COMMENTARY



Meningococcal Disease in the Post–COVID-19 Era: A Time to Prepare

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ABSTRACT

The global invasive meningococcal disease (IMD) landscape changed considerably during the COVID-19 pandemic, as evidenced by decreased incidence rates due to COVID-19 mitigation measures, such as limited social contact, physical distancing, mask wearing, and hand washing. Vaccination rates were also lower during the pandemic relative to pre-pandemic

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F. Martinón-Torres Centro de Investigación Biomédica en Red de Enfermedades Respiratorias (CIBERES), Instituto de Salud Carlos III, Madrid, Spain levels. Although policymakers may have shifted their focus away from IMD vaccination programs to COVID-19 vaccination programs, strong arguments support implementation and prioritization of IMD vaccination programs; IMD cases have increased in some countries and IMD rates may even have exceeded pre-pandemic levels. Additional concerns include increased susceptibility due to vaccination coverage gaps, increased incidence of other respiratory pathogens, immunity debt from lockdown restrictions, and

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K. Schley (🖂) Pfizer Pharma GmbH, Linkstr. 10, 10785 Berlin, Germany e-mail: Katharina.Schley@pfizer.com increased IMD epidemiologic variability. The full range of benefits of widely available and effective meningococcal vaccines needs to be considered, especially in health technology assessments, where the broad benefits of these vaccines are neither accurately quantified nor captured in implementation policy decisions. Importantly, implementation of meningococcal vaccination programs in the current IMD climate also appeals to broader healthcare principles, including preparedness rather than reactive approaches, generally accepted benefit-risk approaches to vaccination, historical precedent, and the World Health Organization's goal of defeating meningitis by 2030. Countries should therefore act swiftly to bolster existing meningococcal vaccination strategies to provide broad coverage across age groups and serogroups given the recent increases in IMD incidence.

Keywords: COVID-19; Epidemiology; Immunization programs; Incidence; Vaccines

Key Summary Points

The COVID-19 pandemic has affected invasive meningococcal disease (IMD) globally.

Recent increases in IMD cases have been observed, most of which were meningococcal serogroup B.

Implementation and prioritization of IMD vaccination programs is necessary.

Health technology assessments need to consider the full range of meningococcal vaccination benefits.

The increasing number of IMD cases highlights the need for preparedness by implementing vaccination programs now instead of reactively.

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INTRODUCTION

Invasive meningococcal disease (IMD), caused by invasion of *Neisseria meningitidis* into a normally sterile site in the body, most often manifests as meningitis or septicemia [1]. IMD is characterized by its rapid and severe clinical course, typically commencing with nonspecific symptoms before progressing to a potentially life-threatening illness within hours [2]. Cases are sometimes fatal, with an estimated 8.3% overall case fatality rate [3], and many survivors experience long-term sequelae and short- and long-term reduced health-related quality of life (QoL) [4].

Although IMD cases are relatively rare [5], the capacity of meningococci for continued antigenic change causes a constantly evolving epidemiology characterized by unpredictable outbreaks [6-8]. For example, IMD caused by serogroup W (MenW) was infrequent before 2000, but emergence of hypervirulent clonal complex 11 strains led to marked global increases [9]. Additionally, after implementation of successful serogroup A (MenA) vaccination programs in Africa, serogroup C (MenC), W, and X outbreaks and epidemics were observed [6]. The inherent unpredictability of IMD was further observed in the United Kingdom (UK), where serogroup B (MenB) and MenC caused epidemics for many years during the 1990s, followed by the emergence of MenW in 2013 [10, 11].

Given clinical and epidemiologic factors, the World Health Organization (WHO) has established a goal of defeating meningitis by 2030; vaccination is a key step toward achieving this goal, based on robust evidence of effectiveness of currently available meningococcal vaccines [12, 13]. Infants, toddlers, and adolescents/ young adults are prime targets for vaccination due to higher rates of IMD within those age groups [13, 14], which maximizes direct and indirect conjugate vaccine-mediated IMD protection [15]. The predominant serogroup(s) causing disease vary among countries because of factors such as natural temporal fluctuations, location, and available public health interventions [15]. In this context, current vaccination

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programs vary by country according to targeted age groups and covered serogroups [13, 15].

