Assessing impact of Omicron on SARS-CoV-2 dynamics and public health burden

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NOTE: This preprint reports new research that has not been certified by peer review and should not be used to guide clinical practice.
Summary

SARS-CoV-2 variant Omicron (B.1.1.529) was classified as a variant of concern (VOC) on November 26, 2021. (1, 2) The infectivity, severity, and immune evasion properties of Omicron relative to the Delta variant will determine 1) the probability of dominant future transmission, and 2) the impact on disease burden. (3, 4) Here we apply an individual-based transmission model to identify thresholds for Omicron’s potential dominance, impact on health, and risk to health systems; and identify for which combinations of viral properties, current interventions would be sufficient to control transmission. We show that, with first-generation SARS-CoV-2 vaccines (5) and limited physical distancing in place, the threshold for Omicron’s future dominance will primarily be driven by its degree of infectivity. However, Omicron’s potential dominance may not necessarily lead to increased public health burden. Expanded vaccination that includes a third-dose for adults and child vaccination strategies is projected to have the biggest public health benefit for a highly infective, highly severe variant with low immune evasion capacity. However, a highly immune evading variant that becomes dominant will likely require alternative measures for control, such as strengthened physical distancing measures, novel treatments, and second-generation vaccines. These findings provide quantitative guidance to decision-makers at a critical time while Omicron properties are being assessed. (6) We emphasize the importance of both genomic and population epidemiological surveillance.
Introduction

SARS-CoV-2 has been mutating continuously since its emergence in December 2019, leading to viral variants with varying infectivity, severity, and immune evading properties. On 26 November 2021, the World Health Organization identified Omicron (B.1.1.529) as a new variant of concern (VOC) after approximately seven months of Delta variant (B.1.617.2) dominating global transmission. (1) Within one week, 24 countries had reported cases of the Omicron variant, (7) with infections also occurring in previously infected and double-vaccinated individuals. (8) Whilst scientific research assessing the infectivity, severity, and immune evasion properties of Omicron are ongoing, understanding the potential scope of Omicron’s public health burden is of top priority. (2)

In many European settings, high vaccination rates - particularly among those most at risk of severe disease - have led to a reduction in disease burden. However, protection of the most vulnerable and maintaining low levels of SARS-CoV-2 transmission in the northern hemisphere are currently under threat for multiple reasons. Firstly, indoor contacts are increasing due to the cooler season. Secondly, immunity of the most vulnerable population (people 65+ and those with comorbidities) is potentially waning since they were primarily vaccinated in the first quarter of 2021. Thirdly, relaxation of most non-pharmaceutical interventions (NPIs) since the summer period and fatigue of COVID-19 restrictions has led to increased contacts. The emergence of Omicron combined with these threats calls into question whether current vaccination strategies will be sufficient.

Mathematical models have been used to represent transmission dynamics of SARS-CoV-2 and have supported decision-makers throughout the pandemic on the implementation and relaxation of control strategies. (9-13) Here we further developed and applied OpenCOVID, an individual-based model of SARS-CoV-2 transmission and COVID-19 disease, which includes seasonality patterns, waning immunity profiles, vaccination and NPI strategies, and properties for multiple
variants. (12) We applied the OpenCOVID model to represent a general European setting and simulated the emergence of a novel variant. We analysed disease dynamics for a wide range of infectivity, severity, and immune evasion properties – relative to the Delta VOC – representing a large range of potential Omicron properties. This allowed us to determine the potential for Omicron to become the new dominant variant, and to estimate its potential future public health burden. We further identified combinations of Omicron’s properties for which first-generation vaccines, in the absence of strong NPIs, may be sufficient to contain transmission and public health burden (i.e., new SARS-CoV-2 infections, ICU occupancy, and COVID-19 related deaths) and identified those combinations for which additional measures may be required.

Results

Disease dynamics projections

We explored a wide range of potential Omicron infectivity and severity levels (between zero and two) relative to Delta, and the full range of immune evading capacity from 0% (similar to Delta) to 100% (no protection from current vaccines and previously acquired natural immunity after infection). Disease dynamics were simulated over a six-month period beginning 1 December 2021 when Omicron emerged, and the cooler weather arrived. We assume an initial effective reproduction number of 1.2, the absence of strict NPIs (e.g., lockdowns), and vaccination coverage by risk group as described in Supplementary Table 1.

