HUMAN VACCINES & IMMUNOTHERAPEUTICS
2024, VOL. 20, NO. 1, 2301186
https://doi.org/10.1080/21645515.2023.2301186

RESEARCH ARTICLE

Invasive meningococcal disease in South-Eastern European countries: Do we need to revise vaccination strategies?

Georgina Tzanakaki[a], Hana Cabrnochová[b], Snežana Delić[c], Anca Draganescu[d], Anna Hilfanova[e], Beáta Onozó[f], Marko Pokorn[g], Anna Skoczyńska[h], and Goran Tešović[i]

[a]Public Health Microbiology, National Meningitis Reference Laboratory, Laboratory for Surveillance of Infectious Diseases, Department of Public Health Policy, School of Public Health, University of West Attica, Athens, Greece; [b]Center of children vaccination in Thomayer University Hospital, and Department of Pediatrics, First Faculty of Medicine, Charles University Prague, Prague, Czech Republic; [c]Serbian Reference Laboratory, Sombor, Serbia; [d]National Institute for Infectious Diseases "Prof.Dr.Matei Bals", Faculty of Medicine, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; [e]Department of Pediatrics, Immunology, Infectious and Rare Diseases, European Medical School of the International European University, Kyiv, Ukraine; [f]Pediatric Department of County Hospital, Miskolc, Hungary; [g]Division of Paediatrics, University Medical Centre Ljubljana, Ljubljana, Slovenia; [h]National Reference Centre for Bacterial Meningitis, Department of Epidemiology and Clinical Microbiology, National Medicines Institute, Warsaw, Poland; [i]University of Zagreb, and Pediatric Infectious Diseases Department, University Hospital for Infectious Diseases, Zagreb, Croatia

ABSTRACT

Invasive meningococcal disease (IMD) is an acute life-threatening infection caused by the gram-negative bacterium, *Neisseria meningitidis*. Globally, there are approximately half a million cases of IMD each year, with incidence varying across geographical regions. Vaccination has proven to be successful against IMD, as part of controlling outbreaks, and when incorporated into national immunization programs. The South-Eastern Europe Meningococcal Advocacy Group (including representatives from Croatia, the Czech Republic, Greece, Hungary, Poland, Romania, Serbia, Slovenia and Ukraine) was formed in order to discuss the potential challenges of IMD faced in the region. The incidence of IMD across Europe has been relatively low over the past decade; of the countries that came together for the South-Eastern Meningococcal Advocacy Group, the notification rates were lower than the European average for some country. The age distribution of IMD cases was highest in infants and children, and most countries also had a further peak in adolescents and young adults. Across the nine included countries between 2010 and 2020, the largest contributors to IMD were serogroups B and C; however, each individual country had distinct patterns for serogroup distribution. Along with the variations in epidemiology of IMD between the included countries, vaccination policies also differ.

ARTICLE HISTORY
Received 30 May 2023
Revised 8 December 2023
Accepted 29 December 2023

KEYWORDS
Age distribution; IMD epidemiology; immunization programs; invasive meningococcal disease; MenB vaccines; meningococcal vaccines; quadrivalent vaccines; serogroup distribution; South-Eastern Europe; vaccination policy

Introduction

Invasive meningococcal disease (IMD) is an acute life-threatening infection caused by the gram-negative bacterium, *Neisseria meningitidis*.[1] The meningococci are often present as commensal species in the rhino-oropharynx, with asymptomatic carriage prevalence varying by age.[2] When the meningococci escape the mucosal barrier and replicates within the blood, the following IMD often progresses rapidly, with a case fatality rate of 8–15% even with suitable and timely antibiotic therapy.[3,4] Up to 20% of patients will also have permanent sequelae such as hearing loss, neurological damage, or loss of a limb.[3,4]

Globally, there are approximately half a million cases of IMD each year,[1] with incidence varying across geographical regions. In Europe, an incidence of 0.6 cases per 100,000 population was reported in 2017.[5] Incidence rates are highest in children <1 year old, followed by a second peak amongst adolescents and young adults.[5] Worldwide the serogroups responsible for the majority of IMD cases are A, B, C, W, X and Y.[1] In Europe, the most prevalent serogroups are B and C; however, in recent years, an increase of IMD infections caused by serogroup W has been reported.[5–8]

Vaccination has proven to be successful against IMD, as part of controlling outbreaks, and when incorporated into national immunization programs (NIPs).[9–16] Consequently, many countries include vaccination against one, or several, meningococcal serogroups into their NIPs, in accordance with local epidemiology. Available vaccines now mainly include conjugated polysaccharide and protein-based meningococcal vaccines.[17] Whilst unconjugated polysaccharide vaccines had been used for years, they cannot induce immune memory and have mostly been replaced by conjugated polysaccharide vaccines.[18] Indeed, monovalent meningococcal serogroup C (MenC) and A (MenA) conjugated vaccines have been instrumental in decreasing meningococcal disease and carriage in Europe and the African meningitis belt, respectively.[17] More recently, there has been a shift across many regions to quadrivalent MenACWY conjugate vaccines

CONTACT Georgina Tzanakaki gtzanakaki@uniwa.gr Public Health Microbiology, Head, Laboratory for Surveillance of Infectious Diseases and National Meningitis Reference Laboratory, and Department of Public Health Policy, School of Public Health, University of West Attica, 196, Alexandras Avenue, Athens 11521, Greece.

Supplemental data for this article can be accessed on the publisher's website at https://doi.org/10.1080/21645515.2023.2301186

to cover a broader range of epidemiological-relevant serogroups. In addition, protein-based MenB vaccines, which have been challenging to develop, have also been shown to reduce real-world MenB IMD risk.[17]

Given the local and global variations in meningococcal epidemiology, as well as differing approaches to vaccination, the South-Eastern Europe Meningococcal Advocacy Group was formed in 2020. The objective was to discuss surveillance, epidemiology, prevention and potential challenges associated with IMD in South – Eastern Europe, including current issues and barriers to vaccine implementation, and to share experiences of national IMD immunization programs, including the link between epidemiological data, vaccine availability and the potential implications for vaccination.

Methods

Representatives from nine South-Eastern European countries, Croatia, the Czech Republic, Greece, Hungary, Poland, Romania, Serbia, Slovenia and Ukraine, met on 10th June 2021 and 10th May 2022 to discuss and exchange experiences on IMD in their countries. Topics that were discussed included: the type of IMD surveillance by each country, case definitions used, microbiological diagnosis, the methodologies used for typing, and whether antimicrobial susceptibility testing is routinely carried out. The attendees also presented information about vaccination strategies and recommendations in their countries, whether there was an impact due to vaccine hesitancy, and whether there were guidelines on IMD management. During these meetings, the representatives also presented epidemiological data for IMD in their country, including incidence, case fatality rates (CFR), serogroup and age distribution. Following these meetings, epidemiological data were completed and updated using sources provided by each representative,[19–25] or from the European Centre for Disease Prevention and Control Surveillance (ECDC) Atlas for Infectious Diseases as collected through The European Surveillance System (TESSy).[26]

Results

IMD surveillance and diagnosis

IMD surveillance is in place in all nine South-Eastern European countries represented in the advocacy group, although there are variations in the type of surveillance used (Table 1). Notifications are either case-based, laboratory-based, or a combination of the two systems (e.g. the Czech Republic) and can be compulsory (e.g. the Czech Republic, Greece, Croatia, Poland and Slovenia) or passive (e.g. Hungary, Romania,[25] Serbia and Ukraine). Microbial diagnosis is performed in all included countries, with variation in the typing methods (Table 2). Serogrouping, through genogrouping by PCR or rapid agglutination tests of isolates, is used in all countries, while multilocus sequence typing (MLST), whole genome sequencing (WGS), PorA and fetA are used for further characterization in the Czech Republic, Greece, Hungary, Poland, Serbia and Slovenia. Additionally, the Czech Republic, Greece and Poland have implemented typing methods such as factor H binding protein (fHbp) and other antigen

Table 1. IMD case definition and type of surveillance across the included countries.

