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A country-specific model of COVID-19 vaccination coverage needed for herd immunity in adult only or population wide vaccination programme

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ABSTRACT

We present a country specific method to calculate the COVID-19 vaccination coverage needed for herd immunity by considering age structure, age group-specific contact patterns, relative infectivity and susceptibility of children to adults, vaccination effectiveness and seroprevalence prior to vaccination. We find that across all six countries, vaccination of adults age 60 and above has little impact on R_{eff} and this is could be due to the smaller number of contacts between this age group and the rest of the population according to the contact matrices used. If R_0 is above 6, herd immunity by vaccine alone is unattainable for most countries either if vaccination is only available for adults or that vaccine effectiveness is lower at 65% against symptomatic infections. In this situation, additional control measures, booster shots, if they improve protection against infection, or the extension of vaccination to children, are required. For a highly transmissible variant with R_0 up to 8, herd immunity is possible for all countries and for all four scenarios of varying relative infectivity and susceptibility of children compared to adults, if vaccine effectiveness is very high at 95% against symptomatic infections and that high vaccination coverage is achieved for both adults and children. In addition, we show that the effective reproduction number will vary between countries even if the same proportion of the population is vaccinated, depending on the demographics, the contact rates and the previous pre-vaccination seroprevalence in the country. This therefore means that care must be taken in extrapolating population level impacts of certain vaccine coverages from one country to another.

1. Introduction

As COVID-19 vaccines are rolled globally, important questions remain about their role in relation to other public health interventions that have been implemented to control the ongoing COVID-19 pandemic.

A number of countries, including the UK (Moore et al., 2021; Hogan et al., 2021; Sandmann et al., 2021), US (Matrajt et al., 2021), Japan and Thailand (Luangasanatip et al., 2021), have undertaken transmission modelling for their country considering different vaccination strategies. Although useful, this approach does not indicate the vaccination threshold needed for herd immunity to be achieved. Evaluating the potential for herd immunity is critical to inform vaccination strategies. If herd immunity is achievable, understanding the vaccination coverage needed in specific population groups will help to prioritize resources and target communication campaigns to improve vaccination uptake. However, if herd immunity is unlikely to be achievable, vaccination goals to reduce pressure on healthcare systems should perhaps be prioritized over strategies aimed at reducing transmission or achieving herd immunity.

A key consideration often overlooked in previous models is the role that children play in SARS-CoV-2 transmission. The differing clinical manifestation of COVID-19 in children compared to adults is well established. However, it is unclear how this translates to the susceptibility and infectivity of children compared to adults. Some systematic reviews (Gaythorpe et al., 2021; Viner et al., 2021) and a modeling result (Davies et al., 2020) suggest that children might be less susceptible and less infectious than adults, though the reasons for these

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differences remain unclear. Children's possible reduced susceptibility to infection and reduced infectivity after infection has important implications for population transmission of SARS-CoV-2, and should be considered in models evaluating population herd immunity. At the time of writing, only one COVID-19 vaccine: Pfizer-BioNTech is available for adolescents aged 12 and above in Singapore and there are several ongoing vaccines trials to evaluate the safety and effectiveness of current vaccines in children.

We present a country specific model to calculate what levels of vaccination coverage in an adult only and population wide vaccination programme would be needed to achieve herd immunity. We demonstrate the model using Singapore as well as selected countries from low, medium and high-income groups. It should be emphasized that the values presented here are theoretical calculations on the estimated vaccination coverage for herd immunity for a given context and assumptions that does not account for the time-dependent changes in the parameters. The ranges of R_0 explored are relevant for delta and omicron transmission.

2. Methodology

The conventional method for calculating the vaccination threshold for herd immunity is $p = (1 - 1/\ R_0)/\varepsilon$ where R_0 is the basic reproduction number, defined as the average number of secondary cases caused by an infected case in a homogeneous population that is completely susceptible and ε is the vaccine effectiveness against infection. However, populations are neither homogeneous nor fully susceptible and thus another method is necessary to get a better estimate of vaccination threshold. The key parameter which determines herd immunity is the effective reproduction number, R_{eff}, which is the average number of secondary cases caused by an infected case in a population that has both susceptible and non-susceptible (infected, vaccinated and recovered) individuals. Therefore, another way to calculate vaccination threshold is to find the vaccination coverage that can reduce R_{eff} below 1. To calculate R_{eff}, we first construct a SIR (Susceptible-Infected-Recovered) model that includes age structure, two infected states with different infectivity (asymptomatic and symptomatic), pre-vaccination seroprevalence and vaccination as shown in Fig. 1. We extended the general method to calculate R_0 by Diekmann et al. (2010) to include the additional conditions. Briefly, Diekmann et al. (2010) define R_0 as the largest eigenvalue of the Next Generation Matrix (NGM), which is constructed by multiplying the rate of infection for each infected state and the time spent in each infected state (refer to Supplementary sections 2 and 3 for a detailed description of this general method and our extended method).

3. Model

We will use an SIR model stratified into three age groups, $i = C$: children age below 16 years old, $i = A$: adults aged between 16 and 59 years old and $i = E$: adults age 60 years old and above, with no transition between different age groups as the whole infection cycle is faster than the timescale we are considering here. This age stratified model is necessary since some key transmission parameters like risk of symptomatic infections, infectivity and susceptibility are age dependent. For simplicity, we will also assume that there is no transition between infected states and that all infected states recover at the same rate γ. The adult population is separated into two because those who are aged 60 and above normally have lower number of contacts (Prem et al., 2017) which are more likely to be household contacts, and hence they contribute lesser to transmission.