We compared two future vaccination scenarios. Firstly, expanded vaccination, with the administration of a third-dose six months after the second dose for individuals older than 12 years of age, and administration of vaccines for children aged 5-11 years. Secondly, we simulated a scenario with no future vaccine rollout (no third-dose vaccination in over 12-year olds and no vaccination of 5-11 year-olds). The latter leading to decay of population-level vaccine-induced immunity over time.
Drivers of Omicron’s potential dominance

Infectivity and immune evasion were identified as the main drivers behind Omicron’s potential dominance, with negligible effect from increasing severity. For an infectivity factor of 1, a 25% immune evasion property is predicted sufficient for dominance, while for a 100% immune evading property an infectivity factor of 0.5 (half the infectivity of Delta) is predicted sufficient. All combinations of properties are presented in Supplementary Figure 1-2. When highly immune evading, Omicron’s chance to dominate would even slightly increase with future expanded vaccination, as vaccines provide a high level of protection against Delta variant infection (14), consequently increasing the relative susceptibility of the population to Omicron infection.

Disease burden

If Omicron is less infective than Delta (below 1), with no immune evading capacity, it would not become dominant and the public health impact due to its emergence will be negligible (Supplementary Figures 2 -3 and Supplementary Table 2). Assuming Omicron has partial immune evading capacity (20%) and higher infectivity (1.2) and severity (1.5) than Delta, we predict it would take approximately five months for Omicron to become dominant. We predict these properties to lead to a relatively low public health burden, particularly with expanded vaccination. However, in scenarios where Omicron has higher levels of immune evasion capacity (50%), infectivity (1.5), and severity (2) relative to Delta, dominance can occur within two months, resulting in a high projected public health burden. For most combinations of properties Omicron becomes dominant within two to three months, we predict a high to very high impact on disease burden.

Projected impact on peak ICU occupancy

Expanded vaccination is predicted to be sufficient to prevent high ICU occupancy (dark grey/black area of Fig. 1, capped at 25 ICU beds per 100,000 people) for settings in which Delta
remains dominant. For a highly infectious (infectivity factor >1.5) but non-immune-evading variant, we predict expanded vaccination may be sufficient to prevent high ICU occupancy, however this probability diminishes with increasing severity. Moreover, there exists a range of infectivity and immune evading properties for which Omicron becomes dominant, but is not expected to lead to high peak ICU occupancy under the assumption of expanded vaccination (Fig. 1 and dotted area in Fig. 3). Similarly, this range diminishes with increasing severity. For a variant with infectivity and severity similar to Delta, we predict expanded vaccination will be insufficient to prevent high peak ICU occupancy for an immune evading property above 75%. For properties that are predicted to lead to high ICU occupancy, settings would benefit from additional measures such as physical distancing, or new treatments and next generation vaccines as they become available.

Fig. 1: Peak daily ICU occupancy (number of beds per 100,000 population over the six-month simulation period) for a range of variant properties. The threshold (50% prevalence, see Supplementary Figure 3) for Omicron’s dominance is presented by red lines (solid for expanded
vaccination, dashed for no future vaccination). Expanded vaccination includes third-doses for adults (six-months after second-dose) and vaccinating 5-11-year-olds. Rows represent Omicron’s potential severity (0 to 2) relative to Delta (1). Horizontal axes represent the range of Omicron’s potential infectivity (0 to 2) relative to Delta (1), left vertical axes Omicron’s potential immune evading capacity (0 to 100%). The peak ICU occupancy per 100,000 people has been capped at 25 per 100,000, a much higher ICU capacity than most countries.

**Impact on COVID-19 infections and deaths**

Omicron’s potential severity will have negligible influence on new infections; however, it heavily influences future mortality (in the absence of additional measures that would likely be implemented before such high mortalities (and ICU occupancy) would be reached, (Supplementary Figures 4 and 5). Fig. 2 presents the percentage of infections and deaths averted through expanded vaccinations for all specified combinations of properties. The highest public health burden in terms of infections and deaths (top right corner of Supplementary Figures 4 and 5), are least likely to be reduced by expanded vaccination (top right of panels in Fig. 2), because of highly immune evading capacity. However, when Omicron becomes dominant, expanded vaccination has an impact for combinations of properties where immune evasion is low (bottom right of panels in Fig. 2). The benefit of expanding vaccination will also be seen for scenarios where Delta remains dominant (area to the left of the black lines in Fig. 2).
Fig. 2: Percentage of COVID-19 infections and deaths averted by third-dose vaccines for adults and vaccinating 5-11-year-olds with doses one and two. The threshold (50% prevalence) for Omicron’s dominance is presented by black lines (solid line for expanded vaccination, dashed for no future vaccination). Left panels represent the percentage infections averted, right panels the percentage of deaths averted due to expanded vaccination, with colour representing % averted. Rows represent Omicron’s potential severity (0 to 2) relative to Delta (1), horizontal axes Omicron’s potential infectivity (0 to 2) relative to Delta (1) and left vertical axes Omicron’s potential immune evading capacity (0 to 100%). Maximum percentage of burden averted is capped at 50%, with blue area extending to values >50%.
Fig. 3: Schematic illustrating a summary of the interplay between potential infectivity, immune evasion of Omicron on its chances of becoming dominant and increasing public health burden.