Country	Case definition	Surveillance
Croatia	EU	Compulsory (nationwide)
Czech Republic	EU	Compulsory (nationwide), active surveillance Case-based and laboratory-based
Greece	EU	Compulsory (nationwide)
Hungary	EU + WHO	Passive (nationwide and case-based)
Poland	EU/PL	Compulsory (nationwide)
Romania	EU	Passive (nationwide and case-based)
Serbia	EU	Passive (nationwide and case-based)
Slovenia	EU	Compulsory (nationwide)
Ukraine	EU	Passive (case-based)

EU, European Union Case definition[27]: **Clinical criteria**: Any person with at least one of the following symptoms: meningeal signs; hemorrhagic rash; septic shock; septic arthritis. **Laboratory Criteria**: At least one of the following four: isolation of *Neisseria meningitidis* from a normally sterile site, or from purpuric skin lesions; detection of *Neisseria meningitidis* nucleic acid from a normally sterile site, or from purpuric skin lesions; detection of *Neisseria meningitidis* antigen in cerebrospinal fluid (CSF); detection of Gram-negative stained diplococcus in CSF. **Epidemiological criteria**: An epidemiological link by human-to-human transmission. **Case Classification**: A) Possible case, any person meeting the clinical criteria; B) Probable case, any person meeting the clinical criteria with an epidemiological link; B) Confirmed case, any person meeting the laboratory criteria.

PL, Poland. Case definition the same as for EU, but with exclusion of possible cases.

WHO, World Health Organization. **WHO suggested invasive meningococcal outbreak case definition**[28]: Suspected case, any person with sudden onset of fever (>38.5°C rectal or 38.0°C axillary), neck stiffness, OR other meningeal signs (including bulging fontanel in infants). Probable case, any suspected case with macroscopic aspect of CSF turbid, cloudy or purulent, or a CSF leukocyte count > 10 cells/mm3, or bacteria identified by Gram stain in CSF, or positive *Neisseria meningitidis* antigen detection (e.g., by latex agglutination testing). In infants, CSF leucocyte count > 100 cells/mm3, or CSF leucocyte count 10–100 cells/mm3 and either an elevated protein (>100 mg/dl), or decreased glucose (<40 mg/dl) level). Confirmed case, any suspected case that is laboratory confirmed by culture or polymerase chain reaction (PCR) detection of Neisseria meningitidis in the CSF or blood. Excluded case, suspected case where laboratory test shows another pathogen.

WHO suggested IMD surveillance case definition[28]: Suspected IMD case, no standard case definition. Probable IMD case, any person with clinical diagnosis of meningitis or septicemia AND at least one of the following: purpuric rash where IMD is considered the most likely cause (linked to confirmed cases with other causes of hemorrhagic rash excluded or considered less likely); or gram-negative diplococci identified from normally sterile site or from a purpuric skin lesion; or positive *Neisseria meningitidis* antigen detection (e.g., by latex agglutination testing) from any normally sterile site or purpuric skin lesion. Confirmed IMD case, *Neisseria meningitidis* is identified via culture or PCR from a purpuric skin lesion or any normally sterile site.

Table 2. Diagnostic methods across the included countries.

Country	Microbial diagnosis	Typing	Antimicrobial suspect testing
Croatia	Yes	Serogrouping (PCR at 1 site)	Yes
Czech Republic	Yes	Serogrouping, PCR, PorA, fetA, MLST, WGS, fHbp, nhba, nadA	Yes
Greece	Yes	Serogrouping, PCR, PorA, fetA, fHbp, nhba, nadA, MLST, WGS	Yes
Hungary	Yes	Serogrouping, WGS, PorA, fetA, MLST	Yes
Poland	Yes	Serogrouping, PorA, fetA, fHbp, MLST, WGS	Yes
Romania	Yes	Serogrouping	Yes
Serbia	Yes	Serogrouping, PorA, fetA	Yes
Slovenia	Yes	Serogrouping, WGS	Yes
Ukraine	Yes	Serogrouping	Yes

fHbp, factor H binding protein; MLST, multilocus sequence typing; nadA, neisserial adhesion A; nhba, neisserial heparin binding protein; PCR, polymerase chain reaction; WGS, whole genome sequencing

genes of MenB vaccines. Antimicrobial susceptibility testing is consistently applied across all participating countries.

Epidemiology of IMD

Incidence

Across the nine South-Eastern European countries, the average notification rate for the pre-pandemic period (2010–2019) varied from 0.13 per 100,000 population per year in Serbia to 0.82 per 100,000 population per year in Croatia (Figure 1). Between 2010 and 2019 the IMD notification rate remained fairly consistent across most of the countries, with some declines observed in Greece and Poland (Table 3). IMD notification rates were consistently lower in Serbia than in any other country, although this may have been due to underreporting. In 2020 (COVID-19 pandemic period) there was a significant decrease in IMD cases in most countries, which was likely due to the impact of COVID-19, social distancing and 'lockdowns' (Table 3).

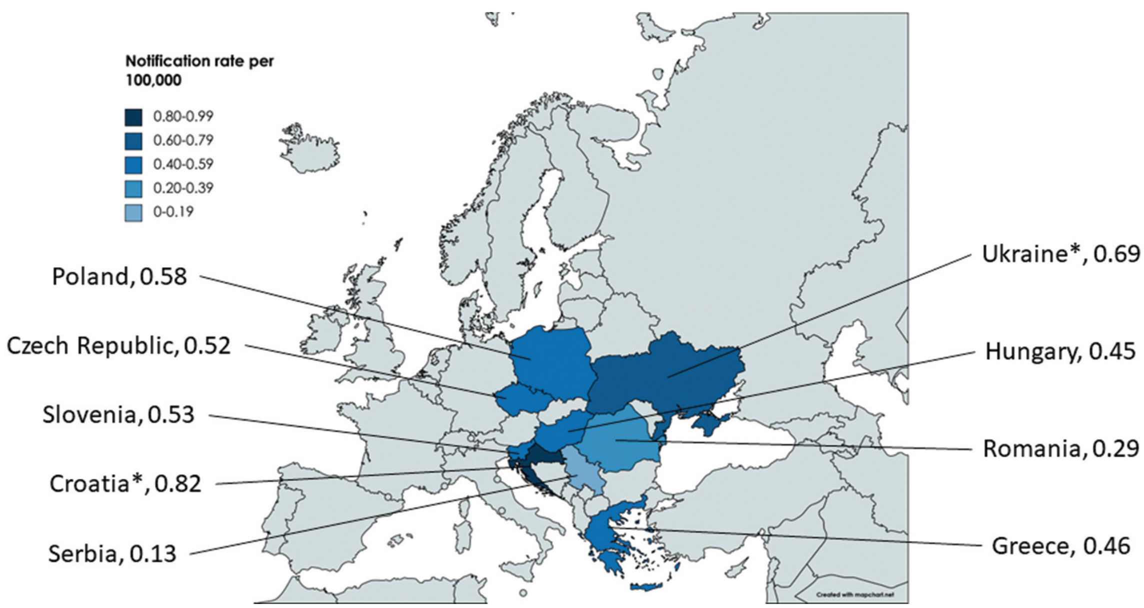

Figure 1. Average notification rates for IMD across the included countries for the period 2010 to 2019. *Data available for 2012–2019

Table 3. Notification rates (confirmed cases) per 100,000 population across the included countries, 2010 to 2020.

Notification rate, per 100,000	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Croatia	NA	NA	0.96	0.61	0.78	0.99	0.72	0.89	0.76	0.83	0.34
Czech Republic	0.57	0.60	0.56	0.56	0.40	0.46	0.41	0.63	0.53	0.46	0.23
Greece	0.49	0.47	0.53	0.54	0.55	0.50	0.48	0.39	0.32	0.30	0.20
Hungary	0.37	0.67	0.51	0.47	0.33	0.36	0.48	0.40	0.41	0.47	0.33
Poland	0.60	0.74	0.63	0.66	0.49	0.58	0.44	0.60	0.52	0.51	0.28
Romania	0.26	0.34	0.35	0.26	0.34	0.25	0.28	0.25	0.33	0.26	0.12
Serbia	0.20	0.18	0.15	0.05	0.17	0.11	0.07	0.17	0.11	0.11	0.03
Slovenia	0.44	0.63	0.44	0.53	0.39	0.78	0.34	0.44	0.87	0.43	0.24
Ukraineb	1.00	1.10	0.75	0.92	0.74	0.72	0.63	0.77	0.63	0.71	0.33

Notification rates from the ECDC Atlas[26] are calculated per 100,000 population: the number of reported confirmed cases, divided by the official Eurostat estimate of the population for that year, multiplied by 100,000.
[a]Serbia, incidence rate per 100,000 population from the Health Statistical Yearbook Republic of Serbia.[20]
[b]Ukraine, incidence rate per 100,000 population from Ministry of Health of Ukraine Public Health Centre.[21]
NA, not available.

