National Immunisation Advisory Committee

RECOMMENDATIONS FOR SPRING 2024 COVID-19 VACCINATION

NIAC 15.02.2024

About NIAC

NIAC membership includes nominees from the Royal College of Physicians in Ireland, its Faculties and Institutes, the Royal College of Surgeons in Ireland, the Irish College of General Practitioners, the National Immunisation Office, the Nursing and Midwifery Board of Ireland, the Infectious Diseases Society of Ireland, the Travel Medicine Society, the National Virus Reference Laboratory and lay members. Meetings are attended by representatives from the Department of Health and the HSE. Representatives of the Health Products Regulatory Agency attend to provide regulatory advice in relation to vaccines.

NIAC considers the evidence about vaccines and provides advice to the Chief Medical Officer and the Department of Health. The Department and the Minister for Health make policy decisions on vaccines which are implemented by the Health Service Executive.

RECOMMENDATIONS FOR SPRING 2024 COVID-19 VACCINATION

1. A Spring COVID-19 vaccine is recommended for:
    - those living in long term care facilities for older adults
    - those aged 80 years and older
    - those aged 5 years and older with immunocompromise associated with a suboptimal response to vaccination.[1]
2. Access to a Spring vaccine should be available for those aged 70 to 79 years who, following discussion with a health care provider (e.g., GP, pharmacist or vaccination centre), request vaccination.
3. The Spring COVID-19 vaccination campaign should aim for completion by end of April 2024.
4. COVID-19 vaccines may be given to the above-mentioned risk groups irrespective of the number of previous doses or types of COVID-19 vaccines, with an interval of six months recommended following any previous COVID-19 vaccine dose or infection. A minimum interval of three months is permissible in exceptional circumstances e.g., planned immunosuppressive therapy or operational reasons.
5. The most recently adapted mRNA COVID-19 vaccine, Comirnaty Omicron XBB.1.5, is the preferred vaccine for use in Spring 2024.
6. Protein based vaccines may be used as alternatives for those in whom mRNA vaccine is contraindicated or declined. Nuvaxovid XBB.1.5 is the preferred alternate.

Recommendations may be updated when more information becomes available.

1. EXECUTIVE SUMMARY

- SARS-CoV-2 has not exhibited a distinct seasonal pattern to date, however surges of infection in winter months have greatest impact due to co-circulation of other winter viruses and increased pressure on the health care systems.
- While vaccination just prior to the winter season likely provides the greatest benefit for the majority of individuals requiring revaccination, certain very high-risk groups require more frequent vaccination, hence a dose in Spring is indicated.
- Wastewater surveillance indicates that SARS-CoV-2 virus continues to circulate in the community and has done so at a relatively consistent level throughout 2023.
- A new variant, JN1 which is more immune evasive than XBB.1.5, has become the dominant variant since the end of December 2023. While it has 30 mutations difference compared to

the XBB.1.5 variant, the XBB.1.5 adapted vaccine has demonstrated good cross reactivity against JN1 in a number of immunogenicity studies.

- Despite the increased immune evasiveness of recent variants, indicators of disease severity were overall improved in 2023 compared to previous years.
- In 2023, the rates of COVID-19 hospitalisations, ICU admissions, and deaths while still significant, were lower than in preceding years. The peak number of inpatients with COVID-19 in January 2024 was 384, compared to peaks of 629 in January 2023, and 1,600 in March 2022.
- The age profile of those who develop severe COVID-19 remains unchanged. Rates of hospitalisation and death increase incrementally with advancing age.
- Those with immunocompromising conditions associated with an impaired response to vaccination continue to be at high risk of severe disease and death from COVID-19, especially those with solid tumours, haematological malignancies, transplant recipients and end stage renal disease.
- In Ireland, the uptake of targeted Spring and Autumn COVID-19 vaccination campaigns in 2023 in older adults was modest; 40% in Spring and 60% in Autumn in those 70 years and older. Uptake among those 80 years and older was higher in Autumn at 69%.
- Early vaccine effectiveness studies from the Netherlands, Denmark and the US indicate that those who received an XBB.1.5 adapted vaccine in 2023 had a 63-75% reduced risk of hospitalisation with COVID-19 compared to those who did not receive the updated vaccine.
- Emerging evidence on the effectiveness of revaccination against hospitalisation and death suggest that time since the last COVID-19 vaccine dose is a more important factor than the total number of prior doses received.
- Evidence regarding the duration of protection afforded by the newest XBB targeted vaccine formulations is limited as these vaccines have only been in use since Autumn 2023. However, duration of protection of the original monovalent vaccines against severe disease has been shown to persist up to 12 months in immunocompetent adults aged 60 years and older.
- Protection from natural infection against severe disease has been shown to persist up to 14 months. Hybrid immunity provides higher protection than either infection or vaccination alone.
- In Ireland, the proportion of those with serological evidence of previous infection decreases with increasing age. In those aged 18-49 years, 90% demonstrate serological evidence of previous infection whereas this decreases to 72% in those aged 80 years and older.
- Those with immunocompromise are more susceptible to severe disease and the protection they achieve from vaccination is less robust and of more limited duration necessitating more frequent revaccination.
- The WHO COVID-19 vaccination roadmap has recommended, that for the immunocompromised and for adults aged over 75 or 80 years, revaccination should be considered at 6-12 month intervals.