To aid interpretation of Omicron’s properties on its chance of becoming dominant and overall impact on public health burden in a vaccinated population, we summarised our findings in a schematic (Fig. 3). The darkness of colour in the heat map indicates the level of disease burden (infections and deaths) and risk to health systems (ICU occupancy) at the corresponding level of relative infectivity and immune evasion. The dashed line indicates when Omicron would become the dominant variant without future vaccinations, the solid line when it would become dominant with expanded vaccination. The dotted area indicates when Omicron would become dominant without increased disease burden or risk to health systems. Area A indicates variant property space where expanded vaccination alone will not prevent increased transmission and would lead to increased infections, ICU occupancy, and deaths. Additional measures would be needed in the case of very high immune evading variant including second-generation vaccines and/or novel treatment once available, or strengthened NPIs in their absence. Area B indicates space where expanded vaccination with first-generation vaccines will have the highest impact.
on reducing disease burden and health system risk. In case of low severity in area B, expanded vaccinations may be sufficient for control.

Discussion

Using our OpenCOVID individual-based transmission model, we simulated the interplay of Omicron's potential combinations of infectivity, severity, and immune evasion properties. We first identified the threshold of Omicron becoming the dominant variant (over Delta), for which infectivity was found to be the main driver followed by immune evasion. Increased disease severity of Omicron was found to have limited effect on dominance, but when dominant, to increase ICU occupancy and number of deaths. If Omicron has increased infectivity and severity to Delta, then expanding first-generation vaccination with a third-dose and vaccinating 5-11-year-olds could avert many cases and deaths. However, should Omicron be highly immune evading, first-generation vaccines will not suffice, and additional measures will be required to control transmission until vaccines are updated.

Besides additional preventive measures such as strengthened NPIs and second-generation vaccines, new treatments currently under development to reduce ICU occupancy and mortality may need to be implemented. Maximum ICU capacity will have to be considered as it differs between countries, ranging from five to 35 beds per 100,000-population capita in Europe. (15). In a worst-case scenario of highly immune evading and increased severity of Omicron, for many countries, our predictions reach or surpass maximum ICU capacity. However, very high occupancy rates are unlikely to be reached as countries would implement additional measures sooner.

Although our analysis focuses on ICU occupancy and mortality as a higher priority public health risk, even rising SARS-CoV-2 infections due to lower severity Omicron may lead to a substantial risk of increased long-COVID (16) and should not be neglected in response...
planning. Furthermore, as we considered expanding vaccination with third-doses, the global
inequity of vaccine access, and the selective pressure and emergence of new variants in settings
with low vaccination rates is a global health emergency that needs to be addressed (17).

Our transmission model is based on assumptions that influence its outcomes. In our model
predictions, we identified that Omicron’s potential severity had little effect on the number of
new cases, also because no impact on viral load was assumed. Higher viral load in the model is
associated with increased transmissibility. The two vaccination scenarios we present in this
study, expanded vaccination (with a third-dose for those 12 years of age and older, and two-
dose vaccines for children aged 5-11 years) and no future vaccination, are examples of two
extreme scenarios. The reality will lie in between and will be region dependent. Waning
immunity is assumed to reduce linearly to zero in approximately one year. However, should
immunity wane much slower, then the population would be protected for a longer period against
either Delta (or a new non-immune evading variant), and our outcomes would prove too
pessimistic. Our outcomes would be too optimistic should immunity wane faster than assumed.

A higher or lower value of 1.2 for the effective reproduction number at the start of the winter
period, prior to introduction of Omicron, may influence peak ICU occupancy estimates,
however the relative impact of vaccination is not sensitive to this parameter.

SARS-Cov-2 mutations have been identified throughout the pandemic and new variants are
likely to continue to emerge. Compared with the Alpha variant, Delta has severity ratios
reported as 1.3- to 2.3-times higher for ICU admissions and deaths. (18) Both vaccine-acquired
and naturally acquired immunity will not suffice to prevent infection or disease if a new variant
is highly immune evading. Based on these predictions we stress that vaccines may need
adjustment to respond to current or future viral mutations. We further advocate for continued
genomic surveillance and see it crucial to quickly test and continue improving assays that
elucidate immune evasion properties of a new VOC, to better understand the risk for increased infectivity and/or severity.