Age standardized rates of IMD

In 2019 (the most recent year of data not influenced by COVID-19), age standardized rates were highest in infants < 1-year-old in the Czech Republic, Greece, Hungary, Poland and Romania (Figure 2(a–e). No age standardized rates were available for Croatia, Serbia or Ukraine. In Slovenia, there were no reported cases in infants < 1-year-old in 2019 (Figure 2(f)), although age standardized rates were highest for this age group from 2010–2018 In general, children aged 1–4-years old had the next highest age standardized rate, followed by 15–24-year-olds (except in Slovenia).

Case fatality rates

CFRs (or number of fatalities) also remained broadly consistent between 2010 and 2020 for each country, although there were variations between the countries, with higher CFRs in Hungary (between 9.4% in 2014 and 25.7% in 2015), and lower CFRs in Croatia (2.8% in 2015 to 10.0% in 2016), Greece (0 in 2020 and 2011 to 11.8% in 2018) and Poland (3.8% in 2020 to 13.5% in 2019) (Table 4).

Serogroup distribution

Across the nine included countries between 2010 and 2020, the largest contributors to IMD were serogroups B and C. Each individual country, however, had distinct patterns for the contributing serogroups (Figure 3). In Croatia, for all years apart from 2017, the majority of cases were due to serogroup B, with cases due to serogroup Y occurring at around 2 per year, and cases due to serogroup W uncommon (Figure 3(a)). In the Czech Republic, while serogroup B was the main contributor throughout the study period, cases appeared to decrease (Figure 3(b)). By contrast, cases of serogroup C increased in 2017 and remained high, making this the predominant serogroup by 2019, with distribution across all age groups (Table S1). This increase in serogroup C cases in 2017 coincided with an increase in the IMD notification rate in the Czech Republic (Table 3). In Greece, serogroup B predominated between 2010 and 2020, although cases steadily declined (Figure 3(c)). Cases due to serogroups C, W and Y occurred at a low frequency throughout the study period. However, the proportion of cases attributed to

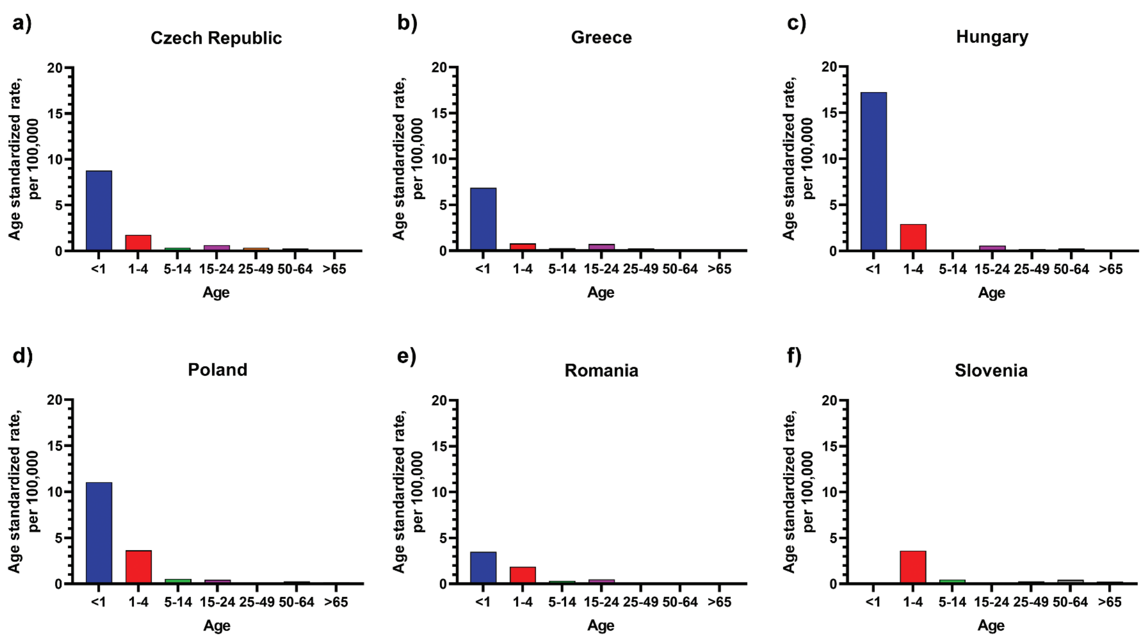

Figure 2. Age standardized rates of IMD per 100,000 population across included countries for 2019.[26] Serbia: In 2019, 1 case in 2 year old, 1 case 10–14, 1 case 15–19, 1 case 40–49, 1 case 50–59 and 2 cases ≥60 years (Health Statistical Yearbook Republic of Serbia).[20] Ukraine: In 2019, 30 cases in up to 1 years, 26 cases in 2–4 years, 18 cases 5–9 years, 11 cases 10–14 years, 3 cases 15–17 years, 30 cases ≥18 years (Ministry of Health of Ukraine Public Health Centre, unpublished).

Table 4. Number of deaths and case fatality rates across the included countries, n deaths (CFR %) 2010 to 2020.

n deaths (CFR %)	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Croatia[a]	4 (9.3)	4 (7.4)	3 (7.3)	1 (3.8)	1 (3.1)	1 (2.8)	3 (10.0)	3 (7.9)	3 (9.7)	2 (5.9)	2 (14.3)
Czech Republic[b]	5 (8.3)	8 (12.7)	3 (5.1)	3 (5.1)	5 (11.9)	3 (6.3)	6 (14.0)	10 (14.9)	3 (5.4)	3 (6.1)	3 (12.0)
Greece[b]	3 (5.5)	0 (0.0)	6 (10.2)	3 (5.1)	5 (8.3)	1 (1.9)	4 (7.7)	3 (7.1)	4 (11.8)	3 (9.4)	0 (0.0)
Hungary[b]	4 (10.8)	12 (17.9)	6 (11.8)	9 (19.6)	3 (9.4)	9 (25.7)	9 (19.6)	6 (18.8)	6 (15.0)	8 (17.4)	5 (15.6)
Poland[b]	22 (9.6)	21 (7.4)	21 (8.8)	25 (10.0)	14 (7.5)	20 (9.1)	25 (15.0)	30 (13.3)	23 (11.6)	26 (13.5)	4 (3.8)
Romania[b]	6 (11.5)	9 (13.2)	9 (12.7)	4 (7.7)	4 (6.0)	8 (16.0)	8 (14.5)	6 (12.0)	13 (20.3)	10 (20.0)	2 (8.3)
Serbia[c]	1 (6.7)	0 (0.0)	1 (9.1)	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	2 (16.7)	2 (25.0)	0 (0.0)	1 (50.0)
Slovenia[b]	1 (11.1)	1 (7.7)	0 (0.0)	1 (9.1)	1 (12.5)	2 (12.5)	1 (14.3)	0 (0.0)	2 (11.1)	0 (0.0)	0 (0.0)
Ukraine[d†]	68	103	58	NA	60	60	NA	49	39	46	NA

[a]Data from the Croatian health statistics yearbook 2019[19]; [b]Data from the ECDC Atlas[26]; [c]Data from the Health Statistical Yearbook Republic of Serbia.[20] [d]Data from the WHO European Health Information Gateway.[29]
NA, not available.
[†]Only n deaths available.