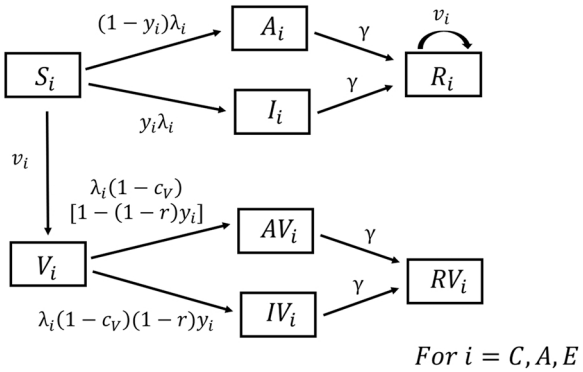

Fig. 1. Transmission model which includes vaccination for all ages.

For each age group i, we suppose that the recovered compartment (R_i/RV_i) has complete protection from infection and this protection is life-long. Before vaccination, the number of people in R_i equals to the pre-vaccination seroprevalence of a given country, while the rest of the population assumed to be susceptible (S_i). There are two infected compartments: symptomatic (I_i/IV_i) and asymptomatic (A_i/AV_i), where the relative infectivity of an asymptomatic case to a symptomatic case is 0.35 (Buitrago-Garcia et al., 2020). The age group specific y_i represents the proportion of all infections that will be symptomatic while (1-y_i) is the asymptomatic proportion of all infection, which is obtained from the weighted average of the asymptomatic percentages among all ages in each age group (asymptomatic percentages for ages 0 to above 75, in 5 year intervals, range from 20% to 55% (Buitrago-Garcia et al., 2020; Ng et al., 2020) decreasing linearly with age (Davies et al., 2020)). y_i is country dependent (refer to Supplementary Table 2) as it is based on the population distribution. v_i represents the percentage in each age group that are vaccinated in a particular context. Under the assumption that vaccination occurs independently of the serostatus of the vaccinee, those who are in R_i compartment are vaccinated as well but since they are completely immune to infection, they remain in the recovered compartment. The number of individuals in the Vaccinated (V_i) compartment is the v_i proportion of the number in S_i pre-vaccination.

Here, λ_i is the force of infection that represent the sum of all infection rates due to all infected states. The effects of vaccine on transmission are indicated by two parameters c_V and r where c_V represents the vaccine effectiveness in reducing infections and r represents the vaccine effectiveness in reducing the probability of being symptomatic when infected.

4. Variables needed for the analysis

4.1. Population age structure and age group-specific contact patterns

Population age structure affects transmission of SARS-CoV-2 as the susceptibility, infectivity and patterns of social contact are age dependent, which will be elaborated on below. It also changes the proportion of the age-group specific symptomatic proportion among infections as described in the model. In this analysis, we follow the age group contact matrices provided by Prem et al. (2017) and the population demographic from the United Nations World Population Prospect (United Nations Department of Economics and Social Affairs, 2019). The information regarding age group contact patterns can be updated with local studies when available.

4.2. Relative infectivity and susceptibility of children with respect to adults (f_a and μ_a respectively in Supplementary Section 3).

There is still no consensus on the relative infectivity and susceptibility of children (age $\leq$ 15) compared to adults. Household studies in Rome (Buonsenso et al., 2021) and Barcelona (Brotons et al., 2020) showed that children are equally as susceptible to infection as adults while modelling results by Davies et al. (2020) suggests that children have half the susceptibility of adults. Bullard et al. (2021) showed that children have higher median Ct values (lower viral load) compared to

adults. However, in that study there was a higher percentage of children who were asymptomatic compared to adults, and the relationship between Ct value and infectivity is still unclear. Other studies show conflicting results (Polese-Bonatto et al., 2022; Heald-Sargent et al., 2020). Hence, we will assume that the relative infectivity and susceptibility of children is either equal to or half of the value of adults.

4.3. Vaccination effectiveness (c_V and r) and action

Phase 3 trial results of the Moderna (Baden et al., 2020), Pfizer-BioNTech (Polack et al., 2020), Oxford-AstraZeneca (Voysey et al., 2021) and Gamaleya (Logunov et al., 2021) vaccines, and cohort studies in UK (Hall et al., 2021a) and US (Thompson et al., 2021), havcainst infection (asymptomatic and symptomatic) and also reduce the probability of being symptomatic when infected. Moreover, the work by Levine-Tiefenbrun et al. (2021) suggests the possibility of vaccines being able to reduce the infectivity of infected individuals, as vaccinated individuals who are infected have a higher Ct value than those unvaccinated. For the analysis, we will consider two vaccine effectiveness, 1) the best possible values following the result from the SIREN study (Hall et al., 2021a): 86% effectiveness in reducing infections, 65% effectiveness in reducing probability of being symptomatic when infected and overall 95% effectiveness in reducing symptomatic infections and 2) a lowered vaccine effectiveness due to waning of protection over time as observed in cohort studies (Andrews et al., 2021; Tartof et al., 2021): 55% effectiveness in reducing infections, 23% effectiveness in reducing probability of being symptomatic when infected and overall, 65% effectiveness in reducing symptomatic infections. Vaccine effectiveness is taken to be uniform across all age groups as from the above-mentioned studies, the differences between age groups are small and the recent results from Pfizer (Reis et al., 2021) and Moderna (Ali et al., 2021) vaccines also showed similar effectiveness for adolescents between ages 12 and 15. Vaccine is assumed to have no effect on the infectivity of infected cases, i.e. those symptomatic/asymptomatic cases have the same infectivity regardless of their vaccination status, though vaccination changes the proportion that are symptomatic.