2. INTRODUCTION

Throughout 2023, SARS-CoV-2 continued to circulate at high prevalence in Ireland as reflected in Ireland's wastewater surveillance data. While there was an overall decline in the numbers of COVID-19-related hospitalisations and fatalities compared to preceding years, intermittent surges in hospitalisations have been experienced, and over 700 deaths were reported.

Unlike many respiratory viruses, SARS-CoV-2 has thus far not exhibited a distinct seasonal pattern. However, surges of infection in winter months have greatest impact due to co-circulation of other winter viruses, exerting increased burden on the health care system when it is under most pressure. Hence, administering vaccines annually, just before the winter season, yields maximal benefits for the majority of individuals who need revaccination.

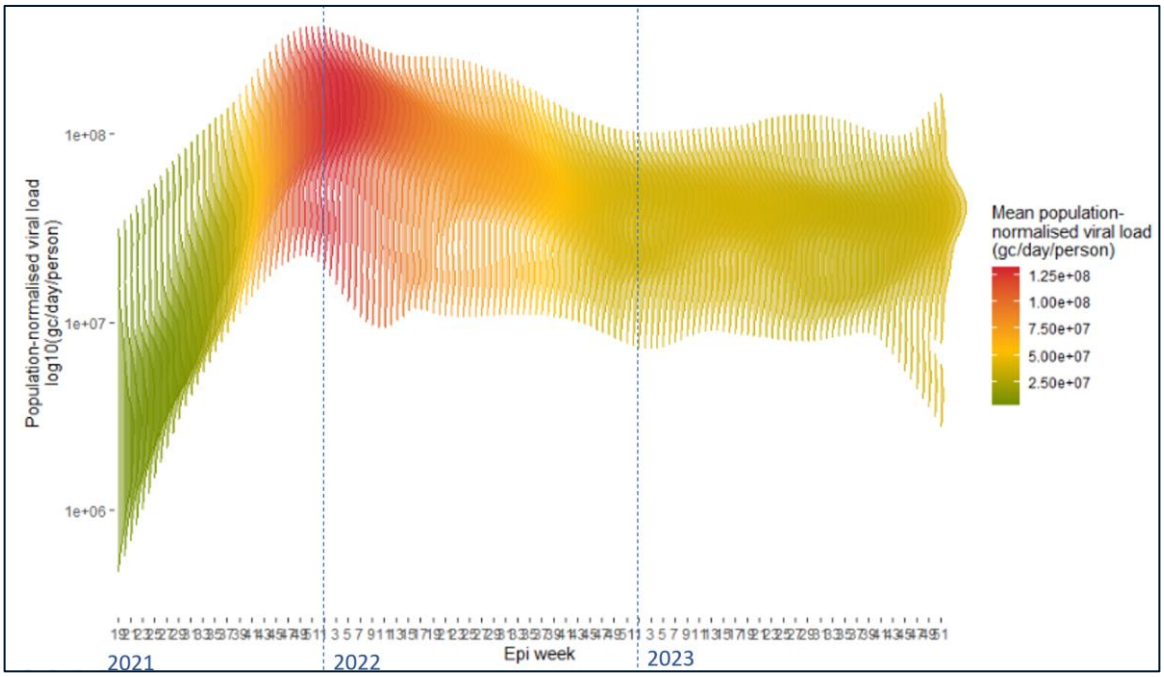
Nevertheless, for those at very high risk of severe disease, the need for more frequent vaccination should be considered and is the basis of this evidence review and recommendation. This very high-risk cohort is characterised by impaired vaccine response, lower levels of hybrid immunity and increased vulnerability to severe COVID-19.

These recommendations are based on review of contemporary scientific evidence, national and international epidemiology and on reflection of the uptake observed in the preceding year's vaccination campaigns.