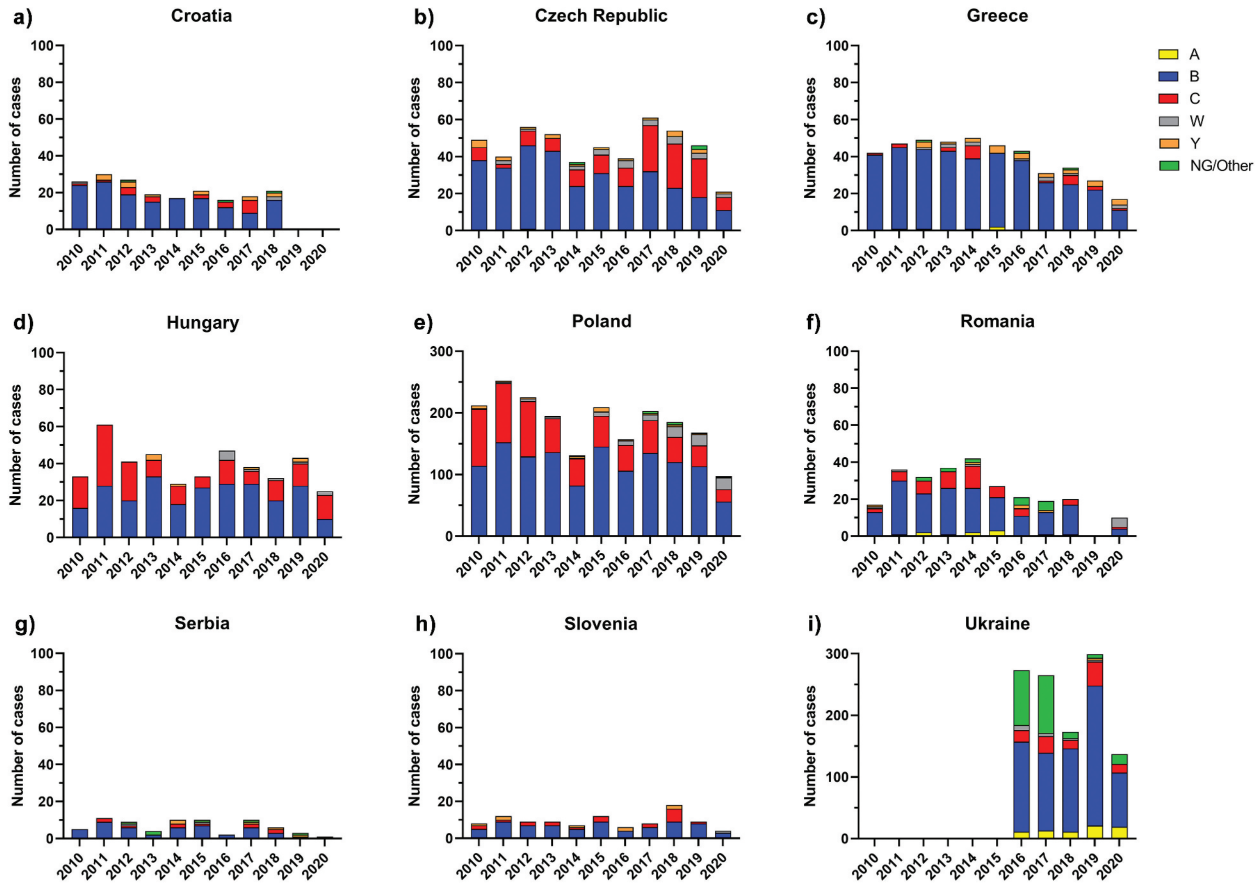

Figure 3. Number of reported cases by serogroups, 2010 to 2020 in selected age groups, as indicated in Table S1.[26] Serbia: In 2019, 1 case in 2 year old, 1 case 10–14, 1 case 15–19, 1 case 40–49, 1 case 50–59 and 2 cases ≥60 years.20 Ukraine: In 2020, 30 cases in up to 1 years, 26 cases in 2–4 years, 18 cases 5–9 years, 11 cases 10–14 years, 3 cases 15–17 years, 30 cases ≥18 years (Ministry of Health of Ukraine Public Health Centre, unpublished). Romania: Data from the National Center of Surveillance and Control of Infectious Diseases, Annual report for 2012,[30] 2014[31] and 2015.[32]

serogroup C appeared to be lower in Greece than in any other country. By contrast, the total number of cases due to serogroup C in Hungary remained high throughout (Figure 3(D)), with cases across all age groups (Table S1). Serogroup B constituted a sizable proportion of case throughout the study period, with a small number of serogroup W cases reported since 2016. An increase in the number of cases due to serogroup W was also observed in Poland, with about a 2-fold increase (from 7 cases to 13 cases) between 2017 and 2018, mostly in infants (Table S1); cases due to serogroup B remained relatively consistent throughout the study period (Figure 3(E)). Romania was one of the few countries that report cases due to serogroup A, although the numbers were small (Figure 3(F)). The numbers of cases due to serogroup B and C declined, with cases due to serogroups W or Y uncommon. Few cases of IMD were reported in Serbia, with serogroup B the predominant serogroup until 2017; with a greater proportion of cases due to serogroups C and Y reported since 2018 (Figure 3(G)). Slovenia also had low numbers of reported cases of IMD throughout the study period, predominantly due to serogroup B and serogroup C to a less extent, with sporadic cases of serogroup Y (Figure 3(H)). In 2018, there was a higher proportion of cases due to serogroup C compared to previous years, but this was not attributed to an outbreak. Cases due to serogroup A were also seen in Ukraine, although most cases reported were due to serogroup B (Figure 3(I)).

Serogroups and age distribution

For the countries with data available from the ECDC Atlas (the Czech Republic, Greece, Hungary, Poland, Romania, and Slovenia), the number of cases due to each of the serogroups B, C, W and Y over the years 2010 to 2020 by age group is shown in Table S1. For these countries, cases due to serogroup B were generally highest in the youngest age groups (<1 year and 1–4 years) and cases due to serogroup C were more frequent in the age groups 1–4 years and 15–24 years. There were few cases due to serogroup W, with these distributed across all four of the examined age groups (<1 year, 1–4 years, 15–24 years and ≥50 years). While the number of cases due to serogroup Y was also low, in the Czech Republic, Greece, and Poland cases appeared most frequently in those in the older age groups.

Vaccination against IMD

Along with variations in IMD epidemiology between the included countries, vaccination policies also differ (Table 5). In most of the countries, MenB and MenACWY vaccines are available; however, despite high vaccine availability,

Table 5. Meningococcal vaccination strategies and recommendations for each included country.

	MenB vaccination	MenC vaccination	MenACWY vaccination
Croatia	High risk groups		High risk groups
Czech Republic	High risk groups (reimbursed), infants (reimbursed since 2020), adolescents in the 15th year of life (reimbursed since 2022)		High risk groups (reimbursed), toddlers in the 2nd year of life (reimbursed since 2020), adolescents in the 15th year of life (reimbursed since 2022)
Greece	Recommended + high risk (not reimbursed) Available privately (since 2014)	12 months (reimbursed since 2005)	Adolescents (reimbursed since 2012), infants >2 months, high risk (reimbursed since 2017)
Hungary	Recommended infants and adolescents (not reimbursed since 2014)	Up to 2 years (reimbursed since 2006)	Recommended adolescents (not reimbursed since 2010)
Poland	Recommended (not reimbursed)	Recommended (not reimbursed)	Recommended (not reimbursed)
Romania	Available privately		High risk Available privately[33]
Serbia			High risk (since March 2016)
Slovenia	Recommended for high risk (reimbursed)		Recommended for high risk (reimbursed)
Ukraine			High risk (not reimbursed) Available privately

reimbursement for specific patient groups is infrequent. MenB vaccination has been reimbursed in the Czech Republic for infants and high-risk groups since 2020, for adolescents (in the 15th year of life) since 2022 and is recommended for high-risk groups only in Croatia, Greece and Slovenia. MenC vaccination has been reimbursed in infants/young children in Hungary since 2006 and in Greece since 2005. The use of quadrivalent MenACWY vaccines has been reimbursed in toddlers (in the 2nd year of life) and high-risk individuals since 2020, and in adolescents (in the 15th year of life) since 2022 in the Czech Republic, adolescents in Greece since 2012, and recommended for high-risk individuals in Croatia, Romania, Serbia (since 2016) and Slovenia. Definitions of high-risk groups by country are reported in Table S2 and the licensed vaccines in each country are shown in Table S3.