Conclusion

As the properties of Omicron or any future SARS-CoV-2 VOC become known, our analyses elucidate interpretation of the variant’s potential dominance and subsequent public health burden. Combined with VOC genomic (19) and population epidemiological surveillance (20), alongside antibody neutralisation testing (21) our findings provide crucial quantitative guidance to decision-makers at a critical time.

References

1. Organization WH. Classification of Omicron (B.1.1.529): SARS-CoV-2 Variant of Concern 2021 [updated 26 November 2021. Available from: https://www.who.int/news/item/26-11-2021-classification-of-omicron-(b.1.1.529)-sars-cov-2-variant-of-concern.

2. Organization WH. Update on Omicron 2021 [Available from: https://www.who.int/news/item/28-11-2021-update-on-omicron.

3. Burioni R, Topol EJ. Has SARS-CoV-2 reached peak fitness? Nature Medicine. 2021;27(8):1323-4.

4. Iftekhar EN, Priesemann V, Balling R, Bauer S, Beutels P, Calero Valdez A, et al. A look into the future of the COVID-19 pandemic in Europe: an expert consultation. The Lancet Regional Health – Europe. 2021;8.

5. Commission E. Safe COVID-19 vaccines for Europeans 2021 [Available from: https://ec.europa.eu/info/live-work-travel-eu/coronavirus-response/safe-covid-19-vaccines-europeans_en.

6. Control ECIDPa. SARS-CoV-2 variants of concern as of 3 December 2021 2021 [Available from: https://www.ecdc.europa.eu/en/covid-19/variants-concern.

7. Dyer O. Covid-19: South Africa’s surge in cases deepens alarm over omicron variant. 2021;375:n3013.

8. Chen J, Wang R, Benovich Gilby N, Wei G-W. Omicron (B.1.1.529): Infectivity, vaccine breakthrough, and antibody resistance. arXiv e-prints. 2021:arXiv:2112.01318.

9. Kerr CC, Stuart RM, Mistry D, Abeyesuriya RG, Rosenfeld K, Hart GR, et al. Covasim: An agent-based model of COVID-19 dynamics and interventions. PLOS Computational Biology. 2021;17(7):e1009149.

10. Hinch R, Probert WJM, Nurtay A, Kendall M, Wymant C, Hall M, et al. OpenABM-Covid19—An agent-based model for non-pharmaceutical interventions against COVID-19 including contact tracing. PLOS Computational Biology. 2021;17(7):e1009146.

11. Sonabend R, Whittles LK, Imai N, Perez-Guzman PN, Knock ES, Rawson T, et al. Non-pharmaceutical interventions, vaccination, and the SARS-CoV-2 delta variant in England: a mathematical modelling study. The Lancet. 2021;398(10313):1825-35.

12. Shattock AJ, Le Rutte EA, Dünner RP, Sen S, Kelly SL, Chitinis N, et al. Impact of vaccination and non-pharmaceutical interventions on SARS-CoV-2 dynamics in Switzerland. medRxiv. 2021:2021.04.14.21255503. Under final revisions at Epidemics, pdf provided

13. Czyzewski A. Modelling an unprecedented pandemic: The vital role of team-based, collaborative epidemiology and disease modelling in managing pandemics [Available from: https://www.imperial.ac.uk/stories/coronavirus-modelling/.
14. Pouwels KB, Pritchard E, Matthews PC, Stoesser N, Eyre DW, Vihta K-D, et al. Effect of Delta variant on viral burden and vaccine effectiveness against new SARS-CoV-2 infections in the UK. Nature Medicine. 2021.
15. Bauer J, Brüggmann D, Klingelhöfer D, Maier W, Schwettmann L, Weiss DJ, et al. Access to intensive care in 14 European countries: a spatial analysis of intensive care need and capacity in the light of COVID-19. Intensive Care Med. 2020;46(11):2026-34.
16. Sudre CH, Murray B, Varsavsky T, Graham MS, Penfold RS, Bowyer RC, et al. Attributes and predictors of long COVID. Nature Medicine. 2021;27(4):626-31.
17. Organization WH. Vaccine Equity 2021 [Available from: https://www.who.int/campaigns/vaccine-equity.
18. Fisman DN, Tuite AR. Progressive Increase in Virulence of Novel SARS-CoV-2 Variants in Ontario, Canada. medRxiv. 2021:2021.07.05.21260050.
19. Robishaw JD, Alter SM, Solano JJ, Shih RD, DeMets DL, Maki DG, et al. Genomic surveillance to combat COVID-19: challenges and opportunities. The Lancet Microbe. 2021;2(9):e481-e4.
20. Torjesen I. Covid-19: Omicron may be more transmissible than other variants and partly resistant to existing vaccines, scientists fear. BMJ. 2021;375:n2943.
21. News N. Omicron likely to weaken COVID vaccine protection 2021 [updated 08 December 2021. Available from: https://www.nature.com/articles/d41586-021-03672-3.