The global IMD landscape changed considerably during the COVID-19 pandemic [16]. IMD incidence rates decreased globally in connection with COVID-19 mitigation measures, such as limiting social contact, physical distancing, mask wearing, and hand washing [16, 17]. Simultaneously, 2020 childhood vaccination rates in general were much lower than pre-pandemic rates worldwide [18]. During the pandemic, many parents delayed or canceled scheduled meningococcal vaccination appointments for their children [19]. However, a resurgence in IMD has recently been observed in several countries, such as England and France [20, 21]. Therefore, using a preparedness approach with well-tolerated and effective vaccines should be considered during this time of increasing IMD cases. A meningococcal vaccination program is also a key component of the WHO's initiative to defeat meningitis by 2030, with goals that include improving QoL after meningitis due to any cause, eliminating bacterial meningitis epidemics, and reducing IMD cases, disability, and deaths [12]. Here, we outline arguments supporting the implementation of IMD vaccination programs in the current climate of IMD resurgence and increased incidence rates as a crucial approach in moving toward the WHO goal of defeating meningitis. This article is based on previously conducted studies and does not contain data from any new studies with human participants or animals performed by any of the authors.

INVASIVE MENINGOCOCCAL DISEASE EPIDEMIOLOGY IN THE COVID-19 ERA

Lockdown Restriction Effects

In many countries, IMD incidence rates decreased after the onset of the COVID-19 pandemic [16]. Notably, IMD rates were already decreasing in many regions before the pandemic due to combined effects of vaccination programs and secular trends [13]. Pandemic-

associated incidence reductions varied across countries: given the caveat that countries differed in COVID-19 mitigation measures and surveillance programs [22], the largest decreases generally occurred in countries with established meningococcal vaccination programs. For example, in Spain, which has a comprehensive vaccination program that includes infant and toddler MenC vaccination and adolescent meningococcal serogroups A, C, W, and Y (MenACWY) vaccination, a single case of IMD was reported by Week 31 of 2021 compared with 24 cases in 2018 and 21 in 2019 [23]. In Poland, which recommends MenC vaccination for those aged 2 months to 19 years, 62 cases were observed by Week 39 of 2021 compared with 116 and 121 in 2018 and 2019, respectively [23, 24]. In South America in 2020, Brazil and Chile reported reductions of 65.0% and 91.3%, respectively, of confirmed IMD cases in 2019 [19]. Brazil's vaccination program includes infant, toddler, and adolescent MenC vaccination and adolescent MenACWY vaccination, whereas Chile's immunization program includes MenACWY vaccination in 12-montholds and MenACWY or MenB vaccination for atrisk populations [25, 26].

As with IMD, meningococcal carriage rates were initially expected to decrease during the pandemic. However, the evidence regarding meningococcal carriage during the COVID-19 pandemic is conflicting. In a review of COVID-19-related childhood immunity debt, lockdown measures were associated with decreased asymptomatic meningococcal carriage [17]. Alternatively, a study of Australian university students found meningococcal carriage rates were higher after COVID-19 containment measures (3.7% in February/March 2020 versus 6.8% in August/September 2020); however, these rates might also relate to students being locked down in residence halls, thereby increasing close contacts [27]. The role of reduced incidence of seasonal respiratory viruses, particularly influenza, during the first 2 years of the pandemic as a contributing factor to the decrease of IMD rates also deserves indepth studies.