Public anti-vaccination sentiments were reported in almost all the countries, the Czech Republic, Poland, Romania, Serbia, Slovenia and Ukraine. Hungary has also reported increased anti-vaccination sentiment since COVID-19. Participants from Romania, Slovenia and Ukraine additionally reported that vaccine hesitancy impacted vaccination against IMD.

Discussion

The incidence of IMD across Europe has been relatively low over the past decade; for the period 2010 to 2020 the average notification rate (confirmed cases, excluding 2020) was 0.65 per 100,000 for countries included in the ECDC Atlas.[26] Of the South-Eastern countries that joined the Meningococcal Advocacy Group, the endemicity of IMD was low, with notification rates (confirmed cases) lower than the European average for almost every country (except Ukraine and Croatia). The age distribution for cases of IMD is well established,[5] and as observed in the included countries, the highest rates were in infants and children, and most countries had another peak in adolescents and young adults.

Although all countries represented in this study align on the case definition of IMD and employ IMD surveillance, there was variation in the surveillance methods used. In general, those countries with a passive surveillance system tended to have lower reporting rates than those with compulsory surveillance, with the exception of Ukraine, which had one of the highest reporting rates throughout the study period. This may be due to incomplete reporting and may include misdiagnoses, leading to underestimation of the true burden of IMD.[34,35] As such, compulsory surveillance or laboratory-based reporting is preferred. Further, access to molecular-based methodologies, such as polymerase chain reaction (PCR) and whole genome sequencing (WGS), is vital to not only to improve diagnostic accuracy and allow timely treatment, but also to inform future vaccination strategies.[36,37] In addition, such techniques can also provide a greater understanding of serogroup-specific burden.[37] Studies incorporating such techniques have highlighted that the incidence and contributing serogroups to IMD vary over time. Previous assessment of IMD in Greece, over the period 2006 to 2016, showed a decrease in incidence over that period, compared to the previous decade and a similar pattern of serogroup distribution to this study.[38] The proportion of cases attributed to serogroup C appears to be lower in Greece than in any other country, which may reflect the fact that MenC vaccination has been reimbursed in infants in this country since 2005, and MenACWY vaccination has been reimbursed in children and adolescents since 2012. By contrast, the total number of cases due to serogroup C remained high in Hungary, despite the fact that since 2006 MenC vaccination of infants has been reimbursed. This may be explained by low vaccine coverage in poorer socioeconomic areas of the country since the vaccine is not mandatory. Incidence of IMD in the Czech Republic has also previously been demonstrated to have decreased since 2000.[39] In the 1990s and early 2000s, serogroup C was the most prevalent serogroup in the Czech Republic; however, serogroup B became predominant in the mid-2000s. Our data show that serogroup B continued to predominate from 2010 until 2017, although its incidence has decreased recently. In a study of bacterial meningitis in children in Romania during the 2000–2002, an unexpectedly high proportion of meningococcal cases were due to serogroup A,[40] whereas in our current report over the period 2010 to 2020, there were only sporadic cases due to serogroup A. This highlights the shifting patterns and trends and illustrates the need for decision makers to understand the current epidemiology of IMD. In this respect, compulsory laboratory-based surveillance should be the guiding principle for informed decision making regarding diagnosis and vaccine policy in these countries.

Similarly, there is a lack of uniformity across Europe with regard to vaccination strategies, with different IMD vaccines inconsistently incorporated into NIPs.[16,41,42] The factors influencing country-specific vaccine strategy are likely multifactorial. For example, the low notification rates of IMD in the South-Eastern Meningococcal Advocacy Group countries will have an impact on the benefit-risk estimates for vaccination programs since the current WHO recommendations for IMD vaccination programs focus on high (>10 cases per 100,000 inhabitants per year) or medium (2–10 cases/100,000) IMD incidence.[41] While non-epidemiology-related factors, such as clinical outcome, cost-effectiveness and disease burden, also interplay into public health decisions for the introduction of vaccination programs, fluctuating epidemiology remains one of the key determinants.[16,41] Consequently, different countries make different decisions about how to implement vaccines against IMD in their NIPs. Notably, there were differences in the definition of high-risk groups between the countries. Some of the risk groups are age-related (infants, toddlers, adolescents and young adults), while others are chronic condition related (immunodeficiency, complement-deficiency, etc.) or life-style related (people entering/living in closed communities, people who are exposed to meningococcal exposure during work, etc.).

As serogroup B was the predominant serogroup across the participating countries, it is unsurprising that many recommend MenB vaccines either for high-risk groups or for other patient groups. However, MenB vaccination has only been reimbursed for infants, high-risk groups, and adolescents (in the 15th year of life) in the Czech Republic since 2020 and 2022, respectively, and there is no indication of an impact of MenB vaccination across the South-Eastern Meningococcal Advocacy Group countries. The introduction of MenB vaccination in the UK for all infants as part of the NIP in 2015 was shown to lead to a reduction of IMD due to serogroup B in the following years,[43] highlighting the potential benefits for MenB vaccination.

Cases of IMD attributed to serogroup A are typically low in Europe. Despite this, serogroup A cases were reported by Romania and Ukraine for some years, although the number of cases was small. These countries may choose to report these cases as a result of high case numbers in Romania and Russia reported around 20 years ago, which may have played a role in the emergence of serogroup A in Greece due to increased immigration.[44,45] It is unsurprising that these cases are also reported in Ukraine as Romania and Ukraine are neighboring countries.

The use of MenC or MenACWY vaccines was also less widespread in the Meningococcal Advocacy Group countries. MenC is recommended and reimbursed in Hungary and Greece; however, MenACWY is only recommended and reimbursed for adolescents ≥11 years of age in Greece, for toddlers (in the 2nd year of life), people in high-risk categories, and adolescents (in the 15th year of life) in the Czech Republic and those at high-risk in Slovenia. Cases due to serogroup C were the second largest contributor to IMD, particularly for the Czech Republic, Hungary and Poland, with a notable increase in cases noted since 2017 in the Czech Republic. In 2017, there was a higher proportion of cases due to serogroup C in Croatia compared to other years; this was not due to an outbreak but could potentially have been imported by tourists. In Greece, prior to 2000, a much larger proportion of cases were due to serogroup C, with a peak in the late 1990s.[14] While the number of cases were already declining in Greece, the introduction of MenC vaccination in 2001 has been proposed to account for the greatly reduced incidence of cases since that time,[14,15] with less than seven cases per year attributed to serogroup C in the period 2010 to 2020. Furthermore, the introduction of the MenACWY vaccine to Greece in 2012 led to the reduced incidence of serogroups W and Y compared with the high incidence experienced by Western European countries between 2013 and 2017.[6] The MenACWY vaccine was only introduced into the NIP in the Czech Republic in 2020, which is too short a period to observe a change in the number of cases, while in Hungary MenC has been used in the NIP since 2006.

The proportion of IMD cases due to serogroup W across Europe as a whole has been increasing over the past decade,[8] with increases particularly observed in countries such as the Netherlands, Norway and Spain.[6] There are concerns regarding the potential for the spread of a MenW hypervirulent strain, which is highlighted by the cases following the Hajj in 2000,[46] the UK between 2010 and 2013,[47] and the World Scout Jamboree in 2015.[48] While numbers of notified cases due to serogroups W and Y are low in the South-Eastern Meningococcal Advocacy Group counties, an increase has been reported in recent years. Hence, careful monitoring and a responsive vaccination strategy is of high importance in order to ensure no further increase in incidence.[49] In contrast, further typing of MenW isolates by WGS in the Czech Republic revealed that many of these cases have a different lineage to much of Europe, with the hypervirulent strain responsible for only a minority of cases[50]; however, MenY isolates were shown to generally follow the trend observed for European isolates.[51] These observations contributed to the Czech Republic's decision to reimburse the MenACWY and MenB vaccine in children from 2020.