4.4. Vaccination coverage for different age groups (v_i) and priority groups for vaccination

In alignment with SAGE's recommendation on vaccine allocation (World Health Organization, 2020), most countries have prioritized vaccination of healthcare workers and the elderly. However, some countries like Singapore (Kok, 2021; Lim, 2021) have also prioritized vaccines for certain occupations considered as essential for socio-economic function or high risk of multiple contacts (e.g. taxi drivers, delivery personnel, dormitory residents etc.). The speed and uptake of vaccines is also dependent on external factors like vaccine supply, vaccination capacity and willingness to vaccinate. The latter is itself dependent on many factors (Lazarus et al., 2020) like age, gender, educational level and socio-economic status. Hence, we will not follow a specific vaccination schedule and instead consider various combinations of the percentage of people that are vaccinated in each age group in a particular context and calculate the effective R value. We will also assume that vaccination is independent of the serostatus of the person. This is because vaccination recommendations are the same regardless of prior infection.

4.5. Seroprevalence prior to vaccination (Number in R_i)

Due to the pandemic, a proportion of the population will already have been infected, and infected individuals have some immunity against infection (Hansen et al., 2021; Hall et al., 2021b). Therefore, it is necessary to include the population cumulative infection proportion in the calculation of the effective R. This proportion can be estimated from seroprevalence studies (Bobrovitz et al., 2020; Rostami et al., 2021).

Seroprevalence varies within (Buss et al., 2021; Grant et al., 2021) and across countries (Bobrovitz et al., 2020), ranging from 18% in South Asia to 1% in Southeast Asia, East Asia and Oceania, with most regions below 10%. It also varies across age groups (Rostami et al., 2021; Stringhini et al., 2020); in general, seroprevalence in children and the elderly has been lower than in adults. Estimates of seroprevalence are often biased due to the limitations (Bobrovitz et al., 2020) in the conduct of seroprevalence studies, including not correcting for test sensitivity and specificity, not using representative samples and not using appropriate statistical analysis. This problem is compounded by the heterogeneity in the rate of waning antibodies as shown by Chia et al. (2021) and the type of serological test used hence seroprevalence is dependent on when and how the study was conducted. In addition, not all antibody assays are equivalent, because they measure responses to different virus antigens. However, serological studies generally measure viral exposure history, not immune function. Studies that measure neutralising antibody are arguably more useful, because they measure a functional characteristic of immunity. Despite this, antibodies are not the only protection mechanism. Cell mediated responses are likely to be important as well, but are less easily measurable than antibody responses.

For simplicity, we equate pre-vaccination seroprevalence as the proportion of the population that is totally protected from infection, even though presence of certain antibodies in not a definitive indicator of protection. In our calculations, it is assumed that seroprevalence of children and the elderly are negligible and the seroprevalence for adults is taken to be either 0% or 10%. Real time estimates of pre-vaccination seroprevalence in different countries and territories can be obtained from the a website SeroTracker (Arora et al., 2021), developed and funded by WHO, the Public Health Agency of Canada and the German Federal Ministry of Health.

4.6. R_0

R_0 of the population is dependent on the interaction patterns within the population and the transmissibility of the circulating virus. It has been estimated that for the current dominant strain Delta, R_0 is between 3 and 8, with an estimated overall estimate of 5.08 (Liu and Rocklöv, 2021). In this analysis, we would not be modeling specific strains as the same strain could have different R value in different settings, but instead conduct theoretical analysis by assuming that R_0 in different countries are either 4, 6 or 8.

5. Results

Singapore is used as an example to illustrate the application of the method. The number of contacts between the age groups [children ($i = 1$), adults aged between 16 and 59 ($i = 2$) and adults aged 60 and above ($i = 3$)], denoted by the matrix β_{ij} is the weighted average number of individuals in age group j that an individual in age group i has contact with per day. We considered 4 scenarios, scenario A: relative susceptibility and infectivity of children are half of adults, scenario B: relative susceptibility of children is half of adults and relative infectivity of children is equal to adults, scenario C: relative susceptibility of children is equal to adults and relative infectivity of children is half of adults and scenario D: relative susceptibility and infectivity of children are equal to adults. In all scenarios, we assumed that all safe management measures (SMMs) like social distancing, mask wearing and trace, test and isolate are absent (i.e. no measures are in place to prevent infected individuals from transmitting infection).

Figs. 2 and 3 below show the four scenarios under the adult only vaccination programme and the population wide (adult and children) vaccination programme with pre-vaccination seroprevalence assumed to be 0%. The yellow boxes indicate vaccination coverages where R_{eff} is less than 1 and transmission is interrupted by vaccination alone.