3. EPIDEMIOLOGY IN IRELAND

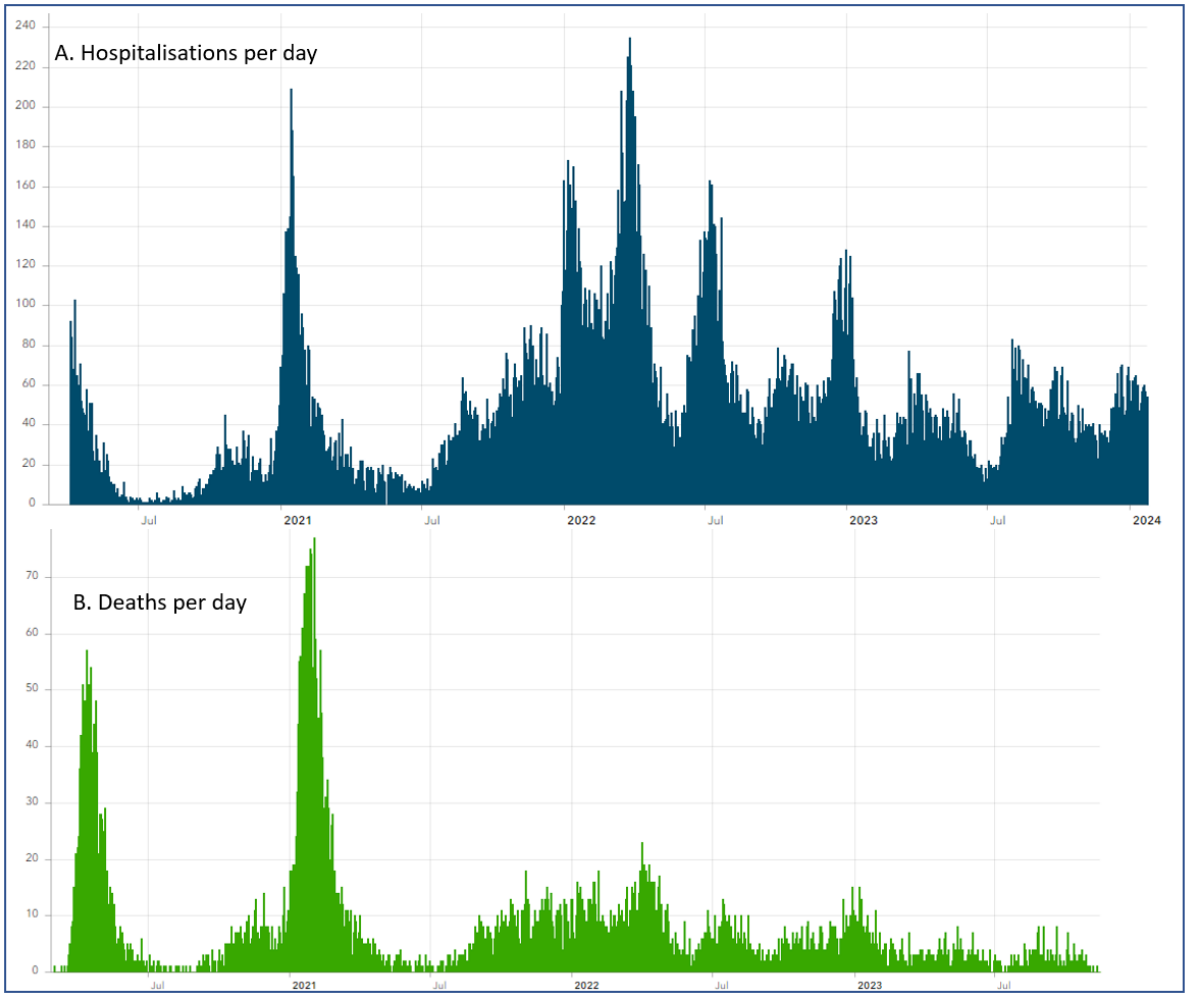
In 2023, SARS-CoV-2 continued to circulate in the community throughout the year with peaks and troughs in clinical indicators but relatively consistent levels in wastewater surveillance indices. As community testing for SAR-CoV-2 in now limited, wastewater surveillance is the most accurate way to monitor levels of SARS-CoV-2 outside of healthcare settings. Wastewater sampling was positive for SARS-CoV-2 in 90-100% of samples collected each week in 2023.[2] Furthermore, the viral load detected also remained relatively stable throughout 2023 in the majority of catchment areas. (Figure 1)

Figure 1. Weekly distribution of population-normalised SARS-CoV-2 viral load week 19 2021 to week 51 2023. Source: National Wastewater Surveillance Programme.[2]



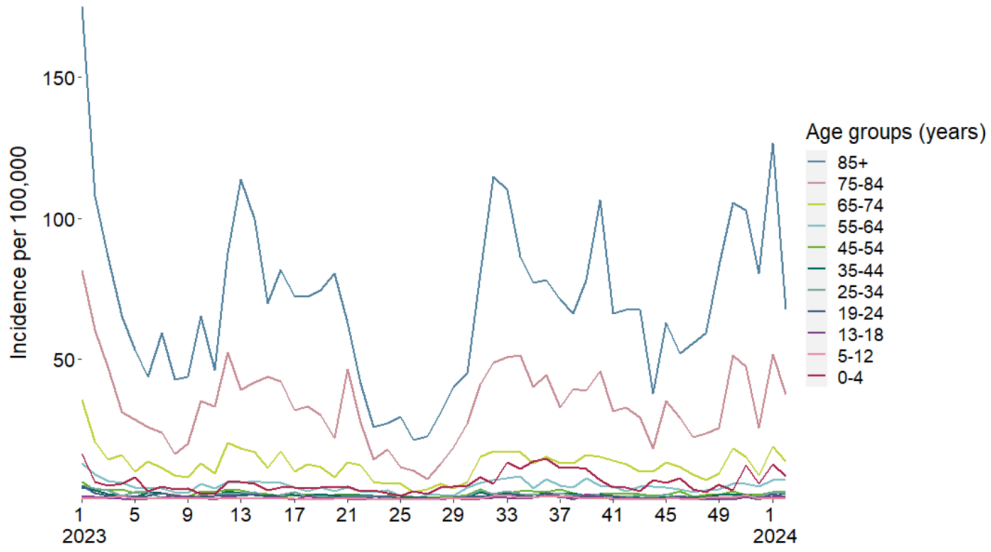
In 2023, surges in hospital admissions were observed, however the peaks were not as high as those seen in preceding years, with similar patters observed with ICU admissions and deaths related to COVD-19. (Figure 2)[3]

Figure 2. A: Total number of confirmed cases of COVID-19 admitted to hospital per day, 3 April 2020 to 22 January 2024. B: Total number of COVID-19 deaths per day, 1 March 2020 to 10 November 2023. Source: COVID-19 Data hub.[3]



