

OPPORTUNITY FOR HEALTHY AGEING: LESSENING THE BURDEN OF ADULT PNEUMOCOCCAL DISEASE IN CENTRAL AND EASTERN EUROPE, AND ISRAEL

REVIEW AND ANALYSIS OF THE PROBLEM

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SUMMARY

The population of the Region (Central Europe, Eastern Europe, and Israel) is ageing, necessitating preventative programmes to maintain a healthy and active lifestyle in older age groups. Invasive pneumococcal disease (including bacteremic pneumonia, bacteremia without a focus, and meningitis) has higher incidence, morbidity and mortality in older adults and is a substantial public health burden in the ageing population.

Surveillance in the Region establishes a significant burden in older adults of invasive pneumococcal disease (IPD), which still appears to be under-estimated as compared with other countries, and this warrants an improvement in surveillance systems. The largest proportion of IPD in adults is bacteremic pneumonia. Community-acquired pneumonia (CAP), largely attributable to *S. pneumoniae*, can be bacteremic or non-bacteremic; the non-bacteremic forms of CAP also represent a significant burden in the Region.

The burden of pneumococcal disease can be reduced with programmes of effective vaccination. Recommendations on pneumococcal vaccination in adults vary widely across the Region. The main barrier to implementation of vaccination programmes is low awareness among healthcare professionals on serious health consequences of adult pneumococcal disease and of vaccination options.

The Expert Panel calls on healthcare providers in the Region to improve pneumococcal surveillance, optimize and disseminate recommendations for adult vaccination, and support awareness and education programmes about adult pneumococcal disease.

Key words: invasive pneumococcal disease (IPD), community-acquired pneumonia (CAP), Central and Eastern Europe (CEE), Israel, pneumococcal vaccines, vaccination, elderly adults

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Healthy Ageing: a Growing Public Health Issue

The proportion of adults in the Region (Central Europe, Eastern Europe, and Israel) over the age of 50 years has nearly doubled

in the past six decades (Fig. 1) and is forecasted to double again by 2040 (1). As a consequence, the Region will increasingly face the issue of “healthy ageing” (i.e. maintaining the general level of health, quality of life and active lifestyle in an ageing population).

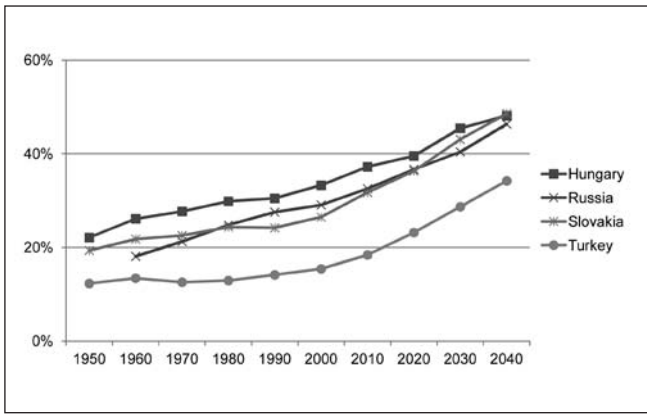


Fig. 1. Proportion of population over 50 years of age is growing in the countries of the Region. National census data from 1950 to 2000 (Hungary (43, 44), Turkey (45)) or 2010 (Russia (46), Slovakia (47)). Country forecast through 2040 by US Census Bureau (44).

Public health should target preventable diseases associated with older age and related co-morbidities (2) by programmes ranging from already established initiatives for reduction of cardiovascular risks to currently less utilized options for adult vaccination.

Adult Vaccination – the Neglected Solution?

The public health value of prevention through vaccination (i.e. lowering disease incidence in the target population) is well documented in paediatric populations and likewise in adults. The value can expand beyond direct effects like an impact on the incidence of invasive pneumococcal disease (IPD) cases in the target population. For instance, successful pneumococcal vaccination in paediatric programmes has associated individual and economic benefits, such as an impact on the patterns of antibiotic therapy, thus reducing the number of treatment failures linked to antibiotic resistance (3). In adults, pneumococcal vaccination, in addition to its protective effect against pneumococcal disease, may prevent pneumonia-associated cardiovascular events (4) and, when co-administered with influenza vaccina-

tion, may reduce the risk of myocardial infarction and stroke in the elderly (5).

