinated.

A



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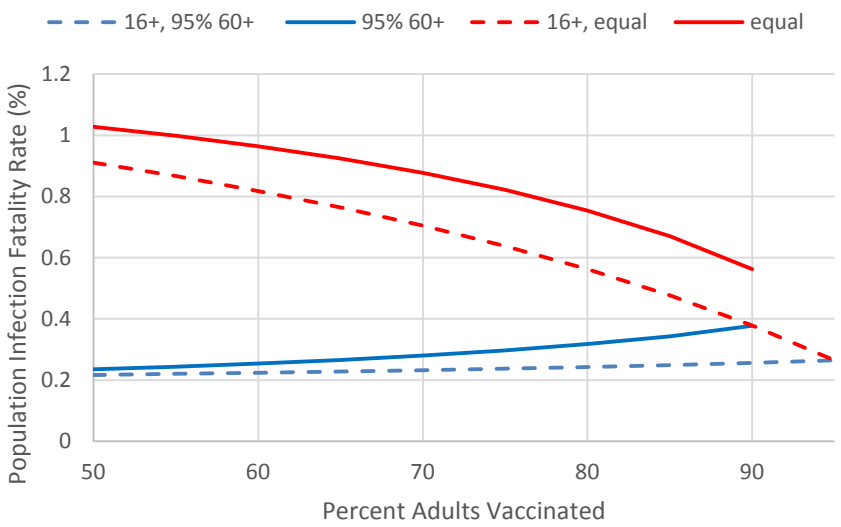

Supplementary Figure 7. Population wide infection fatality rate vs percent adults vaccinated, for different age distributions of vaccine uptake, for the "AZ-mRNA" strategy (A) and the "mRNA" strategy (B), based on the age-dependent IFR for the original strain of SARS-CoV-2.