The potential for vaccination-induced herd immunity against SARS-CoV-2

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Childhood immunisation programmes have led to elimination of viruses with little antigenic variation – such as measles and rubella – in many countries [1]. In contrast, viruses such as influenza undergo frequent antigenic turnover, necessitating regular vaccine updates and re-vaccination [2]. Initial reports of vaccine effectiveness against SARS-CoV-2 have suggested a substantial reduction in risk of infection [3]. However, more transmissible variants such as B.1.1.7 [4] raise questions about the potential for a large-scale immunisation programme against SARS-CoV-2 to generate lasting herd immunity in populations with relatively low seroprevalence, even against variants antigenically similar to vaccine antigens.

The feasibility of attaining vaccination-induced herd immunity depends on vaccine effectiveness in reducing transmission, achievable population vaccine coverage and the transmissibility of the target pathogen. In a scenario where vaccinations are distributed randomly across a population, the herd immunity threshold (HIT) for an immunisation programme is defined as $1 - 1/R_0$, where R_0 is the basic reproduction number [5]. If vaccine effectiveness is below this value, then even vaccination of the entire population would, on its own, be insufficient to ensure control (i.e. the effective reproduction number, accounting for immunity, would remain above 1). Comparing this theoretical HIT with estimated values of R_0 and vaccine effectiveness for a range of vaccine-preventable diseases (**Figure 1A**), we see that for common immunising childhood infections, vaccine effectiveness is sufficiently high to control transmission if high vaccine coverage is achieved. In contrast, influenza A/H3N2 vaccine effectiveness implies that control in the absence of natural immunity is extremely unlikely, even in theory; we estimate a 2% probability of being above the HIT in an unexposed population with 100% vaccination coverage. Influenza vaccine effectiveness is influenced by antigenic evolution as well as characteristics of the vaccine itself; similar evolution has been observed for seasonal human coronaviruses [2]. For SARS-CoV-2, assuming 86% (95% CI: 76–97) vaccine effectiveness against infection, based on early estimates following two doses of BNT162b2 [3], we estimated a 99% probability of being above the HIT with whole-population coverage, with a 94% probability for B.1.1.7. However, whole-population vaccination would require SARS-CoV-2 vaccines – which are currently only approved for adults – to also be used at high coverage in children, which may be challenging to achieve given the risk of severe disease is lower among younger age groups. Vaccination impact would also be reduced if uptake is lower among groups, such as young adults, that contribute more to transmission [6].

Depending on vaccine coverage and effectiveness against future circulating variants – which may be antigenically dissimilar to B.1.1.7 [7] – herd immunity to SARS-CoV-2 in the absence of other non-pharmaceutical interventions may not be reached until considerable naturally-acquired immunity has also accumulated. Given some countries now have a sizeable subpopulation with protective antibodies acquired through natural infection [8], we estimated the probability of reaching the HIT for SARS-CoV-2 under varying degrees of vaccination

coverage against a background of reduction in transmission from previous naturally-acquired infections (**Figure 1B–C**). We find that for pre-B.1.1.7 SARS-CoV-2 variants, a whole-population immunisation programme could have generated herd immunity regardless of background seroprevalence even if vaccine effectiveness was as low as 70%. However, for B.1.1.7, we would expect ongoing transmission until sufficient naturally acquired protection has been accrued, unless vaccine effectiveness in reducing transmission remains over 85-90% and whole populations can be vaccinated. In the absence of booster campaigns, vaccine impact would also decline as a result of increasing susceptibility from new births, waning protection and antigenic evolution.

As further vaccine effectiveness data emerges, estimates of the potential for vaccination-induced control could be refined. Local differences in population structure and behaviour, as well as biological characteristics of SARS-CoV-2 variants, could also change baseline transmissibility and which groups drive outbreaks [9]. If vaccine impact in reducing transmission is in reality higher than assumed here, the feasibility of elimination would increase; conversely, future variants could reduce the effectiveness of current SARS-CoV-2 vaccines, much as influenza vaccines are less effective against heterotypic strains [10].

Our observations suggest that if highly transmissible or antigenically distinct SARS-CoV-2 variants become dominant in low seroprevalence regions, elimination of infection may only be achievable if some non-pharmaceutical interventions remain in place to reduce R_0 or prevent reintroductions, or next generation vaccines can provide persistently high vaccine effectiveness with cross-protection against antigenic variants. Based on current evidence, reopening strategies in such countries should therefore not assume that even whole-population vaccination will be sufficient to fully prevent future transmission.