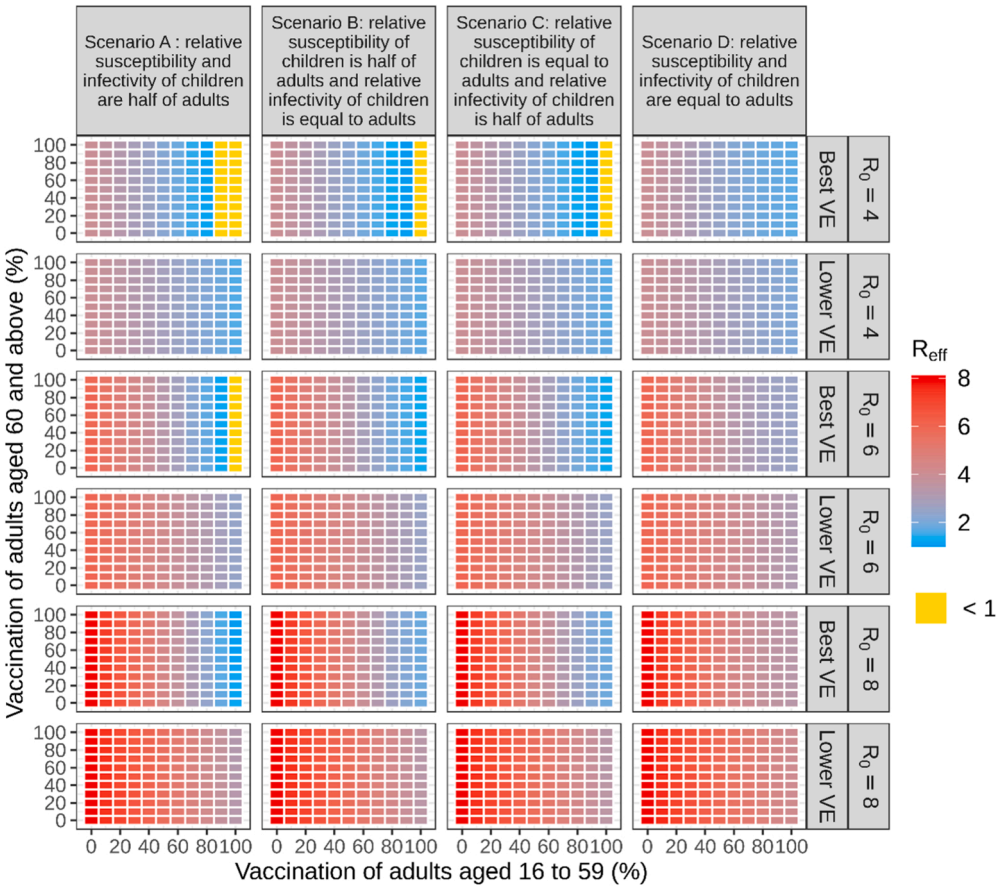

Fig. 2. R_{eff} in Singapore for different vaccination coverages in adult (>=16 y) only vaccination programme for the four different scenarios of varying relative susceptibility and infectivity of children compared to adults. Seroprevalence is assumed to be 0%. Yellow boxes represent R_{eff} is less than 1.

From Fig. 2, it is observed that R_{eff} is mainly influenced by the percentage of vaccinated adults aged between 16 and 59. Given a percentage of adults between ages 16 and 59 that are vaccinated, R_{eff} remains approximately constant regardless of the percentage of adults age 60 and above that are vaccinated. This implies that adults aged 60 and above play a small role in transmission and this is due to the smaller proportion of adults aged 60 and above compared to adults of younger ages in the population (refer to Supplementary Table 3) and the lower number of contacts between the adults aged 60 and above and the rest of the population (refer to Supplementary Table 3) according to the age group contact matrix that is used.

Under the best vaccine effectiveness of 95% against symptomatic infection and a moderate value of R_0 of 6, only scenario A (relative susceptibility and infectivity of children are half of adults) is herd immunity possible in an adult-only vaccination. The herd immunity threshold in this case is 67% of the total population (100% of adults between 16 and 59) which is lower than the 96.9% vaccination threshold obtained from the conventional method for R_0 of 6% and 86% vaccine effectiveness against infection. Herd immunity is also possible in an adult-only vaccination with lower R_0 value of 4 under scenarios A to C. The herd immunity threshold is 90% of adults between 16 and 59 for scenario A and 100% for scenarios B and C. If vaccine effectiveness decreases to 65% against symptomatic infection, herd immunity is not achievable for all scenarios under all R_0 values of 4, 6 and 8.

As shown in the columns of scenarios B to D, as relative susceptibility and infectivity of children increase and approach adult levels, the R_{eff} given the same vaccinated proportions in each group increases, indicating that herd immunity by vaccination alone is increasingly unlikely. For example, for the R_0 of 6 and best vaccine effectiveness, if 100% of all those aged 16 and above are vaccinated, the R_{eff} increases from 0.79 to 1.37–2.54 from scenario A to scenario B/C to scenario D.

Compared to Fig. 2, Fig. 3 shows that if vaccination of children below 16 is possible, for the best vaccine effectiveness, herd immunity is attainable for R_0 between 4 and 8 in all scenarios A to D. A high vaccination coverage is required where at least 100% of all adults aged 16 and above needs to be vaccinated for R_0 between 6 and 8. Similarly for R_0 of 4, at least 90% of all adults aged 16 and above needs to be vaccinated. For the case of the lower vaccine effectiveness, herd immunity from vaccine alone is impossible even if the whole population is vaccinated. This implies that other measures are needed to complement vaccines to limit transmission if vaccine effectiveness against the circulating strain is moderate either due to the waning of immunity acquired from vaccine or the reduced effectiveness against a new variant.