However, the preventative value of vaccination in adults is under-recognised. Healthcare providers traditionally associate vaccination programmes with paediatric practice. “Vaccination for kids” is the current paradigm that needs to be transformed to address the substantial but not fully appreciated public health needs of the ageing population. Preventive potential of adult pneumococcal vaccination is particularly neglected in the Region, due to low awareness of the burden of pneumococcal disease in adults and under-recognition of the potential of preventive measures (6).

Pneumococcal Disease: a Major Preventable Health Burden

S. pneumoniae causes invasive and non-invasive pneumococcal diseases. IPD includes bacteremic pneumonia, bacteremia without a focus, and meningitis. The majority of IPD cases in adults presents as bacteremic pneumonia (7–11). The incidence, morbidity and mortality of IPD are especially elevated in older adults and present a significant burden to individuals and to society (Fig. 2). Among the other risk factors for pneumococcal disease such as co-morbidities, residence in a long-term care facility or smoking, age is an independent risk factor. The most prevalent form of pneumococcal disease in older adults is community-acquired pneumonia (CAP), which presents a substantial clinical and economic burden (12–15). Moreover, *S. pneumoniae* is a major contributor to exacerbations of COPD (16), the disease burden in the Region is at least comparable to, and may even exceed, that of CAP (13, 17). Therefore, the burden of pneumococcal disease in adults is immense.

The Burden of IPD – How Much Remains Hidden?

Diagnosis of IPD (via positive blood or cerebrospinal fluid culture) requires laboratory analysis that cannot be established without adequate infrastructure and resources. Therefore, reliable epidemiological data on IPD depend on the quality of surveillance systems and in particular on collaboration between laboratory and clinical facilities. Diverse surveillance systems in many countries

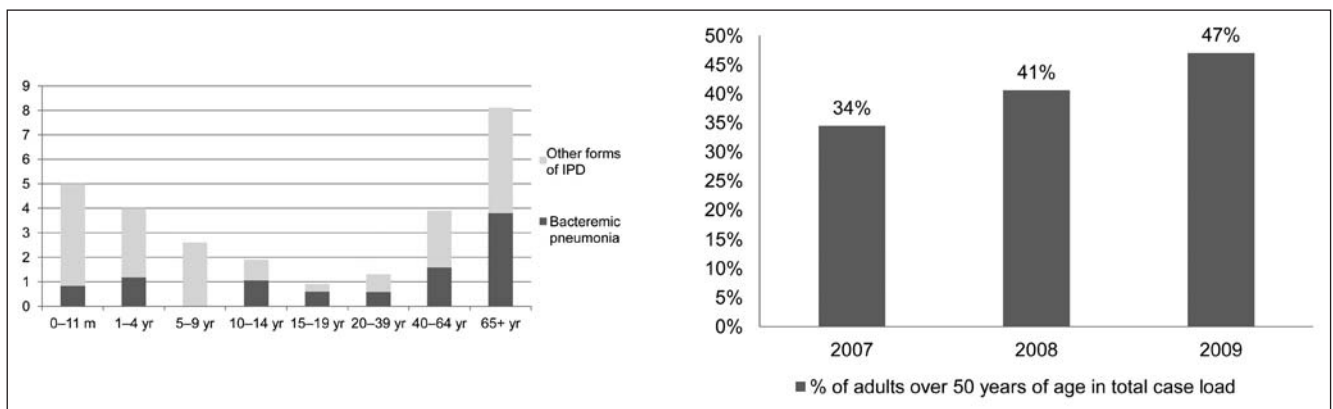


Fig. 2. Older adults have a high incidence of IPD and represent a growing share of national IPD burden. Left panel: IPD incidence (per 100,000) by age group, Czech Republic, 2009 (10). Right panel: Share of adults over 50 (%) in IPD case load, Poland, 2007–2009 (11).