Methods

OpenCOVID individual-based model

OpenCOVID is a stochastic, discrete-time, individual-based transmission model of SARS-CoV-2 infection and COVID-19 disease (12). The model simulates viral transmission between infectious and susceptible individuals that come in contact through an age-structured, small-world network. The probability of transmission in each exposure is influenced by the infectiousness of the infected individual the immunity of the susceptible individual (acquired through previous infection and/or vaccination), and a background seasonality pattern (reflecting a larger proportion of contacts being in closer contact indoors with cooler temperatures).

Infectiousness is a function of viral variant infectivity and time since infection (which follows a gamma distribution peaking approximately at the time of symptom onset). Once infected, a latency period is followed by a pre-symptomatic stage, after which the individual can experience asymptomatic, mild, or severe infection. Severe cases can lead to hospitalisation, ICU admission, and ultimately death. Recovery after infection leads to development of immunity. This immunity is assumed to wane over time and can be further reduced if exposed to a novel variant with immune evading properties (Supplementary Table 2 for further details).
The model has the capacity to represent a number of containment measures, including non-pharmaceutical interventions such as social distancing and facemask usage, testing strategies such as test-diagnose isolate, mass-testing, and contact tracing, and also pharmaceutical interventions such as vaccination and treatment.

Detailed model descriptions and model equations are described in. (12) Open access source-code for the OpenCOVID model is publicly available at (https://github.com/SwissTPH/OpenCOVID).

**Vaccination**

In this analysis, we simulate the impact of mRNA vaccines Pfizer/BioNTech and Moderna, which together make up 78% of the total number of doses secured in Europe. (5) Fully susceptible, partially susceptible, and infected individuals not in hospital are considered eligible to receive a vaccine. Vaccines have a two-fold effect; first, they provide protection against new infection through development of immunity (90% transmission blocking effect modelled). Secondly, once infected, vaccines reduce the probability of developing severe symptoms, leading to reduced hospitalisations, ICU admissions, and deaths. Details regarding targeted vaccination groups and assumed durations between doses and vaccine efficacies are described in the Supplementary Information 2.2-2.3. Associated waning immunity profiles after infection and vaccination are described in Supplementary Information 2.4.

**Variant properties**

Delta (B.1.617.2) is assumed to be the dominant transmission variant at the time of Omicron (B.1.1.529) emergence. A full factorial range of Omicron properties were considered:1) infectivity (transmission multiplication factor per exposure relative to Delta), ranging from 0 to 2, 2) disease severity (multiplication factor per infection, relative to Delta ranging from 0 to 2), and 3) immune evasion capacity from 0-100%. In the model, once infected with a new variant, severity influences the chance to manifest severe symptoms, rather than mild or no symptoms.
One hundred percent immune evasion means fully evading any previously naturally or vaccination-acquired immunity, making an individual susceptible to infection with a new variant. Full model details on the variant properties are described in Supplementary Information 2.5 alongside probabilities that immunologically naïve infected with develop severe disease in Supplementary Table 3.

Model initialisation

All model simulations were designed to be pseudo-representative of a European setting at the beginning of December 2021. We assume 30% of the population have been previously infected with SARS-CoV-2 over a 630 day period (representing epidemic outbreak in Europe in March 2020). We assume the effective reproduction number ($R_e(\tau)$) on 1 December 2021, is equal to 1.2. This represents an average scenario of increasing case numbers across Europe at the start of the winter period prior to the emergence of Omicron. This level of $R_e(\tau)$ is lower than levels in some European countries with strongly increasing cases as of early December, however also higher than those that implemented strong NPI before 1st December. The average number of daily contacts required to achieve an $R_e(\tau)$ of 1.2 inherently considers any non-pharmaceutical interventions in place at the beginning of the winter period in Europe prior to the emergence of Omicron. Seasonality is assumed to follow a cosine function, with a peak in seasonal infectivity occurring 6 weeks from model initialisation (representing mid-winter see Supplementary Information Figure 6).