Unfortunately, reliable vaccine coverage data are not publicly available in most of the countries assessed. As such, further research is needed to investigate vaccine coverage rates.

Analyses from other countries have also examined recent changes in epidemiology and the role of vaccination in controlling IMD. Analysis of IMD in Italy from 2011 to 2017 identified an increase in cases, probably due to improvements in surveillance and diagnosis. An increase in cases of serogroups C, Y and W was also observed, leading the authors to call for the use of MenACWY over MenC in order to broaden protection.[52] In Malta, which has a relatively high incidence of IMD compared to the rest of Europe, including a recent increase in cases due to serogroups W and Y (2014 to 2017), there has been a call for the introduction of MenACWY and MenB vaccines into the NIP.[53] In France in the period 2011 to 2018, a trend for a decrease in cases due to serogroup

B, alongside an increase in cases due to W and Y, has led to the proposal for the switch from MenC to MenACWY as part of the vaccine schedule and the introduction of MenB infant vaccination.[54] IMD in Germany has also steadily decline over recent years, attributed to decreases in cases due to serogroups B and C following the introduction of vaccines, so that now cases due to serogroups W and Y are more frequent.[55]

Although the most important strategy to be implemented would be vaccine reimbursement, other measures should be also considered. In order to protect vulnerable populations, consideration should be given to including meningococcal vaccination of risk groups in NIPs. Recommendations from scientific communities are compelling tools to support the everyday practice of healthcare practitioners. Furthermore, education of healthcare practitioners on the diagnosis, treatment and prevention of meningococcal disease is an essential strategy against infection. Another strategy would be to promote disease awareness campaigns (preferably from trusted sources such as healthcare authorities and scientific communities) for the general public. Informing parents and patients about risk factors, signs and symptoms, as well as short and long-term effects of the disease and available prevention strategies, can be an effective tool to increase vaccination rates. Additionally, vaccine manufacturers must ensure that adequate amounts of vaccine remain available, especially in the event of an outbreak. Overall, a holistic approach to defeating IMD could be achieved through open and frequent discussions between all key stakeholders (policy, research, science and pharma partners).

The WHO has announced a call to eliminate meningitis by 2030, through tackling the main causes of acute bacterial meningitis: *Neisseria meningitidis, Streptococcus pneumoniae, Haemophilus influenzae* and *Streptococcus agalactiae* (group B).[56] Five pillars have been identified for achieving this goal; prevention and epidemic control, diagnosis and treatment, disease surveillance, support and care for people affected by meningitis, and advocacy and engagement. The advocacy group concluded that in order to fulfill the criteria set by the WHO, a coordinated policy at the regional level of active and passive surveillance is needed, as this would provide accurate epidemiology data of South-Eastern Europe. Furthermore, a regionally coordinated prevention strategy emphasizing the importance of broad-spectrum vaccination (against serogroups A, B, C, W, Y) in the exposed population, especially in high-risk groups, is strongly recommended. Most South-Eastern European countries have recommendations to vaccinate high-risk groups; however, we have seen differences between countries in terms of 'risk group' definition which must be rectified. Age-related risk categories, such as infants and toddlers, are part of NIPs in some countries. However, the inclusion of adolescents in NIPs are scarce, despite the fact that vaccination of this age group should be prioritized as they are the main carriers of the disease, and transmission can be reduced by conjugate vaccines. Further, by vaccinating adolescents, a direct benefit on this age group, as well as an indirect benefit on other age groups, can be gained due to herd immunity.[57] Additionally, the lack of vaccine equity leads to inequality in access and distribution of vaccines in general, which is even more pronounced in the case of IMD, as this disease primarily affects those from lower socio-economic backgrounds.[58,59] Therefore, revision of the countries' reimbursement strategies related to IMD is strongly recommended. Lastly, further data collection in this region in the post-COVID-19 era is warranted, as the number of IMD cases reported across Europe are progressively increasing after removal of social restriction measures, and this increasing trend in IMD cases will likely to be seen in this region in the near future.[60]

Acknowledgments

Editorial assistance with preparation of the manuscript was provided by Nicola Truss PhD, of inScience Communications, Springer Healthcare Ltd, UK, and was funded by Sanofi.

Disclosure statement

Prof. Georgina Tzanakaki reports contract work on behalf of the University of West Attica for Pfizer and GSK and has received personal fees for Advisory Boards from Sanofi, Merck, Pfizer and GSK.

MUDr. Hana Cabrnochová has participated in Advisory Boards for Sanofi, MSD, Pfizer, GSK and Moderna, received lecture fees from Sanofi, AstraZeneca, MSD, Pfizer, GSK and Moderna, and has participated in non-monteary performance for Sanofi and Pfizer.

Dr Snežana Delić has no conflicts of interest to disclose.

Dr. Anca Draganescu has been the Principal Investigator in a meningococcal vaccine trial by Sanofi outside the scope of the submitted work, and has participated in an Advisory Board for Pfizer and Sanofi outside of the submitted work.

Dr. Anna Hilfanova reports speakers fee from LLC Sanofi Ukraine and Pfizer Ukraine.

Dr. Beáta Onozó receieved funding for travel to Espid2022 from Sanofi.

Dr. Marko Pokorn has recieved honoraria for lectures from Pfizer, Sanofi and MSD.

Prof. Anna Skoczyńska has received unrestricted grants from Pfizer paid directly to her home institution, non-financial support from Pfizer, and personal fees (for being on an advisory board and speaker fees) from Pfizer, and Sanofi Pasteur.

Prof. Goran Tešović has received grants and personal fees from AstraZeneca, GlaxoSmithKine, Merck, Sharp and Dohme, Pfizer and Sanofi outside the submitted work.

Funding

This work was funded by Sanofi.

Author Contributions

All authors contributed to data acquisition, and interpretation of the data. All authors critically revised the manuscript, gave final approvals, and are accountable for its accuracy and integrity.

Data Availability Statement

The data that support the findings of this study are included in the study/ or can be requested from the corresponding author upon reasonable request.