of the Region merit improvement (18); in particular, systems of active surveillance are under-represented. In many cases, blood culture is not performed at all, or performed at later stage, or the results are not reported correctly. Furthermore, national compulsory surveillance for IPD does not exist in several countries. A specific issue in the Region is the lack of continuity in the funding of such systems. Surveillance systems in some countries, such as Poland and the Czech Republic, have recently been improved, and in 2009 the reported figures for the burden of IPD in adults in these countries were greater than in previous years, possibly due to these improvements (10, 11) (Fig. 2). The largest age-specific IPD mortality rate values were 44% (55–64 years) and 59% (65+ years) in Poland (10, 11). In the Czech Republic, the 65+ years age group had the greatest age-related IPD incidence of 8.8 per 100,000 population per year (and it was 3.3 per 100,000 for age group 40–64 years) (10). By contrast, these reported IPD incidence rates are substantially lower than the 51.9 and 18.1 per 100,000 in the same age groups in Israel for pneumococcal bacteremia (9). Comparisons with current data from other European countries also suggest that IPD may still be dramatically under-reported in the Region, especially in adults in the 50+ years age group (19). Publications from the Region also report a significant burden of adult IPD in terms of healthcare costs and resource utilization (15, 20, 21).

The Burden of CAP – Are Antibiotics an Easy Cure?

A significant proportion of CAP is attributable to *S. pneumoniae*. In multiple European studies investigating the aetiology of CAP, *S. pneumoniae* was the most frequently identified pathogen (12, 22) regardless of age group, clinical severity or country. *S. pneumoniae* is also the most frequently identified cause of bacteremia in CAP (23). Aetiological verification of CAP and detection of bacteremia in clinical practice may be challenging because of initiation of antibiotic therapy before obtaining cultures, and cultures are often not performed due to limited practice of collecting bacteriological material in hospital settings and/or limited laboratory capacity. Given the current reliance on clinical examination and X-ray diagnosis in CAP, there may be insufficient recognition that this disease is predominantly caused by the pneumococcus. This may be especially true in primary care, where a vast majority of CAP patients receive empiric antibacterial therapy.

Improvement of diagnostic and treatment pathways alone, without a clear preventative strategy, may not be sufficient to adequately control the burden of CAP. Rates of CAP hospitalization and CAP mortality remain especially high in older patients in spite of apparent advances in therapy. According to a German nationwide hospital audit, hospital mortality in CAP significantly increases from the age of 40 years and hospitalization rates significantly increase from the age of 50 years (24). Early recognition and adequate antibiotic therapy in the first hours after admission improve the outcomes of hospitalization in both bacteremic and non-bacteremic CAP (25, 26), although antibiotic resistance of *S. pneumoniae* may lead to some treatment failures (12). Moreover, hospital mortality is especially high in the first 4 days after admission, which may be explained by the fact that pneumonia is a severe inflammatory illness, with the gravity of disease compounded by delayed referral of (potentially severe) cases by primary care physicians (PCPs) and/or delayed initiation of antibacterial treatment.

Bacteremia in pneumococcal CAP is more frequent in older adults and may be a risk factor for greater likelihood of severity and mortality (27, 28). Referral decisions can be ameliorated by the application of validated risk scales, such as CRB65 (Severity score for CAP based on: Confusion, Respiratory rate, Blood pressure, and 65 years of age and older) (25). Furthermore, the burden of CAP remains profound even after recovery and discharge from the hospital (24–32). Symptoms can take weeks to resolve (29), and a substantial proportion of patients hospitalized with CAP require re-hospitalization within 30 days (30). Of even more concern is long-term mortality, which remains significantly higher than in the general population for several years after the initial episode, especially in CAP caused by *S. pneumoniae* (31, 32).

Pneumococcal Vaccinations in Adults: Recommendations vs. Implementation

Recommendations for pneumococcal vaccination in adults exist in most countries of the Region and predominantly call for a single dose of plain polysaccharide vaccine in adults older than 65 years of age (33) or in younger adults with well-established risk factors. At the same time, the actual uptake of pneumococcal vaccination in adults has been negligible (34). Consequently, the content of national recommendations from different bodies needs to be accurate, uniform, simple and practical. More importantly, their implementation needs to be addressed to improve the impact of adult pneumococcal vaccination.