INVASIVE MENINGOCOCCAL DISEASE EPIDEMIOLOGY IN THE POST-COVID-19 ERA

Return to Pre-pandemic Behavior Effects

As expected, easing of COVID-19 lockdown restrictions has been associated with increased IMD rates in several countries. Incidence of meningococcal disease increased in 2022 in the United States (US), following a decline in IMD rates during 2020-2021 [28]. In England, IMD cases dropped steeply in March 2020 but substantially increased from September through November 2021 after in-person learning resumed in schools and universities; nearly all new cases were MenB [20]. Importantly, case numbers among 15- to 19-year-olds during this period exceeded pre-pandemic levels, and 41.5% of IMD cases occurred in this age group compared with 11.8% in 2018 and 14.3% in 2019 [20]; currently, no MenB vaccination program exists for this age group in the UK. In France, lockdown measures during COVID-19 were associated with more than 2 years of reduced IMD incidence [21]. However, case numbers in December 2022 exceeded pre-pandemic levels. The majority of cases were MenB (53%) and were mainly observed among infants and those 15–24 years old [21]. Importantly, MenB rates in December 2020 were higher than pre-pandemic levels, especially among 15- to 24-year-olds [21]. This is of notable concern because France lacks a mandatory MenB vaccination program for adolescents/young adults (although vaccination is recommended in those at high risk of contracting the disease) [23, 29, 30], and occurrence of MenB disease in this age group may indicate the emergence of hypervirulent strains [31]. Moreover, health officials in Brazil have emphasized the importance of meningococcal vaccination among children and adolescents due to a recent MenC outbreak in São Paulo [32].

The epidemiology of IMD after the return to pre-pandemic behaviors in countries with vaccination programs likely depends on the serogroups that these vaccination programs cover. For instance, the swift and steep MenB case increase observed in England in 2021 may reflect a combination of high carriage and transmission primarily in adolescents/young adults, and may indicate a need for an adolescent MenB vaccination program [20]. Similarly, the increase in MenB cases in France in December 2022 further highlights the need for an adolescent MenB vaccination program [21, 23]. Importantly, recent reports of meningococcal outbreaks (e.g., the MenC outbreak in Florida among gay and bisexual men and the IMD outbreak in the Democratic Republic of Congo) and rising case numbers (e.g., MenB cases among adolescents/young adults in England) show that IMD is a continued public health threat [20, 33, 34]. Furthermore, the inherent unpredictability of IMD [6] raises concerns that serogroup distribution may change in post-pandemic periods, potentially limiting effectiveness of existing vaccination programs and leading to more complicated and costly outbreak management.

Although the effect of lifting COVID-19 mitigation measures on meningococcal carriage rates is not established, the capability for meningococcal carriage to rise rapidly with increased social activity was documented before COVID-19 emergence. A study of British university students found that meningococcal carriage increased from 6.9% on the first day of classes to 23.1% three days later, with average carriage rates among students living in catered halls increasing from 13.9% in October to 34.2% in December [35]. A more recent study of students newly admitted to a university dormitory in South Korea also reported an increase in meningococcal carriage rates over time, from 2.7% at baseline to 6.3% at 1 month and to 11.8% at 3 months [36]. Furthermore, studies have established that visits to bars or other crowded venues and kissing are significant risk factors for meningococcal acquisition [35, 37, 38].

Gaps in Vaccination Coverage and Immunity Debt

As physical distancing measures have abated, immune protection against IMD may have

declined relative to pre-pandemic levels because of decreased vaccine uptake and increased susceptibility to infectious diseases in the postpandemic period, termed "immunity debt" [17, 39, 40]. Reductions in sales of recommended pediatric vaccines in the US, including non-influenza and measles-containing vaccines, further illustrate the effects of the COVID-19 pandemic [41]. Overall doses ordered were lower in 2020 than in 2019, with the decrease in orders more prominent among those aged 24 months to 18 years [41]. The reduction in routine pediatric vaccine sales, and similar trends in reduced dose administration, highlight the vulnerability of US children to vaccinepreventable disease outbreaks [41]. Similar findings were observed in California, USA, where human papillomavirus vaccine uptake among 9- to 12-year-olds fell in March/April 2020; in May 2020, however, uptake rates increased to similar levels observed in 2019 [42]. MenC vaccine uptake among French infants during the first lockdown was lower than expected for the first dose given to 5-montholds (10.9% decline) and the booster given to 12-month-olds (20.7%), with overall 2.8% and 13.8% declines, respectively, through Q4/2020 [43]. The meningococcal vaccination rate decline during the pandemic is further evidenced by survey results indicating that 50% of parents in eight countries (Argentina, Australia, Brazil, France, Germany, Italy, UK, US) delayed meningococcal or canceled vaccination appointments during the pandemic, with main reasons including lockdowns, concerns of catching COVID-19, or needing to care for someone with COVID-19 [44].