Analyses

For the full range of variant properties specified, we simulated two vaccination scenarios from the introduction of the new variant to six months into the future. For the first scenario, no future vaccinations are implemented. The second scenario is identical up to 1 December 2021, but simulates expanded vaccination with first-generation vaccines administering as third-doses in adults (six months after second-dose) and scale up of first- and second-dose in 5-17 year-olds.
Each simulation provided the relative prevalence of Omicron over the next 6 months compared with Delta, as well as daily and cumulative numbers of new SARS-CoV-2 infections, maximum ICU occupancy, and COVID-19-related deaths. To reflect the element of chance that naturally occurs in transmission dynamics, 10 random stochastic simulations were performed per scenario for which we present the mean. In this analysis we do not explore the effect of varying NPI intensity over time. As such, our analysis reflects predicted disease dynamics and public health burden in the absence of strong NPIs, such as lockdowns.

**Data availability statement**

Data sharing is not applicable to this article as no datasets were generated or analysed during the study. Data informing model parameters are described in Shattock et al. (12)

**Code availability statement**

All model code and Figure code are open access and publicly available at [https://github.com/SwissTPH/OpenCOVID](https://github.com/SwissTPH/OpenCOVID). For this paper model code and Figure code are version 2.0 of OpenCovid.

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**Author contributions**

EALR and AJS conceived the study, performed the analyses, prepared figures, and conducted model and analysis validation. AJS further developed the model with input from EALR, SLK, and MAP. All authors contributed to interpretation of the results, writing the draft, and final version of the manuscript, and gave final approval for publication.
Competing interests
The authors declare no competing interests.

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Supplementary Information:

Assessing impact of Omicron on SARS-CoV-2 dynamics and public health burden

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1. Supplementary Figures 1-6 and Tables 1-3

Supplementary Table 1. Overview of two vaccination scenarios. No future vaccination, and expanded vaccination through third-dose in adults (six months after second-dose) and scale up in 5-17 year-olds with first-generation vaccines. Additional details are provided in section 2.3.

| Group                        | As of 1 December 2021 | No future vaccination | Expanded vaccination |
|------------------------------|-----------------------|-----------------------|----------------------|
| 65+ or comorbidities         | 90% coverage          | 90% coverage          | 90% coverage of third dose* 180 days after second dose |
| Adults 18-64                 | 70% coverage          | 70% coverage          | 70% coverage of third dose* 180 days after second dose |
| Adolescents 12-17            | 50% coverage          | 50% coverage          | Scale up to 70% coverage within 2 months |
| Children 5-11                | 0% coverage           | 0% coverage           | Scale up to 50% coverage within 4 months |
| Total number of doses in future | zero                  | 16,000 per 100,000 people over six-months |

*5% dropout included between those receiving second and third-dose (95% acceptance rate for third dose for these with two doses)

Supplementary Table 2. Summary of seven combinations of Omicron’s potential properties including infectivity, severity, and immune evasion. Probability of Omicron becoming the dominant variant, associated public health burden of Omicron emergence, and the effect of expanded vaccination through third-dose in adults (six months after second-dose) and scale up in 5-17 year-olds with first-generation vaccines.

| Simulation | Infectivity (relative to Delta) | Severity (relative to Delta) | Immune evasion | Probability of Omicron dominance | Public health impact | Expanded vaccination* effect |
|------------|---------------------------------|------------------------------|----------------|----------------------------------|----------------------|-----------------------------|
| 1          | 1                               | 1                            | 0%             | Low                              | Negligible           | High                        |
| 2          | 2                               | 1                            | 0%             | Very high                        | High                 | High                        |
| 3          | 2                               | 2                            | 0%             | Very high                        | High                 | Very high                   |
| 4          | 1                               | 1                            | 100%           | Very high                        | High                 | Moderate                    |
| 5          | 1.2                             | 2                            | 20%            | High                             | Low                  | Moderate                    |
| 6          | 1.5                             | 2                            | 50%            | Very high                        | High                 | Low                         |
| 7          | 2                               | 2                            | 100%           | Very high                        | Very high            | Negligible                  |