References

1. Nadel S, Ninis N. Invasive meningococcal disease in the vaccine Era. Front Pediatr. 2018;6:321. doi:10.3389/fped.2018.00321.
2. Christensen H, May M, Bowen L, Hickman M, Trotter CL. Meningococcal carriage by age: a systematic review and meta-analysis. Lancet Infect Dis. 2010;10(12):853–61. doi:10.1016/S1473-3099(10)70251-6.
3. European Centre for Disease Prevention and Control. Factsheet about meningococcal disease. European Centre For Disease Prevention And Control; 2019 [accessed 2023 Dec 5]. https://www.ecdc.europa.eu/en/meningococcal.disease/factsheet.
4. Pace D, Pollard AJ. Meningococcal disease: clinical presentation and sequelae. Vaccine. 2012;30(Suppl 2):B3–9. doi:10.1016/j.vaccine.2011.12.062.
5. European Centre for Disease Prevention and Control. Invasive meningococcal disease annual epidemiological report for 2017. Stockholm: European Centre for Disease Prevention and Control; 2019 [accessed 2023 Dec 5]. https://www.ecdc.europa.eu/sites/default/files/documents/AERfor2017-invasive-meningococcal-disease.pdf.
6. Krone M, Gray S, Abad R, Skoczyńska A, Stefanelli P, van der Ende A, Tzanakaki G, Mölling P, João Simões M, Křížová P, et al. Increase of invasive meningococcal serogroup W disease in Europe, 2013 to 2017. Eur Surveill. 2019;24:1800245. doi:10.2807/1560-7917.ES.2019.24.14.1800245.
7. Whittaker R, Dias JG, Ramliden M, Ködmön C, Economopoulou A, Beer N, Pastore Celentano L. The epidemiology of invasive meningococcal disease in EU/EEA countries, 2004–2014. Vaccine. 2017;35:2034–41. doi:10.1016/j.vaccine.2017.03.007.
8. Nuttens C, Findlow J, Balmer P, Swerdlow DL. Tin Tin Htar M. evolution of invasive meningococcal disease epidemiology in Europe, 2008 to 2017. Eur Surveill. 2022;27:2002075. doi:10.2807/1560-7917.ES.2022.27.3.2002075.
9. Larrauri A, Cano R, García M, de Mateo S. Impact and effectiveness of meningococcal C conjugate vaccine following its introduction in Spain. Vaccine. 2005;23(32):4097–100. doi:10.1016/j.vaccine.2005.03.045.
10. Trotter CL, Andrews NJ, Kaczmarski EB, Miller E, Ramsay ME. Effectiveness of meningococcal serogroup C conjugate vaccine 4 years after introduction. Lancet Child Adolesc Health. 2004;364:365–7. doi:10.1016/S0140-6736(04)16725-1.
11. Vuocolo S, Balmer P, Gruber WC, Jansen KU, Anderson AS, Perez JL, York LJ. Vaccination strategies for the prevention of meningococcal disease. Hum Vaccin Immunother. 2018;14(5):1203–15. doi:10.1080/21645515.2018.1451287.
12. Mbaeyi S, Pondo T, Blain A, Yankey D, Potts C, Cohn A, Hariri S, Shang N, MacNeil JR. Incidence of meningococcal disease before and after implementation of quadrivalent meningococcal conjugate vaccine in the United States. JAMA Pediatr. 2020;174(9):843–51. doi:10.1001/jamapediatrics.2020.1990.
13. Campbell H, Andrews N, Parikh SR, White J, Edelstein M, Bai X, Lucidarme J, Borrow R, Ramsay ME, Ladhani SN. Impact of an adolescent meningococcal ACWY immunisation programme to control a national outbreak of group W meningococcal disease in England: a national surveillance and modelling study. Lancet Child Adolesc Health. 2022;6:96–105. doi:10.1016/S2352-4642(21)00335-7.
14. Kafetzis DA, Stamboulidis KN, Tzanakaki G, Kremastinou JK, Skevaki CL, Konstantopoulos A, Tsolia M. Meningococcal group C disease in Greece during 1993–2006: the impact of an unofficial single-dose vaccination scheme adopted by most paediatricians. Clin Microbiol Infect. 2007;13(5):550–2. doi:10.1111/j.1469-0691.2007.01704.x.
15. Ladomenou F, Tzanakaki G, Kolyva S, Katsarakis I, Maraki S, Galanakis E. Conjugate vaccines dramatically reshaped the epidemiology of bacterial meningitis in a well-defined child population. Acta Paediatr. 2020;109(2):368–74. doi:10.1111/apa.14957.
16. Martinón-Torres F, Taha M-K, Knuf M, Abbing-Karahagopian V, Pellegrini M, Bekkat-Berkani R, Abitbol V. Evolving strategies for meningococcal vaccination in Europe: overview and key determinants for current and future considerations. Pathog Global Health. 2022;116:85–98. doi:10.1080/20477724.2021.1972663.
17. Pizza M, Bekkat-Berkani R, Rappuoli R. Vaccines against meningococcal diseases. Microorganisms. 2020;8(10):1521. doi:10.3390/microorganisms8101521.
18. Bröker M, Berti F, Costantino P. Factors contributing to the immunogenicity of meningococcal conjugate vaccines. Hum Vaccines Immunother. 2016;12:1808–24. doi:10.1080/21645515.2016.1153206.
19. Croatian Institute of Public Health. Croatian health and statistical yearbook for 2019. 2019 [accessed 2022 May 6]. https://www.hzjz.hr/hrvatski-zdravstveno-statisticki-ljetopis/hrvatski-zdravstveno-statisticki-ljetopis-za-2019/.
20. Institute for Public Health of Serbia. Health and statistical yearbook of the republic of Serbia. 2020 [accessed 2022 May 6]. https://www.batut.org.rs/index.php?content=77.
21. Public Health Center of the Ministry of Health of Ukraine. Infectious disease in the population of Ukraine. 2022 [accessed 2022 May 6]. https://phc.org.ua/kontrol-zakhvoryuvan/inshi-infekciyni-zakhvoryuvannya/infekciyna-zakhvoryuvanist-naselennya-ukraini .
22. National Institute of Public Health National Center for Surveillance and Control of Communicable Diseases. Analysis of the evolution of communicable diseases under surveillance. 2018 [accessed 2022 May 6]. http://www.cnscbt.ro/index.php/rapoarte-anuale/1302-analiza-bolilor-transmisibile-aflate-in-supraveghere-raport-pentru-anul-2018/file.
23. Koroun National Reference Center for the Diagnostics of Bacterial Infections of the Central Nervous System. Epidemiological data. 2021 [accessed 2023 May 12]. http://koroun.nil.gov.pl/dane-epidemiologiczne/.
24. Krizova P, Honskus M, Okonji Z, Musilek M, Kozakova J. Analysis of epidemiological and molecular data from invasive meningococcal disease surveillance in the Czech Republic, 1993–2020. Epidemiol Mikrobiol Imunol. 2022;71:148–60.
25. National Center of Surveillance and Control of Infectious Diseases. Sistem de supraveghere si control in boala meningococica. 2016 [accessed 2023 February 17]. https://www.cnscbt.ro/index.php/metodologii/boala-meningococica/479-metodologie-supraveghere-boala-meningococica/file
26. European Centre for Disease Prevention and Control. Surveillance atlas of infectious diseases. Stockholm; 2022 [accessed 2022 May 31]. https://atlas.ecdc.europa.eu/public/index.aspx.
27. European Centre for Disease Prevention and Control. EU Case Definitions. 2023 [accessed 2023 May 12]. https://www.ecdc.europa.eu/en/all-topics/eu-case-definitions.
28. World Health Organization. Invasive meningococcal outbreak toolbox. 2022 [accessed 2023 December 5]. https://www.who.int/emergencies/outbreak-toolkit/disease-outbreak-toolboxes/invasive-meningoccocal-outbreak-toolbox.
29. World Health Organization. European health information gateway. 2023 [accessed 2023 June 1]. https://gateway.euro.who.int/en/hfa-explorer/#ViBHUF2xyX.
30. National Center of Surveillance and Control of Infectious Diseases. Analiza evolutiei bolilor transmisibile aflate in supraveghere, Raport pentru anul 2012. 2012 [accessed 2023 February 17]. https://www.cnscbt.ro/index.php/rapoarte-anuale/546-analiza-evolutiei-bolilor-transmisibile-aflate-in-supraveghere-raport-pentru-anul-2012.
31. Diseases NCoSaCoI. Analiza evolutiei bolilor transmisibile aflate in supraveghere, Raport pentru anul 2014. 2014 [accessed 2023 February 17]. https://www.cnscbt.ro/index.php/rapoarte-anuale/548-analiza-evolutiei-bolilor-transmisibile-aflate-in-supraveghere-raport-pentru-anul-2014.
32. Diseases NCoSaCoI. Analiza evolutiei bolilor transmisibile aflate in supraveghere, Raport pentru anul 2015. 2015 [accessed 2023 February 17]. https://www.cnscbt.ro/index.php/rapoarte-anuale/549-analiza-evolutiei-bolilor-transmisibile-aflate-in-supraveghere-raport-pentru-anul-2015.