While the overall number of hospital admissions has declined in 2023, the heightened vulnerability of older individuals persists. The age specific incidence rates for hospitalisations increase with increasing age, with those aged over 85 experiencing the highest rates throughout the year.[4] (Figure 3)

Figure 3. Incidence rate by age group of hospitalisations among confirmed COVID-19 cases in Ireland between week 1, 2023 and week 2, 2024. Source: HPSC.[4]

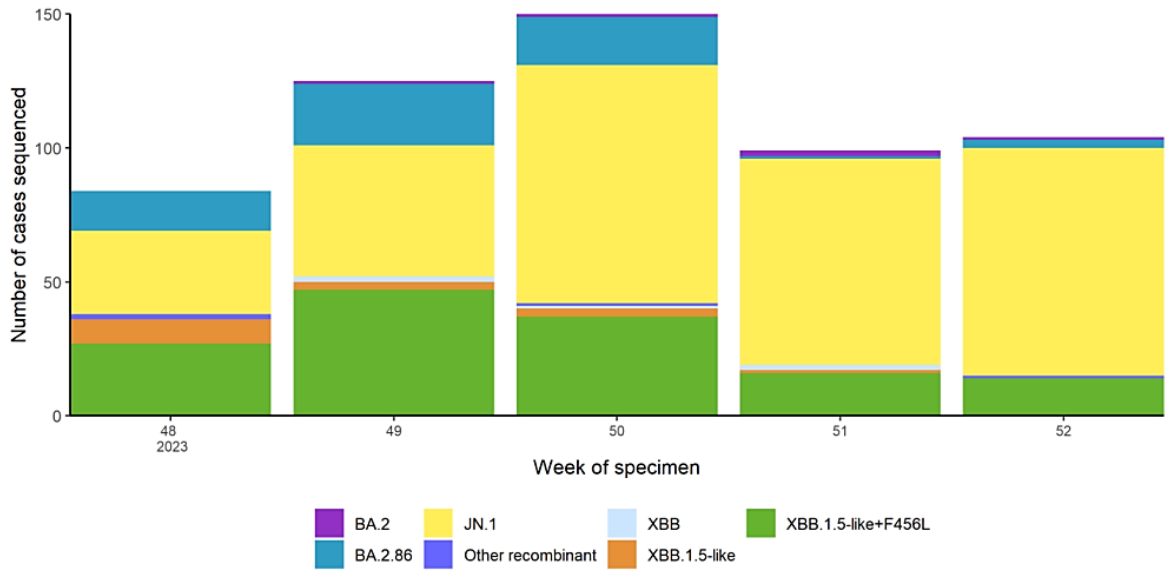


The number of COVID-19 related deaths reported in 2023 was lower than previous years. (Figure 2B) However, the age profile has remained relatively consistent with approximately three quarters of deaths in 2023 occurring in those aged over 75 years, and less than 10% of deaths occurring in those aged less than 65 years. The median age of deaths from 15 Nov 2023 to 6 Jan 2024 was 84 years.[5]

Variants

Variants from the Omicron XBB lineage, upon which the most recently adapted vaccines are based, predominated for most of 2023. However, in late 2023 there was an evolutionary path switch back to a BA.2 derived variant named JN1 noted both nationally and internationally. JN1 accounted for 82% of cases in Ireland in week 52, 2023 as can be seen in Figure 4.[6] This JN1 variant exhibits enhanced immune evasion. Data on clinical impact is limited, as JN1 has only recently become the predominant variant in most countries, however thus far it has not been associated with an increase in disease severity indicators.[7]

Figure 4. SARS-CoV-2 whole genome sequencing results in Ireland from 28 November to 30 December 2023. Source: HPSC.[6]



4. HIGH RISK GROUPS

The available evidence indicates that there have been no substantial changes in the patient profile most susceptible to severe COVID-19 outcomes. In a recent US observational study from Maryland, the risk profiles and outcomes of patients admitted with Omicron XBB.1.5-related COVID-19 were compared to those with earlier XBB and pre-XBB Omicron variant infections.[8] The study revealed no significant differences in the risk of hospitalisation or the profiles of patients in each group. Notably, advanced age, lack of vaccination, immunosuppression, and underlying heart, kidney, or lung conditions consistently showed significant associations with hospitalisation across all groups.[8]

A large observational, population-based study in the UK investigated the impact of COVID-19 on immunocompromised populations during 2022 when Omicron was dominant.[9] Data was analysed from almost 12 million people, of which 470,910 were immunocompromised. The findings revealed a notable disproportion; although immunocompromised individuals constituted 3.9% of the overall population, they accounted for 22% of hospitalisations, 28% of ICU admissions, and 24% of deaths attributed to COVID-19. Furthermore, the study highlighted that within the immunocompromised population certain subgroups have heightened vulnerability to more severe COVID-19. Notably those with solid organ transplants, moderate to severe primary immunodeficiency, stem cell transplant and recent haematological malignancy treatment were at highest risk for hospitalisation.