5.1. Herd immunity threshold for population wide vaccination in high-, middle- and low-income countries

Two countries each from high-, middle- and low-income groups as categorized by the United Nations (United Nations, 2020) are selected and their herd immunity thresholds (HIT) under the population wide vaccination programme for the different scenarios are calculated from Fig. 4. The HIT is defined as the lowest percentage of the whole population that needs to be vaccinated to reduce R_{eff} below 1. In these calculations, it is assumed that R_0 is 6 for all countries, the vaccine effectiveness is the best at 95% against symptomatic infection and that the pre-vaccination seroprevalence is taken to be 0%.

From Table 1, with R_0 of 6 and a high vaccine effectiveness, it is observed that the HIT does not vary considerably with age distribution of the country, where for the six selected countries, HIT of the total

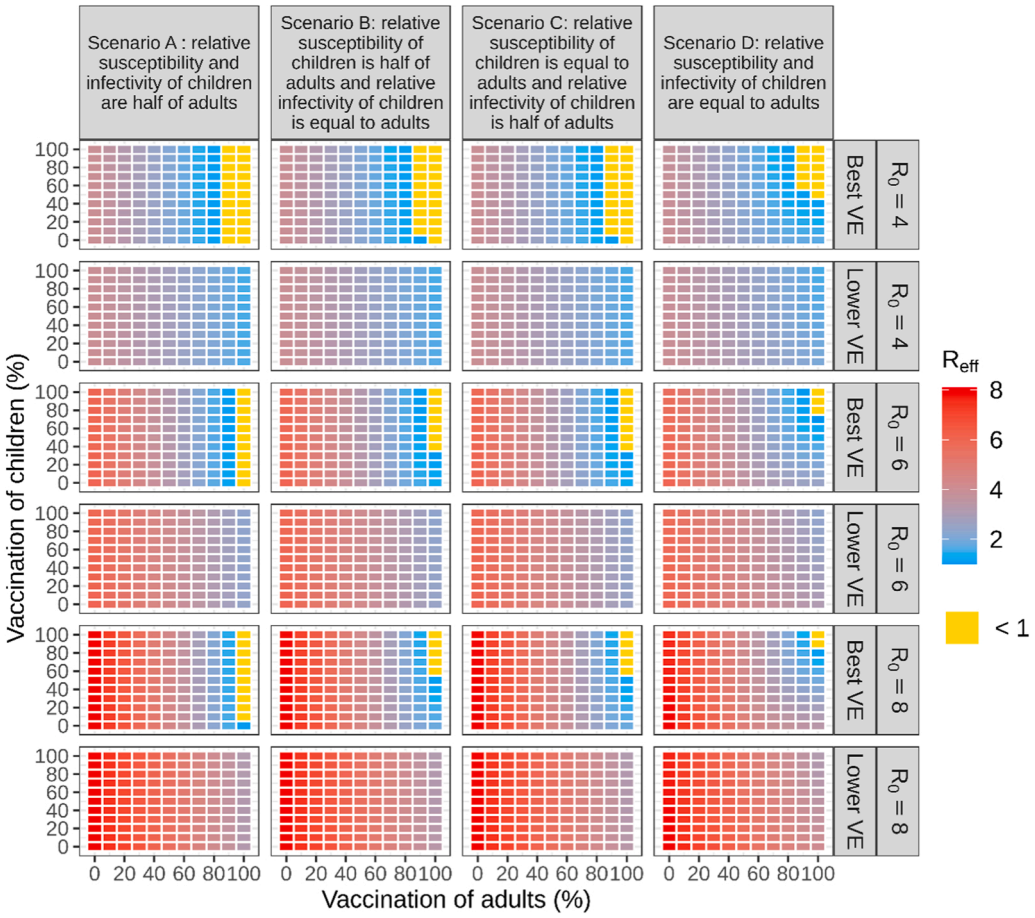

Fig. 3. R_{eff} in Singapore for different vaccination coverages in adult (>=16 y) and children (< 16 y) in a population wide vaccination programme for the four different scenarios of varying relative susceptibility and infectivity of children compared to adults. Seroprevalence is assumed to be 0%. Yellow boxes represent R_{eff} is less than 1.

population ranges from 81.1% to 88.0% for scenario A, 89.8–95.4% for scenario B and 92.6–97.9% for scenario D. However, countries with a larger proportion of children (<16 years) in their population require a higher vaccination coverage among children for herd immunity.

For all countries and in all scenarios, HIT is attained with 100% vaccination coverage in adults (>=16 years) except for India and Uganda in scenario D, where vaccinating 100% of children instead of adults helps to reduce the HIT. This could be because, under the assumed contact matrices used for these two countries (refer to Supplementary Table 3), children have a higher number of total contacts than adults between 16 and 59 years (18.69 vs 15.97 in India and 30.70 vs 19.60 in Uganda) and hence it is more efficient to vaccinate them as they contribute more to transmission.