33. Azoicăi D, Rădulescu A, Pițigoi D, Popovici F. Recomandări de vaccinare a pacienților cu imunodeficiențe de diverse cauze. Editie revizuita si adaugita. Ed. 2. 2020 [accessed 2023 December 5]. https://lege5.ro/gratuit/gyzdcnbugm4q/ghidul-recomandari-de-vaccinare-a-pacientilor-cu-imunodeficiente-de-diverse-cauze-din-05042021.
34. Gómez JA, Wetzler Malbrán P, Vidal G, Seoane M, Giglio ND. Estimation of the real burden of invasive meningococcal disease in Argentina. Epidemiol Infect. 2019;147:e311–e. doi:10.1017/S0950268819002024.
35. Gilbert R, Cliffe SJ. Public health surveillance. Public Health Intelligence. 2016; 27:91–110.
36. Azzari C, Nieddu F, Moriondo M, Indolfi G, Canessa C, Ricci S, Bianchi L, Serranti D, Poggi GM, Resti M. Underestimation of invasive meningococcal disease in Italy. Emerg Infect Dis. 2016;22(3):469–75. doi:10.3201/eid2203.150928.
37. Peterson ME, Li Y, Bita A, Moureau A, Nair H, Kyaw MH, Abad R, Bailey F, Garcia IF, Decheva A, et al. Meningococcal serogroups and surveillance: a systematic review and survey. J Glob Health. 2019;9:010409. doi:10.7189/jogh.09.010409.
38. Flountzi A, Georgakopoulou T, Balasegaram S, Kesanopoulos K, Xirogianni A, Papandreou A, Tzanakaki G, Anastasia A, Athina A, Genovefa C, et al. Epidemiology of invasive meningococcal disease in Greece, 2006–2016. Eur J Clin Microbiol Infect Dis. 2019;38:2197–203. doi:10.1007/s10096-019-03668-y.
39. Jandova Z, Musilek M, Vackova Z, Kozakova J, Krizova P, Hozbor DF. Serogroup and clonal characterization of Czech invasive Neisseria meningitidis strains isolated from 1971 to 2015. PLoS One. 2016;11(12):e0167762. doi:10.1371/journal.pone.0167762.
40. Luca V, Gessner BD, Luca C, Turcu T, Rugina S, Rugina C, Ilie M, Novakova E, Vlasich C. Incidence and etiological agents of bacterial meningitis among children <5 years of age in two districts of Romania. Eur J Clin Microbiol Infect Dis. 2004;23:523–8. doi:10.1007/s10096-004-1169-6.
41. Pinto Cardoso G, Lagree-Chastan M, Caseris M, Gaudelus J, Haas H, Leroy JP, Bakhache P, Pujol JF, Werner A, Dommergues MA, et al. Overview of meningococcal epidemiology and national immunization programs in children and adolescents in 8 Western European countries. Front Pediatr. 2022;10:1000657. doi:10.3389/fped.2022.1000657.
42. Bai X, Borrow R, Bukovski S, Caugant DA, Culic D, Delic S, Dinleyici EC, Eloshvili M, Erdősi T, Galajeva J, et al. Prevention and control of meningococcal disease: updates from the global meningococcal initiative in Eastern Europe. J Infect. 2019;79(6):528–41. doi:10.1016/j.jinf.2019.10.018.
43. Ladhani SN, Andrews N, Parikh SR, Campbell H, White J, Edelstein M, Bai X, Lucidarme J, Borrow R, Ramsay ME. Vaccination of infants with meningococcal group B vaccine (4CMenB) in England. N Engl J Med. 2020;382(4):309–17. doi:10.1056/NEJMoa1901229.
44. Tsolia MN, Theodoridou M, Tzanakaki G, Vlachou V, Mostrou G, Stripeli F, Kalabalikis P, Pangalis A, Kafetzis D, Kremastinou J. et al. Invasive meningococcal disease in children in Greece: comparison of serogroup a disease with disease caused by other serogroups. Eur J Clin Microbiol Infect Dis. 2006;25(7):449–56. doi:10.1007/s10096-006-0155-6.
45. Kremastinou J, Tzanakaki G, Velonakis E, Voyiatzi A, Nickolaou A, Elton RA, Weir D, Blackwell C. Carriage of Neisseria meningitidis and Neisseria lactamica among ethnic Greek school children from Russian immigrant families in Athens. FEMS Immunol Med Microbiol. 1999;23(1):13–20. doi:10.1111/j.1574-695X.1999.tb01711.x.
46. Taha M-K, Achtman M, Alonso J-M, Greenwood B, Ramsay M, Fox A, Gray S, Kaczmarski E. Serogroup W135 meningococcal disease in Hajj pilgrims. Lancet. 2000;356(9248):2159. doi:10.1016/S0140-6736(00)03502-9.
47. Ladhani SN, Beebeejaun K, Lucidarme J, Campbell H, Gray S, Kaczmarski E, Ramsay ME, Borrow R. Increase in endemic Neisseria meningitidis capsular group W sequence type 11 complex associated with severe invasive disease in England and Wales. Clin Infect Dis. 2015;60(4):578–85. doi:10.1093/cid/ciu881.
48. Smith-Palmer A, Oates K, Webster D, Taylor S, Scott KJ, Smith G, Parcell B, Lindstrand A, Wallensten A, Fredlund H, et al. Outbreak of Neisseria meningitidis capsular group W among scouts returning from the World Scout Jamboree, Japan, 2015. Eur Surveill. 2016;21:30392. doi:10.2807/1560-7917.ES.2016.21.45.30392.
49. Booy R, Gentile A, Nissen M, Whelan J, Abitbol V. Recent changes in the epidemiology of Neisseria meningitidis serogroup W across the world, current vaccination policy choices and possible future strategies. Hum Vaccin Immunother. 2019;15(2):470–80. doi:10.1080/21645515.2018.1532248.
50. Honskus M, Okonji Z, Musilek M, Kozakova J, Krizova P, Berbers GA. Whole genome sequencing of Neisseria meningitidis W isolates from the Czech Republic recovered in 1984–2017. PLoS One. 2018;13(9):e0199652. doi:10.1371/journal.pone.0199652.
51. Honskus M, Okonji Z, Musilek M, Krizova P, Lin B. Whole genome sequencing of Neisseria meningitidis Y isolates collected in the Czech Republic in 1993–2018. PloS ONE. 2022;17(3):e0265066. doi:10.1371/journal.pone.0265066.
52. Igidbashian S, Bertizzolo L, Tognetto A, Azzari C, Bonanni P, Castiglia P, Conversano M, Esposito S, Gabutti G, Icardi G, et al. Invasive meningococcal disease in Italy: from analysis of national data to an evidence-based vaccination strategy. J Prev Med Hyg. 2020;61:E152–e61. doi:10.15167/2421-4248/jpmh2020.61.2.1589.
53. Pace D, Gauci C, Barbara C. The epidemiology of invasive meningococcal disease and the utility of vaccination in Malta. Eur J Clin Microbiol Infect Dis. 2020;39(10):1885–97. doi:10.1007/s10096-020-03914-8.
54. Taha M-K, Gaudelus J, Deghmane A-E, Caron F. Recent changes of invasive meningococcal disease in France: arguments to revise the vaccination strategy in view of those of other countries. Hum Vaccin Immunother. 2020;16(10):2518–23. doi:10.1080/21645515.2020.1729030.
55. Gruhn S, Witte J, Greiner W, Damm O, Dietzsch M, Kramer R, Knuf M. Epidemiology and economic burden of meningococcal disease in Germany: a systematic review. Vaccine. 2022;40(13):1932–47. doi:10.1016/j.vaccine.2022.02.043.
56. World Health Organization. Defeating meningitis by 2030: a global road map. World Health Organization; 2021 [accessed 2023 December 5]. https://apps.who.int/iris/rest/bitstreams/1352955/retrieve
57. Burman C, Serra L, Nuttens C, Presa J, Balmer P, York L. Meningococcal disease in adolescents and young adults: a review of the rationale for prevention through vaccination. Hum Vac Immunother. 2019;15:459–69. doi:10.1080/21645515.2018.1528831 .
58. Masaquel C, Schley K, Wright K, Mauskopf J, Parrish RA, Presa JV, Hewlett D Jr. The impact of social determinants of health on meningococcal vaccination awareness, delivery, and coverage in adolescents and young adults in the United States: a systematic review. Vaccines. 2023;11(2):11. doi:10.3390/vaccines11020256.
59. Taha MK, Martinon-Torres F, Köllges R, Bonanni P, Safadi MAP, Booy R, Smith V, Garcia S, Bekkat-Berkani R, Abitbol V. Equity in vaccination policies to overcome social deprivation as a risk factor for invasive meningococcal disease. Expert Rev Vaccines. 2022;21(5):659–74. doi:10.1080/14760584.2022.2052048.
60. Clark SA, Campbell H, Ribeiro S, Bertran M, Walsh L, Walker A, Willerton L, Lekshmi A, Bai X, Lucidarme J, et al. Epidemiological and strain characteristics of invasive meningococcal disease prior to, during and after COVID-19 pandemic restrictions in England. J Infect. 2023;87(5):385–91. doi:10.1016/j.jinf.2023.09.002.