5. UPTAKE & SEROPREVALENCE

Vaccination uptake

The uptake of COVID-19 vaccines in the 2023 Spring campaign was modest with a greater number of older adults coming forward for vaccination in Autumn.[10 11] (Table 1)

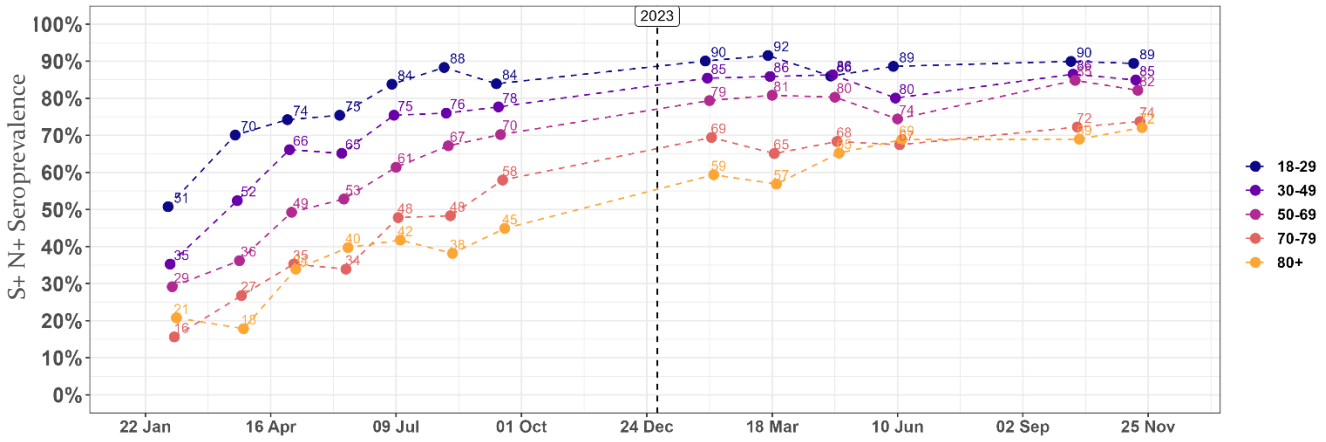
Table 1. Uptake of COVID-19 vaccines in 2023 Spring and Autumn vaccination campaigns in Ireland. Source: HPSC and HSE.[10 11]

Age Group (years)	Percentage Uptake (%)
Spring 2023 as % of completed primary series	
70 - 79	37.7
≥80	42.9
Autumn 2023 as % of 2022 census population	
70 - 74	53.1
75 - 79	64.1
80 - 84	68.6
≥85	68.8

Seroprevalence

The latest cumulative blood donor infection seroprevalence is estimated to be 87% and the latest infection seroprevalence from primary care sources is estimated to be 78%. Across both blood donor and primary care datasets infection seroprevalence in older people is lower than that in younger people. (Figure 5) These data indicate that currently approximately 28% of those aged 80 years and older, and 26% of those aged 70-79 years attending primary care services do not have evidence of protection from previous natural infection.

Figure 5. Percentage of people attending primary care with prior SARS-CoV-2 infection (S+ N+). Source: Lab Surveillance Network data provided directly to NIAC by the Seroepidemiology Unit.



6. VACCINE PREFORMANCE

Safety

Interim safety data from a phase 2/3 trial of monovalent Omicron XBB.1.5-adapted BNT162b2 COVID-19 vaccine in 412 participants aged ≥12 years, indicates a safety profile similar to that of the original and bivalent vaccine formulations. Local reactions reported within seven days of the XBB.1.5-adapted BNT162b2 vaccination were mild to moderate in severity. Within seven days of vaccination, systemic events were predominantly mild to moderate in severity. Fatigue and headache were the most common systemic events. Adverse events were infrequent (7.5% in the total population), and none led to study withdrawal. No confirmed myocarditis or pericarditis reports and no cases of severe COVID-19 infection or of multisystem inflammatory syndrome in children were noted.[12]

Effectiveness

The newly adapted monovalent XBB.1.5 vaccines were authorised in Europe in September 2023 and included in vaccination programmes shortly thereafter. Given the short time since introduction there are limited effectiveness data available to date.

A nation-wide cohort study from Denmark enrolled over 1.3 million adults aged 65 years and above who had received a COVID-19 vaccine in the winter 2022/2023 campaign. There was a 75% reduction in risk of COVID-19 hospitalisation in the group who had received an XBB.1.5 vaccine in October 2023 compared to those who had not.[13]

Similar results were reported in two pre-prints from the Netherlands and USA. In the Netherlands, a cohort study including over 2,000 COVID-19 hospitalisations aged 60 years and above, estimated vaccine effectiveness of the XBB.1.5 adapted vaccine at 70% against hospitalisation, and 73% against ICU admission.[14] A test negative control study, sponsored by the vaccine manufacturer, based in California including 4,232 cases and 19,775 controls reported that in those who had received an XBB.1.5 adapted vaccine, there were reduced odds ratios for hospitalisation (0.37, 0.2-0.67), emergency department visits (0.42, 0.34-0.53) and outpatient visits (0.42, 0.27-0.66) compared to those who had not received an adapted XBB.1.5 vaccine, irrespective of their previous vaccination history.[15]

Despite the presence of 30 mutations difference in the spike protein of JN1 compared to XBB.1.5, immunogenicity studies suggest that there is relatively good cross reactivity of the XBB.1.5 vaccines against the newer JN1 variant. Following administration of the XBB.1.5 vaccine to study participants who had previously had four doses of wild type vaccine and a dose of bivalent BA.4/5 vaccine, serum neutralising antibody (Nab) levels were significantly boosted against JN1, with a 13.3 fold increase in those who were previously uninfected, and a 6.5 fold increase in those with a previous Omicron infection. While the relative fold rise in Nab levels against JN1 in the previously infected group was less, the absolute levels of Nab measured was highest in this group (geometric mean ID_{50} titres:1,504 compared to 196), again highlighting the more robust levels of protection achieved with hybrid immunity.[16] Similar results have been reported from other labs in different population groups internationally.[17-19] Additionally, while immunological imprinting was still evident with the monovalent XBB.1.5 vaccine, imprinting was less than had been observed previously with the bivalent vaccines.[16]