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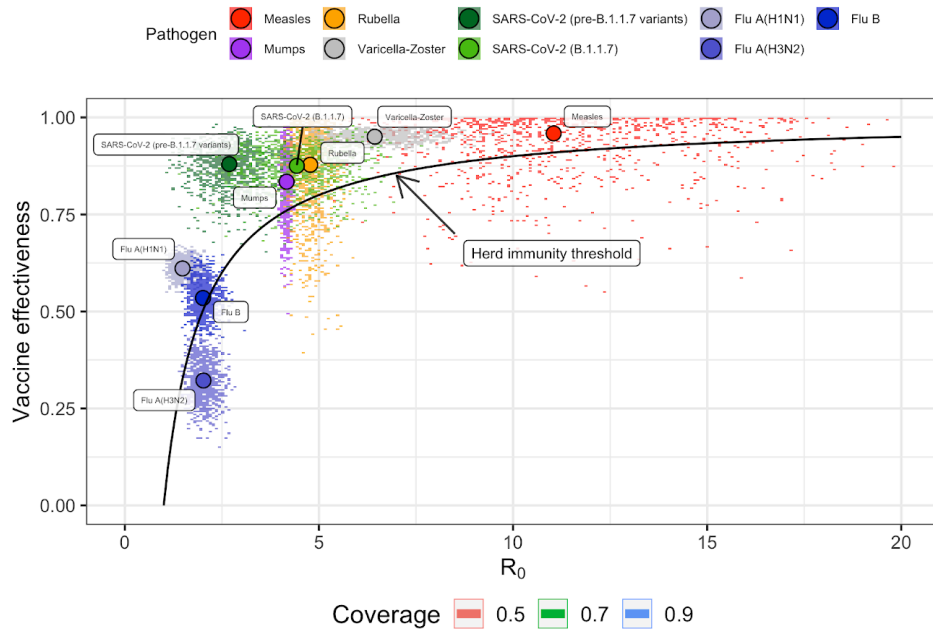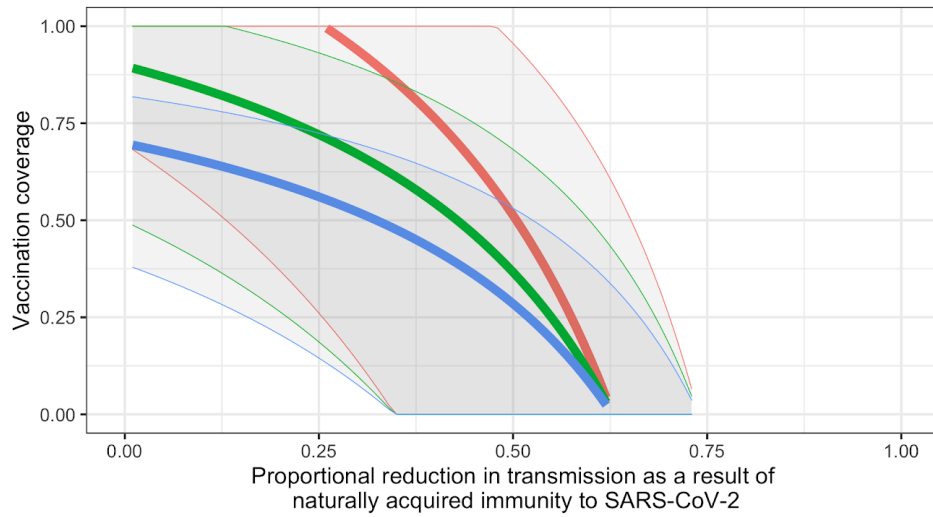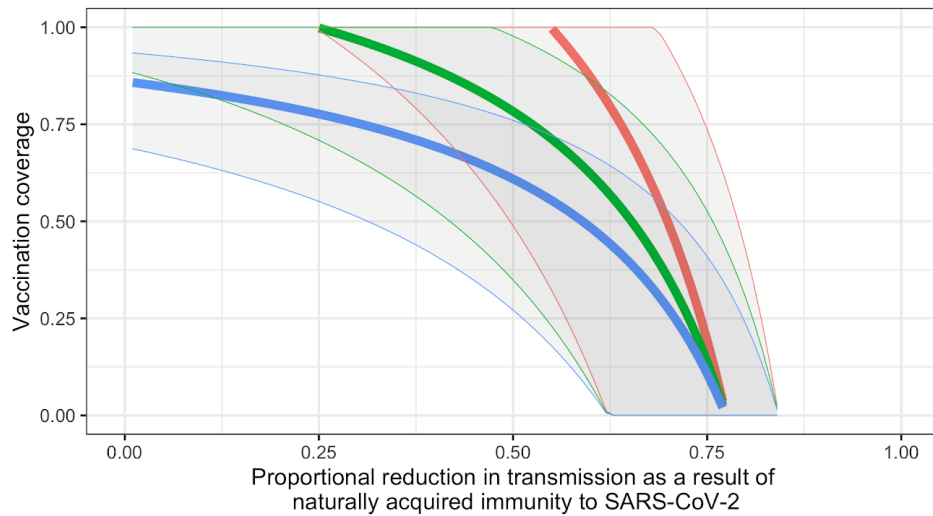
Figure 1: Comparison of vaccine impact and herd immunity thresholds for different vaccine-preventable viral diseases. A) Comparison of the effectiveness of currently available vaccines against the herd immunity threshold for different viruses. The black line shows the minimum vaccine effectiveness needed to achieve herd immunity for given R_0 values. Colour points represent samples from available effectiveness and transmissibility estimates (see Appendix), with large points showing medians. If sampled points are above the line, vaccination of the entire population could in theory lead to epidemic control; the more samples that are above the line, the higher the probability of control. B) Vaccination coverage required to reach herd immunity for pre-B.1.1.7-like transmission and different levels of vaccine effectiveness. Line shows median and shaded region 95% Credible Interval. Blue, 90% effectiveness in reducing transmission; green, 70%; red 50%. C) Vaccination coverage required to reach herd immunity for B.1.1.7-like transmission. Data sources are provided in the supplementary appendix.