Considerations for Vaccination Recommendations

IPD and CAP represent a significant preventable burden in adults from the age of 50 years. With increasing life expectancy, vaccination recommendations should address the extended period of risk. A primary dose of vaccine, followed by the ability to maintain a protective immune response through regular re-vaccination as needed, may provide continued protection even in the face of the immunosenescence associated with aging. Polysaccharide vaccines have shown a certain level of effectiveness against invasive pneumococcal disease but evidence of their effectiveness in all-cause pneumonia is inconsistent. Furthermore, polysaccharide vaccines have a number of limitations with regard to the immune responses in older age groups (35): protection provided by a dose of plain polysaccharide vaccine wanes over time, and re-vaccination is currently not recommended as the benefit is doubtful (36–38). Protection is also less likely to be demonstrated in more elderly age groups or in immuno-compromised individuals (39, 40). Consequently, pneumococcal vaccines are needed that are capable of establishing immune memory initially and that retain the potential for an individual to be re-vaccinated as necessary throughout the aging adult risk period.

Overcoming Barriers to Successful Implementation

A number of barriers hinder the successful implementation of vaccination recommendations in adults (41). Patient barriers include general low health awareness and poor knowledge of the safety and benefits of vaccination in adults. A major barrier for potential vaccine recipients is missing opportunities to have vaccination recommended and administered during their encoun-

ters with healthcare professionals (42), who in-turn may have an incomplete understanding of the seriousness of pneumococcal disease (6). Additional barriers specific to the Region are: inconsistent reimbursement policies in several countries and associated low public compliance to carry out-of-pocket expenses; variability in the age and risk groups for which vaccination is recommended; a negative attitude of the media towards vaccination in general.

For pneumococcal disease in adults, PCPs may play a key part in prevention, diagnosis and referral, especially in those healthcare systems where they play a gatekeeper role. Continual changes in healthcare systems overwhelm PCPs with multiple complex procedures and guidelines, which are often poorly implemented. A key success factor is therefore the implementation of clear and easy-to-follow recommendations and tools to motivate PCPs to vaccinate adults. Other stakeholders such as policy makers, payers, media and the public have low awareness of, and commitment to vaccination in adults. There are even examples of anti-vaccination attitudes among the public and the media. However, the attitude of non-medical audiences is unlikely to change before healthcare professionals manifest improved awareness of, and commitment to pneumococcal vaccination of adults.

Conclusions: Call to Action

The Expert Panel calls on healthcare providers and policy makers in the Region to lessen the burden of pneumococcal disease in adults and to make a concerted effort to address the unmet needs.

Optimised Surveillance Systems and Epidemiology Studies

- Require regional protocols and/or data centres that are optimised to generate consistent and comparable epidemiology data on adult pneumococcal disease (e.g. IPD and CAP).
- Perform sentinel studies in selected locations that may be instrumental in establishing the actual incidence, morbidity and mortality of IPD and CAP.

State-of-the-art Vaccination Recommendations

- IPD and CAP represent significant risks and a preventable burden for adults starting at 50 years of age.
- There is a rationale for immunisation throughout the adult risk period that involves priming by a pneumococcal vaccine that provides a protective immune response, followed by the possibility of regular re-vaccination, if necessary, to provide continued protection, even in the face of any immunosenescence associated with aging.

Coordinated Awareness and Implementation Efforts

- Data on the pneumococcal disease burden and information about successful vaccination programmes should be communicated beyond the specialist community to healthcare professionals, the public and policy makers.
- Public health policy and reimbursement decisions need to be made to allocate sufficient resources for the prevention of pneumococcal disease in adults.

- Educational programmes with clear messages and usable tools should be addressed in a top-down approach to multiple audiences including PCPs and allied healthcare professionals.

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Conflicts of interest

Endre Ludwig: Financial support for participating and working as consultant in advisory boards by Astellas, MSD; Honoraria as speakers in scientific meetings by Bayer

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