For all countries, across the scenarios A to D, as relative infectivity and susceptibility of children get closer to adult, both the percentage of children needed for HIT and the HIT of the population increase, though the increments are not linear. This is due to the increasing contribution to transmission by children and thus more of them have to be vaccinated to control transmission. Comparing between scenario A and D when the relative infectivity and susceptibility of children doubles from half to equal to that of adults, the increase in HIT is within 20% for all countries though, the increase does not correlate with the proportion of children in the population with Brazil having the largest increase of 16.8% and Uganda the smallest increase of 8.4%.

Table 2 shows the minimum R_{eff} in an adult only vaccination programme supposing 100% coverage among adults aged 16 and above which gives us an idea on what level of SMMs is required in addition to vaccination of adults to break transmission if herd immunity using vaccine alone is not achievable. Under the assumptions of the best vaccine effectiveness and R_0 of 6, herd immunity (R_{eff} <1) by vaccinating solely adults can only be achieved in scenario A for three countries – Singapore, Spain and Thailand, that has the three lowest proportion of children. For the other scenarios B and D, for all countries, the R_{eff} are above 1 and thus vaccination of children is needed for herd immunity from vaccine. For each scenario, the R_{eff} increases as the proportion of children increases, for example in scenario D, it increases from 2.54 in Singapore (12% children) to 5.24 in Uganda (46% children). As a result, there is a greater need to make vaccines available for children in countries with larger proportion of children in order for them to decrease their R_{eff} to values to similar to those of countries with lower proportion of children.

6. Discussion

We extended the method proposed by Diekmann et al. (2010) to a specific SIR model and calculated the theoretical effective reproduction number, R_{eff} for different vaccine coverages in different age groups taking into consideration differences in transmissibility of SARS-CoV-2 between children and adults. We looked at three R_0 values and two vaccine effectiveness, relevant for considering the transmissibility of different variants and the diverse vaccine effectiveness of different vaccines against a circulating strain, in view of possible waning of protection from vaccines. In this analysis, we showed that across all countries, vaccination of adults aged 60 and above has little impact on R_{eff} (refer to Supplementary Fig. S4) due to the smaller number of contacts between this age group and the rest of the population according

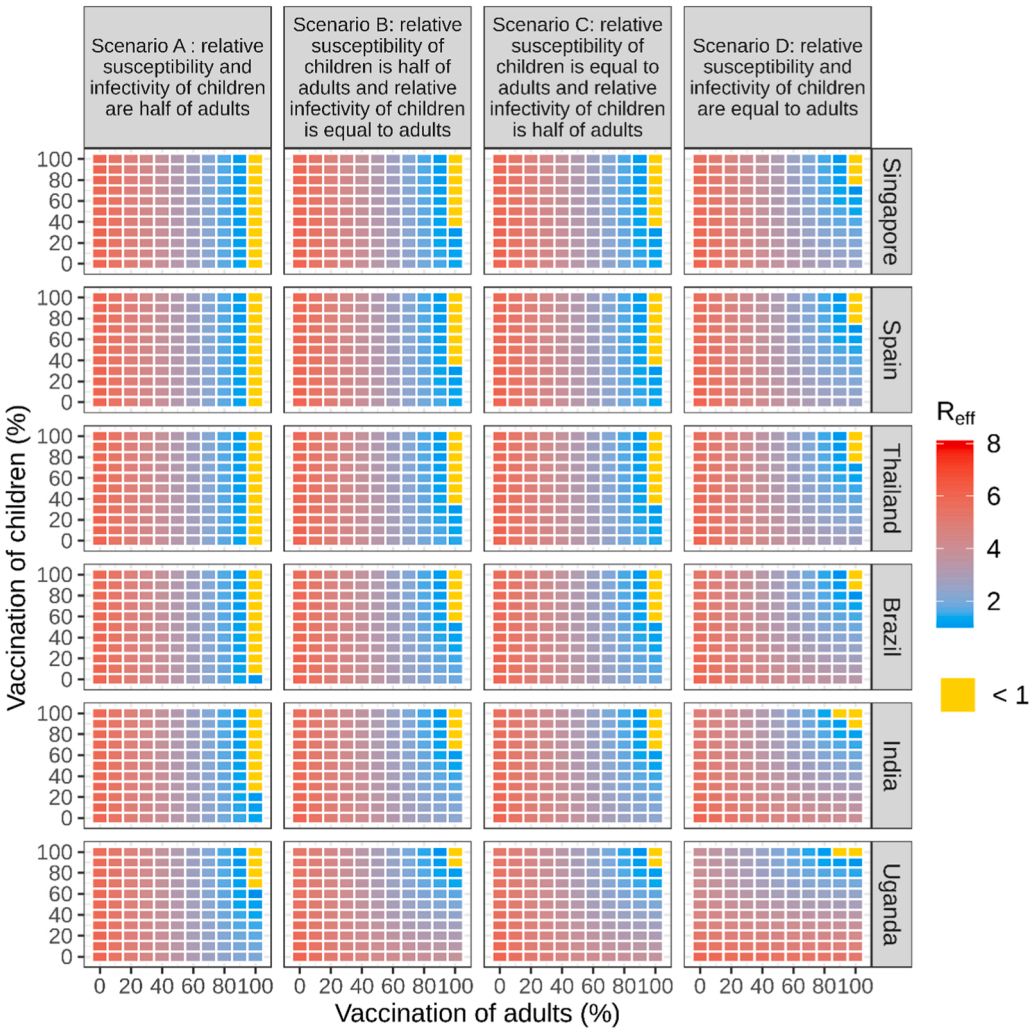

Fig. 4. R_{eff} for some high-, middle- and low-income countries with different vaccination coverages in adult (>=16 y) and children (< 16 y) in a population wide vaccination programme for the four different scenarios of varying relative susceptibility and infectivity of children compared to adults. It is assumed that R_0 is 6, the vaccine has 95% effectiveness against symptomatic infections and seroprevalence is 0%. Yellow boxes represent R_{eff} is less than 1.