* Expanded vaccination through third-dose in adults and vaccinating 5-17 year-olds with first-generation vaccines
Supplementary Figure 1. Temporal epidemiological trends for seven combinations of Omicron’s potential properties under no future vaccination. Public health burden is represented by COVID-19 infections and ICU occupancy per 100,000 population per day. Variant prevalence percentage over time is presented in the bottom row.
Supplementary Figure 2. Temporal epidemiological trends for seven different combinations of Omicron’s potential properties under expanded vaccination. This figure represents a setting with future expanded vaccination through third-dose in adults (six months after second-dose) and scale up in 5-11 year-olds with first-generation vaccines. Public health burden is represented by COVID-19 infections and ICU occupancy per 100,000 population per day. Variant prevalence percentage over time is presented in the bottom row.
**Supplementary Figure 3.** The projected prevalence of the Omicron variant under combinations of infectivity, immune evasion capacity, and severity after six months. Black line represents the threshold (50%) for Omicron to become dominant (areas to the right of the lines). Left column represents a setting with expanded vaccination through third-dose in adults (six months after second-dose) and scale up in 5-17 year-olds with first-generation vaccines. Right column represents a setting with no future vaccination. Horizontal axes represent the range of Omicron’s potential infectivity (0 to 2) relative to Delta (1). Vertical axes represent the range of Omicron’s (or a new VOC’s) potential immune evasion capacity (0 to 100%). Rows represent five levels of Omicron’s potential severity (0 to 2) relative to Delta (1).
Supplementary Figure 4. Cumulative number of SARS-CoV-2 infections (per 100,000 population over the six-month simulation period) for a wide range of variant properties. Solid and dashed black lines represent the threshold (50%) for Omicron to become dominant (area to the right of the black line). Left panels represent a setting with expanded vaccination with first-generation vaccines through third-dose in adults (six months after second-dose) and scale up in 5-17 year-olds, right panels, a setting with no future vaccination. Horizontal axes represent the range of Omicron’s potential infectivity (0 to 2) relative to Delta (1). Left vertical axes represent the range of Omicron’s potential immune evasion capacity (0 to 100%). Rows represent five levels of Omicron’s potential severity (0 to 2) relative to Delta (1).
Supplementary Figure 5. Cumulative number of COVID-19-related deaths (per 100,000 population over the six-month simulation period) for a wide range of variant properties. Solid and dashed black lines represent the threshold (50%) for Omicron to become dominant (area to the right of the black line). Left panels represent a setting with expanded vaccination through third-dose in adults (six months after second-dose) and scale up in 5-17 year-olds using first-generation vaccines, right panels, a setting with no future vaccination. Horizontal axes represent the range of Omicron’s potential infectivity (0 to 2) relative to Delta (1). Left vertical axes represent the range of Omicron’s potential immune evasion capacity (0 to 100%). Rows represent five levels of Omicron’s potential severity (0 to 2) relative to Delta (1).
Supplementary Figure 6. Predicted temporal epidemiological trends for Delta in the absence of Omicron under no future vaccination and expanded vaccination, alongside seasonality profile. Public health burden is represented by COVID-19 infections, ICU occupancy and COVID-19 related mortality per 100,000 population per day. Seasonal infectious and susceptible population over time is presented in the bottom row. Blue illustrates dynamics with expanded vaccination, and red with no future vaccination.

2. Supplementary methods

2.1 Model initialisation

All model simulations were designed to be pseudo-representative of a general Western European setting at the beginning of December 2021. We assume 30% of the population have been previously infected with SARS-CoV-2 over a 630 day period (representing epidemic outbreak in Europe in March 2020). We assume the effective reproduction number on 1 December 2021 is equal to 1.2. This represents increasing case numbers across Europe at the start of the winter period, prior to the emergence of Omicron. The average number of daily contacts required to achieve an initial effective reproduction number of 1.2 inherently considers any non-pharmaceutical interventions in place at the beginning of the winter period in Europe prior to the emergence of Omicron. Seasonality is assumed to follow a cosine function, with a peak in seasonal infectivity occurring 6 weeks from model initialisation (representing mid-winter, Supplementary Figure 6).

2.2 Vaccine rollout

Four distinct risk groups are simulated for vaccination rollout; those 65 years of age and older or live with comorbidities (high-risk group), all other adults (18-64-year-olds), adolescents (12-17-year-olds), and children (5-11-years-olds). In our simulations, vaccinations start in the high-risk group in January 2021 reaching a 90% coverage rate on 1 December 2021. The 18-64-year-olds start vaccination on 1 May 2021, achieving 70% coverage on 1 December 2021. Adolescents 12-17 years of age started vaccinations on 1 October 2021 with a coverage of 50% achieved by 1 December 2021. Children 5-11 years of age start vaccinations of doses 1 and 2 on 1 December 2021 and are only included as part of the extended vaccination scenario.
Vaccination groups, associated vaccination coverages as of 1 December 2021, and the simulated future scenarios are summarized in Supplementary Table 1.