The overall decrease in exposure to pathogens during the pandemic may also lead to immunity debt, possibly resulting from impaired adaptive immunity against specific infectious agents and decreased innate immunity because of lack of immune stimulation [17, 39]. This may invite rebounds in IMD and other vaccine-preventable infectious diseases, as described below [17, 39]. Therefore, relevant and current seroepidemiology data, especially following the COVID-19 pandemic, are needed to help estimate or model the epidemiologic implications of COVID-19 on IMD.

Changing Epidemiology of Other Respiratory Infectious Diseases

Concerns surrounding changes in infectious disease epidemiology in the post-pandemic period are not unique to IMD. In Australia, following relaxations in physical distancing measures, cases of respiratory syncytial virus (RSV) drastically increased beginning in September 2020, far exceeding annual peaks observed in 2012-2019, with median patient age significantly higher than in previous years (18.4 vs. 7.3-12.5 months; P < 0.001) [45]. France and the US also observed delayed RSV seasonality in 2021 [46, 47]. Conversely, in a New York hospital, the median age among those < 18 years old testing positive for RSV was 6 months in 2021 versus 17 months in 2019-2020; additionally, 81% of those admitted were moved to the intensive care unit compared with 45% in the 2019-2020 season [48]. Similarly, an increase in childhood invasive pneumococcal disease cases was observed in England after COVID-19 restrictions were lifted [49]. For respiratory infections, immunity debt may be contributing to this increased potential for more epidemics and higher case numbers [49, 50]. These findings collectively suggest that infectious diseases can increase rapidly following easing of lockdown restrictions; furthermore, reemergence may cause epidemiologic changes or case number increases, which may then exert pressure on healthcare systems. Additionally, infection rate increases for other respiratory pathogens may directly potentiate IMD increases. For example, historical evidence on individual and population levels link IMD with prior influenza infection [51].

PREPAREDNESS AGAINST INVASIVE MENINGOCOCCAL DISEASE

Meningococcal Vaccination Program Effectiveness

Abundant real-world evidence supports the effectiveness of meningococcal vaccination

programs. Successful vaccination programs have been comprehensively reviewed elsewhere [13]; here, we discuss several notable or recent examples. A > 99.9% decrease in confirmed MenA cases was observed across nine African countries following implementation of MenA conjugate vaccination programs beginning in 2010 (Fig. 1A) [52]. In England, the introduction of a MenC vaccination program in 1999 for infants, with a one-time catch-up for children up to 18 years old, was associated with a 93.1% decrease in MenC cases from 1998/1999 to 2003/2004 [53-55]. In 2009, 10 years following the introduction of the MenC vaccination program, a study estimated that 9000 MenC cases had been avoided, resulting in a cumulative savings of £75 million [56]. In 2013, a MenC booster dose was recommended for teenagers aged 14 years to improve protection against MenC disease and to maintain high levels of herd protection, with 97.1% reduction in MenC cases persisting through 2019/2020 (Fig. 1B) [53–55]. In 2015, the single MenC dose for adolescents was replaced by the MenACWY vaccine to combat steep MenW disease increases, with an estimated effectiveness of 94% against MenCWY disease (no cases of diseases by MenA were reported/identified) [57]. Similarly, 2018 implementation of toddler and adolescent MenACWY programs in the Netherlands to address increasing MenW disease rates was associated with 85% and 50% reductions in MenCWY cases in vaccine-eligible and ineligible cohorts, respectively (no cases of diseases by MenA were reported/identified) [58].

Outside Europe, a MenACWY vaccination campaign to combat rising MenW disease rates was initiated in Chile in 2012 for those 9 months to 4 years old, with routine vaccination for 12-month-olds introduced in 2014 [59]. By 2016, a 92.3% MenW disease reduction was observed among 1- to 4-year-olds, the age group that was targeted by the vaccination program (Fig. 1C) [59]. Interestingly, no early indirect effects of the toddler vaccination were observed in 2012–2014, emphasizing the importance of including adolescents (the age groups that usually have the highest carriage rates) in the vaccination programs to achieve indirect protection [59, 60].