Supplementary appendix

Source of vaccine effectiveness estimates
We obtained published estimated for the average and 95% upper and lower confidence intervals for vaccine effectiveness against measles [1], mumps [1], rubella [1], varicella [1], SARS-CoV-2 [2], influenza A/H1N1 (post-2009), A/H3N2, and B [3]. For SARS-CoV-2, we used data from a study estimating vaccine effectiveness in reducing infection among antibody negative healthcare workers who received two doses of BNT162b2 [4]. Two dose effectiveness was estimated at 86% (95% CI: 76-97%), with single dose at 72% (58-86%). This compares with an estimate of 75% (72–84%) single dose effectiveness in Israel [5] and an estimate of 83% (76-87%) lower risk of reinfection among healthcare workers following prior infection [6]. In order to reflect uncertainty in estimates, we generated a set of Monte Carlo samples for each pathogen by fitting the average and upper/lower confidence intervals to a beta distribution and sampling 1,000 values.

Source of pathogen R0 estimates
For mumps, rubella, and varicella, we obtained a set of 1,000 samples by bootstrapping a set of pre-vaccination R0 estimates from various regions [7,8]. For measles, SARS-CoV-2 variants, and influenza subtypes, we obtained estimates of the average, upper confidence interval and lower confidence interval for each to a lognormal distribution in order to sample 1,000 values [9–12]. We assumed that transmissibility of SARS-CoV-2 B.1.1.7 was 67% higher than for pre-B.1.1.7 variants [10].

Code
The code used in this analysis can be found at https://github.com/adamkucharski/hit-analysis

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Pathogen	Vaccine effectiveness (%, mean, 95% CI)	Basic reproduction number (mean, 95% CI)
Measles	96 (72–99)	12.0 (6.0–18.0)
Mumps	86 (65–92)	4.2 (3.6–4.5)
Rubella	89 (58–97)	4.7 (3.4–7.8)

Varicella	95 (92–97)	6.5 (3.3–16.9)
SARS-CoV-2 (pre-B.1.1.7)	86 (76–97)	2.7 (1.5–3.8)
SARS-CoV-2 (B.1.1.7)	86 (76–97)	4.5 (2.5–6.4)
Influenza A/H1N1 (post-2009)	61 (57–65)	1.4 (1.2–2.0)
Influenza A/H3N2	33 (22–43)	2.1 (1.6–2.5)
Influenza B	54 (46–61)	2.1 (1.6–2.5)

Appendix Table 1: Assumed values of vaccine effectiveness and basic reproduction number for different pathogens, based on empirical estimates.