2.3 Vaccine-induced immunity profile

We model an interval of 28 days between the first and second dose, and a maximum of 95% vaccine efficacy to be reached 14 days after the second dose (increasing with a sigmoidal curve). We assume that 90% of vaccination effect is transmission blocking. We assume vaccinated individuals will always be administered two doses and assume that 95% of those vaccinated with doses one and two will accept a third-dose. Third-doses are administered 6 months after the second dose, after which the maximum vaccine efficacy of 95% is again reached.

2.4 Immunity following infection

After recovering from infection with SARS-CoV-2, individuals develop naturally acquired immunity with a maximum level of 90% transmission blocking effect which they maintain for a month, after which their immunity wanes linearly to zero over a period of 335 days \(^1,2\). The level of immunity is the reverse of the susceptibility of the individual, which thus increases over time. Immunity immediately after vaccination is also considered 90% in the model, protection against infection, starting two weeks after the second dose has been administered. One month after the second dose, immunity wanes linearly to zero in 335 days.

2.5 Effect of variant properties on prognosis

The probabilities of 1) a symptomatic case developing severe disease, 2) a severe case becoming critical, and 3) a critical case ultimately leading to death, are all defined as functions of age. For this study, we use functions fitted to the probabilities reported in \(^3\), updated to represent the additional risk of hospitalisation from infection with VOC Delta (B.1.617.2) \(^4,6\).

In additional to age-related risk, the probability that an infected individual will develop severe symptoms is also scaled by the severity factor of the viral variant exposed to.

In this study we use a severity factor of 1 for VOC Delta (B.1.617.2), and consider a range of potential relative severity factors for VOC Omicron (B.1.1.529) between 0 and 2. That is, a variant that has 0%-200% severity of Delta. For vaccinated individuals that become infected (noting that the transmission-blocking action of the vaccine reduces the probability of infection), the probability of developing severe disease is reduced by the disease-blocking action of the vaccine. The level to which the probability of severe disease is reduced is dependent upon the level of immunity at the time of infection.

Vaccine-induced immunity is assumed to wane over time and can be further decreased if exposed to a variant with immune evading capacity. In this study, we consider the full range of potential immune evading properties of Omicron, from 0% to 100%. For this study, the probabilities that immunologically naïve (i.e., unvaccinated, and previously uninfected) individuals with no comorbidities infected with Delta (severity factor 1, 0% immune evading) develop severe disease are given in Supplementary Table 3.
Supplementary Table 3. Probabilities that immunologically naïve (i.e., unvaccinated and previously uninfected) individuals with no comorbidities infected with Delta (severity factor 1, 0% immune evading) develop severe disease (source 3–6)

| Age group | Severe disease (Delta, unvaccinated) |
|-----------|-------------------------------------|
| 0-10      | <1.0%                               |
| 10-20     | 1.0%                                |
| 20-30     | 1.2%                                |
| 30-40     | 2.4%                                |
| 40-50     | 3.9%                                |
| 50-60     | 6.6%                                |
| 60-70     | 16.3%                               |
| 70-80     | 26.0%                               |
| 80-90+    | 33.0%                               |

3. References

1. Wheatley, A. K. et al. Evolution of immune responses to SARS-CoV-2 in mild-moderate COVID-19. Nat Commun 12, 1162, doi:10.1038/s41467-021-21444-5 (2021).
2. Cohen, K. W. et al. Longitudinal analysis shows durable and broad immune memory after SARS-CoV-2 infection with persisting antibody responses and memory B and T cells. Cell Rep Med 2, 100354, doi:10.1016/j.xcrm.2021.100354 (2021).
3. Shattock, A. J. et al. Impact of vaccination and non-pharmaceutical interventions on SARS-CoV-2 dynamics in Switzerland. medRxiv, 2021.2004.21255503, doi:10.1101/2021.04.14.21255503 (2021).
4. Twohig, K. A. et al. Hospital admission and emergency care attendance risk for SARS-CoV-2 delta (B.1.617.2) compared with alpha (B.1.1.7) variants of concern: a cohort study. Lancet Infect Dis, doi:10.1016/s1473-3099(21)00475-8 (2021).
5. Sheikh, A., McMenamin, J., Taylor, B. & Robertson, C. SARS-CoV-2 Delta VOC in Scotland: demographics, risk of hospital admission, and vaccine effectiveness. Lancet 397, 2461-2462, doi:10.1016/s0140-6736(21)01358-1 (2021).
6. CDC. Risk for COVID-19 Infection, Hospitalization, and Death By Age Group. (Atlanta, 2021).