Duration of Protection

As monovalent XBB.1.5-adapted vaccines were first administered in October 2023, long term studies on the duration of protection of this specific vaccine formulation are not yet available. However, longer term studies on the duration of protection of the original monovalent vaccines and subsequent booster vaccines are available and can provide an indication of the likely duration of protection of monovalent XBB.1.5-adapted vaccines. Data from Belgium, Portugal, the UK, Singapore, and Qatar indicate good protection of monovalent vaccines and subsequent vaccine doses against COVID-19 related severe disease and mortality out to six months, and modest protection against the same outcomes out as far 12 to 15 months in immunocompetent older adults.[20-23] Data suggest that time since last dose is a more important factor than the total number of doses administered in the level of protection achieved against both COVID-19 hospitalisation and death. Protection against symptomatic infection wanes more quickly than protection against severe disease.[24] Protection against severe disease wanes more quickly in immunocompromised sub populations than in the immunocompetent and with increasing age.[20 25 26] Protection against severe COVID-19-related disease from natural infection with SARS-CoV-2 has been shown to be high and wane more slowly than protection from vaccination, lasting at

least 14 months, and hybrid immunity has been shown to provide the most robust protection against severe outcomes.[22 27]

7. INTERNATIONAL POSITIONS

Table 2. International positions on COVID-19 revaccination in 2024.

Country	Summary of recommendations for 2024 revaccination	
	Target population	**Recommended timing of revaccination**
WHO[28]	Oldest adults (aged ≥75 or 80 years) Older adults with multiple co-morbidities Immunocompromised (≥6 months)	6-12 month interval
	Older adults (aged ≥50 or 60 years) Other adults with co-morbidities	Approximately 12 month interval
Germany[29]	Immunocompromised	Consider shorter interval (less than 12 months)
	Adults aged ≥60 years Residents of care facilities Those aged ≥6 months with underlying disease associated with increased risk of severe COVID-19 infection Health and care workers Close contacts of those with impaired response to COVID-19 vaccination	Annual revaccination in the Autumn
Netherlands[30]	Certain high risk patient groups as determined by specialists	Consider shorter interval (less than 12 months)
	Adults aged ≥60 years Medical risk groups Healthcare workers	Annual revaccination in the Autumn
United Kingdom[31]	Adults aged ≥75 years Residents in a care home for older adults Immunocompromised ≥6 months	Should be offered revaccination 6 months after previous dose (minimum interval of 3 months)
Canada[32]	Adults aged ≥65 years Long term care residents Immunocompromised	Additional dose in Spring 2024

USA[33]	Those aged ≥5 years	One dose of an 2023-2024 updated vaccine (at least 8 weeks after last dose)
	Those aged ≥6 months	At least one dose of an 2023-2024 updated vaccine (at least 8 weeks after last dose)
	Those aged ≥6 months with moderate to severe immunocompromise	May get an additional dose of a 2023-2024 updated vaccine (at least 8 weeks after last dose)

8. DISCUSSION

Since the beginning of the COVID-19 pandemic, a diverse range of clinical manifestations has emerged, spanning from asymptomatic cases to severe conditions leading to fatality. Encouragingly, the disease's trajectory has evolved, attributed to factors such as increased natural immunity, widespread vaccination, and viral mutations, resulting in an overall reduction in pathogenicity. However, despite this positive trend, certain vulnerable groups continue to face severe outcomes, with reported deaths persisting in Ireland.

While the overall mortality rates have diminished, the demographic profile of those experiencing severe disease has remained relatively consistent. It remains important to shield individuals of advanced age and those with significant immunocompromise from SARS-CoV-2. Given that SARS -CoV-2 continues to circulate in the community, maximising immunity through vaccination is the most effective strategy. NIAC recommends a targeted vaccination approach in Spring 2024 for those at very high risk: those aged 80 years or older, immunocompromised individuals, and residents of long-term care facilities for older adults.

Evidence suggests that most individuals, due to vaccination, infection, or hybrid immunity, exhibit robust and long-lasting protection against severe disease. Duration of protection is longest in vaccinated individuals with previous history of infection (hybrid immunity). Duration of protection from vaccination in those with hybrid immunity is at least 12 months. Thus, the majority of those vaccinated in autumn should maintain protection against severe disease for at least a year. However, very high-risk individuals in whom duration of protection wanes quicker stand to benefit from earlier vaccination.

Those aged 80 years or older face a higher risk due to waning vaccine protection and lower levels of natural immunity. Long-term care facility residents constitute a distinct risk group, encompassing the most vulnerable, frail individuals of advanced age. Additionally, these facilities pose unique challenges in terms of controlling and mitigating outbreaks. Immunocompromised individuals have reduced vaccine responses, reduced duration of vaccine protection and

vulnerability to severe infection. There may be other patients aged 70-79 years, who would benefit from vaccination during the Spring campaign. These include those aged 70-79 years who did not receive a vaccine during the Autumn campaign, or who have a chronic medical condition that significantly increases the risk of severe COVID-19 infection.