Fig. 1 Examples of IMD epidemiology before and after implementation of mass vaccination programs including: A MenA cases in 9 African countries (reproduced with permission from Trotter and colleagues) [52], B MenC cases in England [54], and C MenW incidence by age group in Chile (reproduced with permission from Villena and colleagues) [59]. *IMD* invasive meningococcal disease, *MenA* meningococcal serogroup A, *MenC* meningococcal serogroup C, *MenW* meningococcal serogroup W, *Non-MenA* other meningococcal serogroups, *Non-MenA* pathogens other than *Neisseria meningitidis*

Holistic Approach to the Value of Preventive Meningococcal Vaccination

Although initial cost-effectiveness studies have generally reported MenB vaccination strategies to be cost-ineffective [61], existing health technology assessments generally fail to capture the full range of vaccination benefits [62-64]. For example, although previous cost-effectiveness studies have found MenB vaccination cost-effective only at low prices or cost-ineffective, a recent analysis found a 4-component vaccine that protects against MenB and is cost-effective in England when considering additional aspects of the disease (i.e., 5 "disease burden categories") for a comprehensive analysis of the broad burden of MenB [65]. Similar findings were observed in Germany, where the 4-component MenB vaccine was found to be more cost-effective when considering broader aspects, such as the quality-adjusted life-years effect on patients and caregivers [66]. Additionally, a systematic review found that the effect of IMD sequelae is underestimated because of underreporting and the small available dataset, particularly regarding the real rate of long-term sequelae, but such evaluations are warranted in economic assessments of vaccination programs [67]. Moreover, a recent review of the impact of cost-effectiveness analyses on vaccine policy decisions in the UK, the US, the Netherlands, and Canada reported that vaccine availability, serogroup incidence over time, and the disastrous nature of IMD mainly drive vaccine recwhereas traditional ommendations, costeffectiveness analyses did not play a major role in recommendations, in part because they tend to underestimate the value of vaccination against IMD (i.e., not considering risk reduction for both the vaccinee and their close contacts) [55].

Although calculating the costs of vaccination programs is relatively straightforward, the calculation of benefits is less so, and economists traditionally focus on a narrow range of implications for these programs (e.g., medical costs avoided with children not getting sick) [68]. Other burdens, such as cognitive or psychological problems, family or legal burdens, adaptive measures, concern about meningococcal disease, and social crisis management, are less easily quantifiable and are consistently neglected in cost-effectiveness analyses [69]. Indeed, assessment of indirect costs associated with IMD is highly dependent on sequelae severity, and varies among and within countries. These costs may largely affect low-income countries because a disproportionately large portion of household annual income may be needed to cover costs of utilized resources [69]. Policymakers should therefore consider outcomes to determine the full public health value of vaccines in evidence-based decision-making, including broader, non-health effects, such as social and economic benefits; reductions in disease incidence, transmission, and size/frequency of outbreaks; health system stabilization; and a more balanced view of cost-effectiveness data that balances value, access and profit, and public good [70].

Proper valuation of vaccination is not a purely academic exercise because the process by which the value of vaccination is estimated has consequences for vaccine cost and policy, which in turn have effects on personal health and well-being, especially in disadvantaged groups [71]. Given that health technology assessments do not consider the broader benefits of vaccination consistently, five priority areas for improvement have been suggested: broader healthcare cost offsets, effect on caregiver QoL, transmission value, prevention of antimicrobial resistance, and macroeconomic effects [72, 73]. Suggestions for future policyoriented vaccination studies include evaluating the impact of vaccination on school attendance, educational achievement, cognitive development, employment (including hours worked and earnings), and the development of a calibrated epidemiologic/economic model to estimate vaccination value [71]. The use of experimental and observational studies may be another way to address gaps in evidence that link vaccination to economic benefits other than direct health benefits and reduced medical costs [74].

