

Invasive Meningococcal Disease (IMD) in Older Adults – Current Perspectives and Call for Action

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BACKGROUND

- Invasive meningococcal disease (IMD) caused by *Neisseria meningitidis* is an important global public health concern and is usually associated with high mortality and often life-long sequelae in survivors
- Although meningitis and/or septicemia are the most well-known forms of IMD, atypical presentations are increasingly observed, including meningococcal pneumonia, acute gastrointestinal presentations, and septic arthritis^{1,2}
- Twelve meningococcal capsular groups have been identified and most of the meningococcal infections are due to six serogroups (A, B, C, W, Y and X)³
- Global epidemiological data shows that these capsular subgroups are variably predominant in different geographical regions and can fluctuate over time and with age⁴
- Routine child and adolescent immunisation programmes have substantially reduced IMD incidences and burden in targeted populations
- Recently the proportion and number of IMD cases have increased in older population (≥ 60 years of age) due to the absence of specific recommendations for prevention⁵

METHODS

- In this context, an international multidisciplinary expert working group (EWG) was established to evaluate the existing knowledge on meningococcal disease in older adults and discuss evidence gaps
- The EWG comprised seven members, each specialists in infectious disease epidemiology and clinical management or within broader areas of immunisation policy from across Europe, the United States and the Middle East. An eighth member was a patient advocate (from the Confederation of Meningitis Organisations)
- The proceedings from these initial meetings are reflected in this poster

EXPERT WORKING GROUP PROCEEDINGS

- ### Challenges of IMD in Older Adults
- IMD is typically associated with clinical manifestation of meningitis and/or septicemia. Meningococcal septicemia is associated with higher case fatality rates of up to 40%, with survivors suffering from rare but severe physical sequelae ranging from skin necrosis and subsequent scarring requiring skin grafting to limb amputation⁶
 - Although meningococcal meningitis is associated with lower case fatality, severe long-term neurological sequelae (sensorineural deafness, visual impairment, epilepsy, cognitive impairment, cerebral palsy) and psychological sequelae (depressive and anxiety disorders) are observed with survivors. Physical sequelae range from skin necrosis and subsequent scarring that requires skin grafting to limb amputations (following septicemia)⁶. This may result in potential loss of autonomy ("dependency")
 - Atypical presentation of IMD is common in older adults, particularly bacteremic meningococcal pneumonia (approximately 25% cases), which poses a challenge in the diagnosis of IMD in this age group⁷
 - In older adults, IMD due to hypervirulent MenW and MenY strains is more prevalent and typically associated with atypical presentations, including pneumonia and septic arthritis^{2,8,11}
 - Mortality is the highest (20%) for IMD in older adults compared to other age groups¹²

- ### IMD Epidemiology in Older Adults
- Currently, ~25% of the overall IMD burden in several countries is found in older adults¹³⁻¹⁵
 - Additionally, mortality is higher in the elderly population, with case fatality rates (CFRs) of 30% reported in adults >75 years of age¹⁶. Data from the European Centre for Disease Prevention and Control (ECDC) show CFR rates of up to 17.6% in individuals ≥ 50 years in 2019¹⁷ (Figure 1)
 - A marked rebound in IMD due to W and Y serogroups in adults was reported, particularly in those aged ≥65 years, which accounted for 17% of all IMD cases¹⁸
 - Prior to the Covid-19 pandemic, a significant proportion of all cases in adults ≥50 years were due to serogroups W (21–30%) and Y (20–22%)
 - In 2019, the proportion of cases in older adults aged ≥65 years ranged from 17.5% in Italy to 30.1% in Spain¹⁷ (Figure 2)
 - A sharp decline in IMD cases was observed in most countries and across most age-groups as a result of widespread social and individual restrictions to mitigate the impact of COVID-19 pandemic^{19, 20} (Figure 3). However, despite reduced case numbers, IMD in older adults persisted, often with atypical (respiratory) presentations

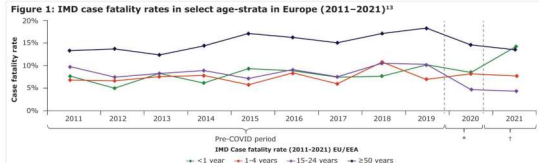


Figure 1: IMD case fatality rates in select age-strata in Europe (2011–2021)¹⁹

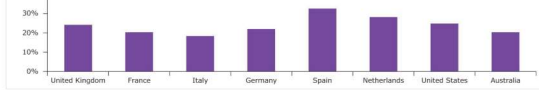
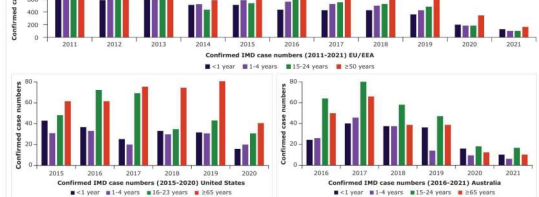


Figure 2: The proportion of confirmed IMD cases due to any serogroups occurring in older adults (≥65 years) in select countries in 2019¹⁷