The overall decline in COVID-19 hospitalisations and deaths reflects improved population-wide immunity, attributed to increased hybrid immunity, high initial vaccination uptake, and diminished pathogenicity of the virus. Ireland's commendable lack of excess mortality compared to other OECD countries in the early years of the pandemic underscores the public's cooperation, healthcare decision-makers' prudence, and healthcare providers' dedication. However, the decline in vaccination uptake with every subsequent vaccine offered, necessitates a renewed focus on facilitating vaccination for those at very high risk.

NIAC recommends offering vaccination in Spring 2024 to those at very high risk of severe COVID-19 infection; the elderly aged 80 years or older, those with immunocompromising conditions and those living in long term care facilities for older adults. Access to a Spring vaccine should be available for those aged 70 to 79 years who, following discussion with a health care provider (e.g., GP, pharmacist or vaccination centre), request vaccination.

ACKNOWLEDGEMENTS

NIAC would like to thank all the individuals and organisations who provided data, time, advice and information in support of this work.

REFERENCES

1. National Immunisation Advisory Committee (NIAC). Table 5a.2 Conditions or treatments associated with very high or high risk of severe COVID-19 disease. National Immunisation Guidelines2024.

2. Health Protection Surveillance Centre (HPSC). National SARS-CoV-2 Wastewater Surveillance Programme. Week 51 2023 2023 [Available from: https://www.hpsc.ie/a-z/nationalwastewatersurveillanceprogramme/2023wastewatersurveillanceprogrammereports/nwsp_main_public_week%2051_2023.html accessed 15 Jan 2024.

3. Ireland Go. Ireland's COVID-19 Data ub 2024 [Available from: https://covid19ireland-geohive.hub.arcgis.com/pages/0814b13a2f2b4458a36105502c8e92e8 accessed 15 Jan 2024.

4. Health Protection Surveillance Centre (HPSC). Weekly report on the epidemiology of COVID-19 in Ireland. Week 2, 2024 2024 [Available from: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/surveillance/epidemiologyofcovid-19inirelandweeklyreports/2024_01_16_Weekly_report_v3.0.pdf accessed 18 Jan 2014.

5. Health Protection Surveillance Centre (HPSC). Report on COVID-19 deaths reported in Ireland 2024 [Available from: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/surveillance/covid-19deathsreportedinireland/2023/COVID-19_Death_Report_Website_v1.8_09012024.pdf accessed 18 Jan 2024.

6. Health protection Surveillance Centre (HPSC). Summary of COVID-19 virus variants in Ireland 2024 [Available from: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/surveillance/summaryofcovid-19virusvariantsinireland/ accessed 15 Jan 2024.

7. World Health Organisation. Initial Risk Evaluation of JN.1 2023 [updated 19 December 2023. Available from: https://www.who.int/docs/default-source/coronaviruse/18122023_jn.1_ire_clean.pdf?sfvrsn=6103754a_3 accessed 15 Jan 2024.

8. Klein EY, Fall A, Norton JM, et al. Severity outcomes associated with SARS-CoV-2 XBB variants, an observational analysis. *Journal of Clinical Virology* 2023;165:105500. doi: https://doi.org/10.1016/j.jcv.2023.105500

9. Evans RA, Dube S, Lu Y, et al. Impact of COVID-19 on immunocompromised populations during the Omicron era: insights from the observational population-based INFORM study. *The Lancet Regional Health – Europe* 2023;35 doi: 10.1016/j.lanepe.2023.100747

10. Centre HPS. COVID-19 Vaccination Uptake in Ireland Reports 2023 [Available from: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/vaccination/covid-19vaccinationuptakereports/2023/ accessed January 2024.

11. Centre HPS. COVID-19 Vaccine Uptake in Ireland Reports 2024 [Available from: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/vaccination/covid-19vaccinationuptakereports/2024/ accessed January 2024.

12. Gayed J, Diya O, Lowry FS, et al. Safety and Immunogenicity of the Monovalent Omicron XBB.1.5-Adapted BNT162b2 COVID-19 Vaccine in Individuals ≥12 Years Old: A Phase 2/3 Trial. *Vaccines* 2024;12(2):118.

13. Hansen CH, Moustsen-Helms IR, Rasmussen M, et al. Short-term effectiveness of the XBB.1.5 updated COVID-19 vaccine against hospitalisation in Denmark: a national cohort study. *Lancet Infect Dis* 2024 doi: 10.1016/s1473-3099(23)00746-6 [published Online First: 20240105]

14. Werkhoven CHv, Anne-Wil V, Bente S, et al. Early COVID-19 vaccine effectiveness of XBB.1.5 vaccine against hospitalization and ICU admission, the Netherlands, 9 October - 5 December 2023. *medRxiv* 2023:2023.12.12.23299855. doi: 10.1101/2023.12.12.23299855

15. Sara YT, Jeff MS, Timothy BF, et al. BNT162b2 XBB1.5-adapted Vaccine and COVID-19 Hospital Admissions and Ambulatory Visits in US Adults. *medRxiv* 2023:2023.12.24.23300512. doi: 10.1101/2023.12.24.23300512

16. Qian W, Yicheng G, Anthony B, et al. XBB.1.5 monovalent mRNA vaccine booster elicits robust neutralizing antibodies against emerging SARS-CoV-2 variants. *bioRxiv* 2023:2023.11.26.568730. doi: 10.1101/2023.11.26.568730