With regard to government budgeting, vaccination program costs may be accurately estimated, with the maximum budget estimated at 100% uptake; however, budgeting for treatment of vaccine-preventable diseases may be more difficult due to variable costs [56]. The cost of disease prevention through vaccination is relatively low given the associated benefits, and, thus, return-on-investment analyses that better estimate short-term vaccination benefits may complement cost-effectiveness analyses [56]. Consideration of all vaccination-related competing priorities (e.g., health, economic growth, equity, education) is necessary for government healthcare budgeting decisions and broader interventions [56, 75].

Disparities in vaccine uptake among socioeconomic and demographic groups because of limitations in access to healthcare and healthcare providers increase risks of IMD. In the US, coverage of >1 dose of MenACWY vaccine among 13- to 17-year-olds ranged from 86.1% to 91.6% in 2020 among those with annual incomes below the poverty line, with rates similar to those at or above the poverty line (85.6%–90.2%) [76]. However, coverage rates were 47.4%-48.6% for >2 doses versus 50.2%-61.2%, respectively. Similarly, a crosssectional study of 16- to 18-year-olds in the immunization Philadelphia registry 2015-2017 reported a significant difference in MenB vaccination coverage by socioeconomic status, where MenB vaccine recipients were more likely to live in a neighborhood with a median income of > US\$100,000 compared with < \$20,000 (*P* < 0.0001) [77]. Additionally, sequelae of IMD may affect people from lowincome backgrounds unequally because resources for IMD survivors may require a large portion of their household income [69].

Many low- and middle-income countries (LMICs) have limited access to some vaccines and therapeutics [78–80]. Limited access to healthcare and vaccination may also lead to epidemics and outbreaks in such low-income regions [81]. Meningococcal vaccination in LMICs may only be available through external support, such as Gavi, the Vaccine Alliance, to fund purchases of vaccines [78, 80]. In a systematic review describing investment cases for vaccines and immunization programs, the authors reported that the investment cases identified research and development gaps in LMICs, including the need for funds to support

clinical trials and purchases of vaccines [82]. The withdrawal of Gavi support in LMICs transitioning to fully self-financing may potentially lead to additional funding gaps experienced by some countries [80].

A 2020 publication presented a taxonomy for MenB vaccine evaluation that includes internalized and externalized health and nonhealth benefits (Table 1), with the goal of comprehensively accounting for the devastating nature of IMD and the corresponding protective impact of vaccination [64]. The authors suggested the need to evaluate more broadly the cost of IMD and the cost benefits of MenB vaccination [64]. A modeling study that assessed the effect of MenB vaccination among college students demonstrated that MenB vaccination not only lowered MenB incidence and number of outbreaks but also reduced costs associated with MenB outbreaks [83]. In a systematic review and synthesis of published evidence [84], mean healthcare costs associated with acute infection in 2014 international dollars were reported at I\$50,796 in the US. Notably, the healthcare costs of IMD were higher than those estimated for influenza and RSV infections, with \$15,163 and \$16,034 (2013 US dollars), respectively, in hospitalized US adults aged ≥ 60 years [85]. These findings illustrate the high burden of IMD on healthcare costs compared with other infections and the importance of preventing IMD disease. Importantly, most IMD analyses focus only on acute infection costs, and a broader analysis should incorporate direct costs of both acute and long-term phases, including all expenses relevant to recovery from infection [64].

The uptick in IMD cases following lockdown restriction relaxations, as demonstrated in some countries [20, 21, 86], will result in lives lost and other far-reaching negative consequences for infected individuals and the broader community. The recent increases in IMD cases highlight the importance of vaccination programs and the need to be proactive during this postpandemic era. Experts have thus called upon policymakers to implement preventive vaccination programs to provide protection from these outcomes [17, 39].