Table 1
Herd immunity threshold of the whole population in a population wide vaccination programme where it is assumed that R_0 is 6, the vaccine has 95% effectiveness against symptomatic infections and seroprevalence is 0%. Scenario A: relative susceptibility and infectivity of children are half of adults, scenario B: relative susceptibility of children is half of adults and relative infectivity of children is equals to adults, scenario C: relative susceptibility of children is equals to adults and relative infectivity of children is half of adults and scenario D: relative susceptibility and infectivity of children are equal to adults. Results from scenario C is omitted because they are similar to those of scenario B.

Country		Scenario A		Scenario B		Scenario D	
	% < 16 year old	% of < 16 years old that need to be vaccinated	% of whole population that need to be vaccinated	% of < 16 years old that need to be vaccinated	% of whole population that need to be vaccinated	% of < 16 years old that need to be vaccinated	% of whole population that need to be vaccinated
Singapore	12	0	88.0	40	92.8	80	97.6
Spain	14	0	86.0	40	91.6	80	97.2
Thailand	17	0	83.0	40	89.8	80	96.6
Brazil	21	10	81.1	60	91.6	90	97.9
India	26	30	81.8	70	92.2	100	92.6
Uganda	46	70	86.2	90	95.4	100	94.6

to the contact matrices used. For the population wide vaccination programme, if vaccine effectiveness is very high at 95% against symptomatic infections, herd immunity from vaccine alone is possible for all four scenarios of varying relative infectivity and susceptibility of children compared to adults, even for a highly transmissible variant with R_0 up to 8 (refer to Supplementary Figs. S5 and S6). If the vaccine effectiveness is lower at 65% against symptomatic infections, for R_0 between 4 and 8, herd immunity is not attainable by vaccine alone for all countries. For adult only vaccination, if R_0 is above 6, herd immunity by vaccine is not possible for most countries even with the best vaccine effectiveness (refer to Supplementary Fig. S4). The high R_{eff} despite 100% coverage in adult only vaccination highlights that vaccinating children, particularly

Table 2
R_{eff} if 100% of adults are vaccinated while no children is vaccinated, under the assumption that R_0 is 6, the vaccine has 95% effectiveness against symptomatic infections and seroprevalence is 0%. Scenario A: relative susceptibility and infectivity of children are half of adults, scenario B: relative susceptibility of children is half of adults and relative infectivity of children is equals to adults, scenario C: relative susceptibility of children is equals to adults and relative infectivity of children is half of adults and scenario D: relative susceptibility and infectivity of children are equal to adults. Results from scenario C is omitted because they are similar to those of scenario B.

Country	Scenario A	Scenario B	Scenario D
Singapore	0.79	1.37	2.54
Spain	0.80	1.39	2.59
Thailand	0.84	1.46	2.67
Brazil	1.03	1.86	3.34
India	1.27	2.30	3.92
Uganda	2.05	3.70	5.24

for those countries with a large proportion of children, will be needed to lower their R_{eff} to manageable levels without applying drastic social measures.

If there is some pre-vaccination seroprevalence (and assuming complete protection - the most extreme assumption)or a particular vaccine coverage, the R_{eff} decreases and thus the HIT is also slightly lower (refer to Supplementary Fig. S1) however, for a vaccine with 65% vaccine effectiveness against symptomatic infections, herd immunity is still impossible with a 10% seroprevalence. When the R_0 is kept constant, changing the age group specific symptomatic proportion among infections to extreme values of either 45% or 80% for all age groups has little effect on both the R_{eff} for a given vaccine coverage and the HIT (refer to Supplementary Figs. S2 and S3). Hence, some uncertainty in age group specific symptomatic proportion among infections would not affect outcomes.

Our findings are similar to other age group stratified mathematical simulation works (Zachreson et al., 2021; Nguyen et al., 2021) where they predicted that herd immunity will not be reached for a highly transmissible virus if vaccination coverage is below 95% even with a highly effective vaccine. Moreover, our results are also supported by real world observations where transmission is still ongoing in countries like Singapore (Ministry of Health, 2021) and South Korea (Anon, 2021) with at least 70% of their total population fully vaccinated (Ritchie et al., 2020) despite some SMMs in place. Our results differ slightly from those of Hodgson et al. (2021) where they showed that if a given vaccination coverage in the population is reached, herd immunity can be achieved. Instead, we showed that the same overall population vaccination coverage will not achieve the same reduction in transmission or HIT in different countries, as this depends on the age-specific contact patterns, children's role in transmission and who the vaccine is allocated to. This is a key consideration when extrapolating vaccination impact from one country to another or using a single HIT as the target for global vaccination programmes.