17. Marking U, Bladh O, Aguilera K, et al. Humoral immune responses to the monovalent XBB.1.5-adapted BNT162b2 mRNA booster in Sweden. *The Lancet Infectious Diseases* 2024 doi: 10.1016/S1473-3099(23)00779-X

18. Tortorici MA, Amin A, Albert JS, et al. Persistent immune imprinting after XBB.1.5 COVID vaccination in humans. *bioRxiv* 2023:2023.11.28.569129. doi: 10.1101/2023.11.28.569129

19. Stankov MV, Hoffmann M, Gutierrez Jauregui R, et al. Humoral and cellular immune responses following BNT162b2 XBB.1.5 vaccination. *The Lancet Infectious Diseases* 2024;24(1):e1-e3. doi: 10.1016/S1473-3099(23)00690-4

20. ECDC. European Centre for Disease Prevention and Control. Interim analysis of COVID-19 vaccine effectiveness against hospitalisation and death using electronic health records in six European countries. Stockholm, 2023.

21. Wee LE, Pang D, Chiew C, et al. Long-term Real-world Protection Afforded by Third mRNA Doses Against Symptomatic Severe Acute Respiratory Syndrome Coronavirus 2 Infections, Coronavirus Disease 19-related Emergency Attendances and Hospitalizations Amongst Older Singaporeans During an Omicron XBB Wave. *Clinical Infectious Diseases* 2023;77(8):1111-19. doi: 10.1093/cid/ciad345

22. Chemaitelly H, Nagelkerke N, Ayoub HH, et al. Duration of immune protection of SARS-CoV-2 natural infection against reinfection. *Journal of Travel Medicine* 2022;29(8) doi: 10.1093/jtm/taac109

23. UK Health Security Agency (UKHSA). COVID-19 Vaccine surveillance report: Week 4 2024 [Available from: https://assets.publishing.service.gov.uk/media/65b3c8a3c5aacc000da683d3/vaccine-surveillance-report-2024-week-4.pdf.

24. COVID-19 Forecasting Team - Past SARS-CoV-2 infection protection against re-infection: a systematic review and meta-analysis. *Lancet* 2023;401(10379):833-42. doi: 10.1016/s0140-6736(22)02465-5 [published Online First: 2023/03/18]

25. Ferdinands JM, Rao S, Dixon BE, et al. Waning of vaccine effectiveness against moderate and severe covid-19 among adults in the US from the VISION network: test negative, case-control study. *BMJ* 2022;379:e072141. doi: 10.1136/bmj-2022-072141

26. Grewal R, Nguyen L, Buchan SA, et al. Effectiveness of mRNA COVID-19 vaccine booster doses against Omicron severe outcomes. *Nature Communications* 2023;14(1):1273. doi: 10.1038/s41467-023-36566-1

27. Bobrovitz N, Ware H, Ma X, et al. Protective effectiveness of previous SARS-CoV-2 infection and hybrid immunity against the omicron variant and severe disease: a systematic review and meta-regression. *Lancet Infect Dis* 2023;23(5):556-67. doi: 10.1016/s1473-3099(22)00801-5 [published Online First: 2023/01/22]

28. World Health Organization. WHO roadmap on uses of COVID-19 vaccines in the context of Omicron and high population immunity. Updated 10 Nov 2023 2023 [Available from: https://iris.who.int/bitstream/handle/10665/373987/WHO-2019-nCoV-Vaccines-SAGE-Prioritization-2023.2-eng.pdf accessed 10 Nov 2023.

29. Robert Koch Institut (STIKO). STIKO: Aktualisierung der COVID-19-Impfempfehlung 2024 [updated 11 Jan 2024. Available from: https://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2024/Ausgaben/03_24.pdf?__blob=publicationFile accessed 13 Feb 2024.

30. Gezondheidsraad (Netherlands). Structural vaccination program against COVID-19 2023 [Available from: https://www.gezondheidsraad.nl/onderwerpen/vaccinaties/alle-adviezen-over-covid-19-vaccinaties/structureel-vaccinatieprogramma-tegen-covid-19.

31. Joint Committee on Vaccination and Immunisation (JCVI). JCVI statement on COVID-19 vaccination in spring 2024 and considerations on future COVID-19 vaccination, 4 December 2023. Published 7 Feb 2024 2024 [Available from: https://www.gov.uk/government/publications/covid-19-spring-2024-and-future-vaccination-programmes-jcvi-advice-4-december-2023/jcvi-statement-on-covid-19-vaccination-in-spring-2024-and-considerations-on-future-covid-19-vaccination-4-december-2023#:~:text=4%2Ddecember%2D2023-,Advice%20on%20spring%202024%20vaccination,care%20home%20for%20older%20adults accessed 12 Feb 2024.

32. National Advisory Committee on Immunisation (NACI). Guidance on an additional dose of COVID-19 vaccines in the spring for individuals at high risk of severe illness due to COVID-19 2024 [Available from: https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/national-advisory-committee-immunization-guidance-additional-dose-covid-19-vaccines-spring-2024-individuals-high-risk-severe-illness-due-covid-19.html accessed 24 Jan 2024.

33. Centres for Disease Control and Prevention (CDC). Stay Up to Date with COVID-19 Vaccines 2024 [Available from: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html accessed 13 Feb 2024.