	Health benefits	Social/economic benefits
Internalized	Direct health gains (I)	Education gains (I)
	Household health externalities (I; F)	Labor market productivity gains (I)
	Prevention and amelioration of comorbidities (I)	Nonmarket productivity and leisure gains (I)
	Reductions in nosocomial infections (H; I)	Caregiver productivity and leisure gains (F)
		Risk reduction gains (C; I)
Externalized	Full public health benefits (B)	Healthcare cost savings (C; I)
		Social preference fulfillment (C)
		Outbreak control gains (C; H)
		Litigation mitigation (F; H; I)
		Macroeconomic gains (B; C; I)
		Institutional disruptions (C; F; I)
		Equity gains (C; F; I)
		Health system efficiency gains (H)

Table 1 Taxonomy of MenB vaccination benefits^a adapted from Stawasz and colleagues (adapted with permission underthe CC-BY license) [64]

B broader society, *C* communities, *F* families, *H* healthcare/hospital, *I* individuals, *MenB* meningococcal serogroup B ^aLetters presented in parentheses denote the group(s) potentially affected by the corresponding benefit. Italicized benefits categories comprise narrow benefits. All other listed benefits are broad benefits

Broader Context of Preventive Meningococcal Vaccination

The COVID-19 pandemic triggered a global reckoning surrounding disease control strategies. One key learning is the importance of a preparedness rather than a reactive approach to public health policy and prevention, with analyses underscoring the chronic underinvestment in healthcare infrastructure and lack of early and comprehensive virus containment measures as major contributors to poor pandemic outcomes [87–89].

Many meningococcal vaccination campaigns were implemented in response to increased IMD rates [13]; however, using a preparedness approach with vaccines that are well tolerated and effective during times of IMD resurgence should be considered from a disease and case minimization context. Another broader consideration in meningococcal vaccination program implementation is that the programs are an important component of achieving the WHO's Defeating Meningitis by 2030 Global Roadmap, which includes the goals of eliminating bacterial meningitis epidemics, reducing vaccine-preventable bacterial meningitis cases by 50% and deaths by 70%, reducing disability, and improving QoL after meningitis due to any cause [12].

The results discussed here do not consider the effect of COVID-19 on IMD epidemiology due to underlying uncertainties in disease unpredictability. Estimating the epidemiologic implications of COVID-19 for the level and future trajectory of IMD should be considered at least at the regional level; however, current seroepidemiology to guide these models is unavailable. Future work should consider evaluations of post-pandemic catch-up meningovaccination options, including coccal vaccination programs that may have improved following the pandemic.



Fig. 2 Summary of arguments supporting implementation of meningococcal vaccination programs in the context of IMD incidence in the COVID-19 pandemic and post-

CONCLUSIONS

The resurgence of IMD incidence in some countries following relaxation of physical distancing and lockdown restriction measures implemented due to the COVID-19 pandemic presents a critical opportunity for implementation of meningococcal vaccination programs. Figure 2 reviews the manifold arguments supporting this conviction. Evidence suggests that IMD incidence in the post-pandemic era has increased and exceeded pre-pandemic levels in some countries, with added concerns including increased susceptibility because of vaccination coverage gaps, increased incidence of other respiratory pathogens, immunity debt from lockdown restrictions, and increased IMD epidemiologic variability. Vaccines targeting the ACWY and B serogroups are widely available and demonstrably effective in many global regions. Given the often devastating nature of IMD, the full range of benefits of these vaccines, including the variant control value of meningitis vaccination, should be considered in health technology assessments. However, vaccines have wide-ranging benefits that are rarely accurately quantified and not captured in implementation policy decisions. Given that traditional cost-effectiveness analyses of vaccination programs may have a limited role in

pandemic eras. *IMD* invasive meningococcal disease, *WHO* World Health Organization

individual country recommendations for IMD vaccination, in part because these traditional evaluations lack broader value assessments of vaccines, analyses that consider the broad benefits of vaccines are needed. Implementation of meningococcal vaccination programs in the current IMD climate also appeals to broader healthcare principles, including preparedness rather than reactive approaches, generally accepted benefit–risk approaches to vaccination, historical precedent, and the WHO goal of defeating meningitis by 2030.

Countries must act swiftly to bolster existing meningococcal vaccination strategies to provide broad coverage across age groups and serogroups. Ultimately, implementation of comprehensive meningococcal vaccination programs is necessary to prepare for IMD incidence fluctuations in the post-pandemic era, as demonstrated by the increases in IMD incidence in some countries following relaxation of the COVID-19 pandemic control measures.

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Declarations

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Ethical Approval. This article is based on previously conducted studies and does not contain any new data from studies with human participants or animals performed by any of the authors.

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