- ### Economic Aspects of IMD in Older Adults
- Infectious diseases in older adults pose a substantial clinical and economic burden. However, some of them, including meningococcal diseases are very preventable²¹
 - Economic burden of IMD in older adults is higher than other forms of bacterial meningitis²² (Figure 4)
 - Cost estimates for the acute disease phase of IMD in patients ≥60 years were between €13,365–14,965 in France, and the index hospitalisation costs increased significantly with age²³ (Figure 5)
 - Management of complications during the initial phase and of subsequent sequelae carries additional direct costs²⁴

Figure 4: The mean cost per capita of the index hospitalisation of IMD increases with age (p<0.001): The highest among ≥60 years in France²³

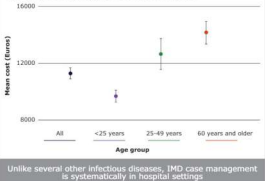
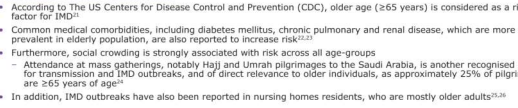


Figure 5: Per capita costs in the year following the index hospitalisation of IMD



- ### Risk Factors for IMD in Older Adults
- Access to the US Centers for Disease Control and Prevention (CDC), older age (≥65 years) is considered as a risk factor for IMD²¹
 - Common medical comorbidities, including diabetes mellitus, chronic pulmonary and renal disease, which are more prevalent in elderly population, are also reported to increase risk^{22,25}
 - Furthermore, social crowding is strongly associated with risk across all age-groups
 - Attendance at mass gatherings, notably Hajj and Umrah pilgrimages to the Saudi Arabia, is another recognised risk for transmission and IMD outbreaks, and of direct relevance to older individuals, as approximately 25% of pilgrims are ≥65 years of age²⁶
 - In addition, IMD outbreaks have also been reported in nursing homes residents, who are mostly older adults^{25,26}

- ### Importance of Considering Older Adults
- According to the WHO, well-being encompasses quality of life and the ability of people and societies to contribute to the world with a sense of meaning and purpose. Healthy ageing is defined as "the process of developing and maintaining the functional ability that enables wellbeing in older age". This implies limitation of any factor that may potentially increase dependency of older adults^{27,28}
 - As a result of established global health measures and decreasing birth rates, this has led to increased life expectancy and significant ageing of the world population. In the present scenario, individuals ≥65 years of age constitute 19% of the population in Europe and North America. Globally, a similar pattern is being observed (increase from 10% at present to 16% by 2050)^{29,30}
 - Presently, lifelong vaccination approach is being increasingly adopted by several countries to accommodate all age groups in the vaccination programmes³¹
 - In this approach, individuals across all age-groups are offered all appropriate vaccinations (including catch-up vaccination when prior scheduled immunisation was missed, and regular boosters). For older adults, although it varies across specific countries, this approach includes immunisation against influenza, pneumococcal infection, pertussis and herpes zoster, in addition to continued SARS-CoV-2 vaccination

Meningococcal Vaccination Strategy Across Age Groups

- Most countries offer infant, toddler and/or adolescent immunization, although specific vaccines, target age-groups, and schedules vary widely across countries
 - Routine meningococcal immunisation in adults is not recommended in any national programmes except those considered at high-risk
- A broad range of meningococcal vaccines are available. While older conjugated polysaccharide vaccines remain in use in some settings (e.g., China and in some countries for use by Hajj/Umrah pilgrims), countries with established programmes use protein-conjugated vaccines in monovalent and quadrivalent forms (MenA, MenC, and MenACWY) raise awareness and increase a better acknowledgement of IMD

- Conjugated vaccines induce T-cell dependent responses, generating a greater immune improved response to booster doses³². In addition, conjugated vaccines reduce *N. meningitidis* carriage and onward transmission, providing indirect "herd" protection across the broader population, including those age-groups not targeted in routine immunisation programmes³³

Call For Action

- There is a need to raise awareness of IMD, within and across medical specialties involved in the care of older adults, in order to communicate greater understanding and improve clinical outcomes
- While most systems report age-demographics, greater focus on IMD in older age-strata can help determine which older individuals are at greatest risk (and may benefit most from vaccination)
- A clearer understanding of any indirect "herd" protection for older adults gained from existing immunisation programmes is important
- In addition, increased education on available vaccines, regardless of reimbursement considerations, is essential to inform patient choices

CONCLUSIONS

- Older adults experience a high burden of IMD cases
 - This burden directly correlates with the elevated number of cases, case fatality rates (CFRs), increasing size (percentages and volume) of older adults, and specificity of serogroups W and Y
- Currently, no specific global recommendation is available against prevention of IMD in adults
- Standardized case definition and diagnostic protocols (to capture all IMD atypical presentations) are required to ensure precise estimation of disease burden
- Global vaccination policies should be balanced and maintain parity between all age groups
- While deciding the national immunisation policies, it is important to understand the cost burden of IMD in older adults, and of the broader impact on survivors in terms of sequelae, loss of autonomy and quality of life (QoL)

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