In this analysis, we evaluated the impact of varying vaccination coverage in different age groups on R_{eff} in the absence of any SMMs. This work can provide policy makers and healthcare professionals with an estimate on the reduction in transmission likely to be achieved from vaccination and hence the level of SMMs that should be put in place, to keep R_{eff} below 1. The minimum reduction in transmission necessary, a given a calculated value of R_{eff} is equals to $1-1/R_{eff}$ if it is assumed that the reduction in transmission due to the interventions is uniform across all age groups, vaccination status and disease status, or by assuming that a is the minimum reduction in transmission across all possible infected states. This inverse relationship between a and R_{eff} means that a does not increase linearly with R_{eff}, which implies that for a more transmissible virus variant with a higher R_{eff}, the level of interventions needed to keep the outbreak under control may not need to increase considerably. However, this inverse relationship also indicates that even for R_{eff} slightly above and close to 1, the level of interventions required remains quite high. Hence, it serves as a reminder that even when R_{eff} is close to 1, interventions should still be kept in place until herd immunity is achieved by vaccination.

There are several limitations in our work. Firstly, in the SIR model we considered, we supposed that there is no transition between the different age groups and ignored the natural birth and death rates and the additional mortality from COVID-19. These assumptions are only valid for the short term and when number of infections is not too high. However, if the pandemic persists for a prolonged period of time, it will be necessary to include the maturity rate for the age group transition and the other parameters that changes the population size. In addition, we assumed a single contact matrix that is uniform across the country, however contact patterns may vary geographically depending on the settings like rural vs urban or single household vs multi-generational household.

Moreover, the outcome of this analysis is the effective reproduction number R_{eff} which relates to the transmission potential given a context. It does not consider the number of cases and the severity of cases in the different age groups. Hence, while it provides a guideline on the vaccination coverage to reach herd immunity, it does not provide information on how different vaccination coverages affect the disease burden, which might be a more important issue for healthcare professionals and policy makers. Our results seem to discourage vaccinating the elderly since doing so will not decrease the R_{eff}, but it is likely that vaccinating the older age groups can help reduce the number of hospitalizations and deaths. Hence, using the R_{eff} as the only outcome in evaluating vaccination strategy is incomplete. Nevertheless, the model could help guide countries in terms of the most appropriate public health vaccination goal to reduce transmission potential as much as possible especially if achieving herd immunity is unrealistic based on country specific parameters and vaccine availability for adults/children. Extensions to this work could also consider the suitable age range for boosting, or the transmission reductions from boosting certain age groups.

Furthermore, while we suggest that this analysis can help guide decision makers on the level of interventions needed to limit transmission, the reduction in transmission in each age group resulting from individual interventions or combined interventions is unknown and may be context-dependent. Therefore, despite knowing the R_{eff} given a vaccination coverage, this work does not provide specific recommendations of what level and what kind of measures are necessary to reduce R_{eff} below one.

Lastly, we assumed that vaccination occurs independently of the serostatus of the person and that the R_0 value is uniform spatially. This is however unrealistic since vaccination coverage in a country can be heterogeneous, as vaccine uptake is related to structural factors as well as individual decision-making (Robertson et al., 2021). In addition, there are subgroups of the population that are in the higher risk groups, due to either the nature of their work which causes them to have higher chance of contacts with infected cases like those in the tourism, healthcare and manufacturing industry or due to overcrowded living conditions that cause them to have higher number of contacts with others. These higher risk groups and communities with lower vaccination coverage can still form local clusters even if herd immunity is achieved at a population level.

In order to conduct our analysis, numerous data sources are necessary. This includes country specific parameters: 1) population demographics and age group contact patterns, 2) vaccine supply and allocation, and general parameters: 1) the transmission rate of the current setting and variant, 2) relative infectivity and susceptibility of children compared to adults, 3) relative infectivity of asymptomatic cases compared to symptomatic cases in vaccinated and non-vaccinated people, 4) vaccine effectiveness parameters for the blocking of infection for the relevant variant. Some of these parameters are changing with the evolving situation while others could be updated according to the latest

findings and surveys (including contact surveys). This implies that HIT is not a constant value but changes with time depending on the situation. Hence, constant monitoring of the emergence of new variants and the waning of vaccine effectiveness is necessary to anticipate how the HIT would change and take actions like implementing SMMs and providing booster shots (Bar-On et al., 2021) to control transmission.

In conclusion, our results show that for a virus with R_0 of 4–8, like the previously dominant delta variant, or the now dominant omicron variant (early 2022), herd immunity by vaccination is not achievable for most countries if vaccine are allocated only to adults ages 16 and above, even with a highly effective vaccine. Therefore, other measures may need to be in place until vaccines are available for most children. Moreover, by using a country specific model, we showed that 1) the herd immunity threshold is different for different places, 2) targets for the of percentage of the population vaccinated to reach herd immunity should consider in which age groups are the vaccinated individuals and 3) that the changes in transmission from a certain percentage of the population being vaccinated in one country may be substantially different to those in another country.

CRediT authorship contribution statement

Fang Ting Goh: Conceptualization, Methodology, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Yi Zhen Chew:** Formal analysis, Visualization, Writing – review & editing. **Clarence C Tam:** Conceptualization, Writing – review & editing. **Chee Fu Yung:** Conceptualization, Writing – review & editing. **Hannah Clapham:** Conceptualization, Supervision, Writing – review & editing.

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Declaration of Competing Interest

The authors have no competing interests.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.epidem.2022.100581.

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