

# Effect of Age on the Manifestations and Outcomes of Invasive Pneumococcal Disease in Adults



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## ABSTRACT

**BACKGROUND:** Although a considerable amount is known about the effect of age on the manifestations and outcomes of pneumonia, the same is not true for invasive pneumococcal disease.

**METHODS:** This was a prospective observational study of all cases (2435) of invasive pneumococcal disease in adults in Northern Alberta from 2000 to 2014. Rates of invasive pneumococcal disease per 100,000, sociodemographic variables, clinical characteristics, and invasive pneumococcal disease–related outcomes were compared for the following age groups: 17–54, 55–64, 65–74, and ≥75 years.

**RESULTS:** The rate of invasive pneumococcal disease per 100,000 increased with increasing age. Although only 27.3% of the cases were in those aged ≥65 years, they accounted for 48% of the deaths. The case fatality rate increased with increasing age, from 9.6% for those aged 17–54 years to 31.7% for those aged ≥75 years. The rate of meningitis decreased with increasing age, as did admission to intensive care and use of mechanical ventilation. There was a marked reduction in the rate of invasive pneumococcal disease due to protein conjugate vaccine 7 and protein conjugate vaccine 13 serotypes in those aged ≥55 years but a much smaller decline in rates for those aged 17–54 years. Replacement with non-vaccine serotypes constituted approximately 50% of the cases.

**CONCLUSIONS:** The rate of invasive pneumococcal disease is highest in the very elderly, and manifestations of invasive pneumococcal disease are influenced by age.

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**KEYWORDS:** Age group; Invasive pneumococcal disease; *Streptococcus pneumoniae*

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**Authorship:** TJM and GJT designed the study, organized the data collection, and had full access to all of the data in the study. DTE conducted all analyses and had full access to the data. All authors contributed to the interpretation of data, wrote the manuscript, revised the manuscript for intellectual content, and approved the manuscript to be published.

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## INTRODUCTION

There is a general understanding that the incidence of invasive pneumococcal disease is highest at the extremes of age.<sup>1</sup> It is also well known that the mortality rate from invasive pneumococcal disease increases with increasing age.<sup>2</sup> In pneumonia, it is well known that older patients report fewer symptoms than those who are younger.<sup>3</sup> Whether this holds true for patients with invasive pneumococcal disease is uncertain because it is not well known how the incidence, predisposing factors, and outcomes (other than mortality) of invasive pneumococcal disease in adults vary by age group.

There are 2 pneumococcal vaccines currently in use in Alberta, Canada. Protein conjugate vaccine 13 was implemented in the pediatric population for those individuals 2 months of age up to 59 months and for high-risk individuals 2 months of age up to and including 17 years of age in 2010.<sup>4</sup>

Before 2010, protein conjugate vaccine 7 was in use and was introduced into the Alberta pediatric population in 2002 and discontinued when protein conjugate vaccine 10 was introduced. The second vaccine, pneumococcal polysaccharide vaccine 23, has been in use since the late 1990s and is indicated for routine immunization in adults aged  $\geq 65$  years and those considered medically at risk.<sup>5</sup>

We used data from a 15-year population-based study of invasive pneumococcal disease in Northern Alberta, Canada to describe the effect of age groups on the incidence, manifestations, outcomes, and prevalent serotypes in invasive pneumococcal disease. Furthermore, we also explored the influence pneumococcal conjugated vaccines have had on the prevalence of invasive pneumococcal disease in specific age groups in our study population.

## METHODS

### Definitions

Cases of invasive pneumococcal disease were defined as per the Canadian national case definition as isolation of *Streptococcus pneumoniae* from a sterile site, such as blood, cerebrospinal fluid, pleural fluid, biopsy tissue, joint aspiration, pericardial fluid, or peritoneal fluid.<sup>6</sup> Invasive pneumococcal disease is listed as a provincially notifiable disease in Alberta. Part of being a notifiable disease is the requirement that all invasive pneumococcal isolates be submitted to the Provincial Laboratory for Public Health for pneumococcal serotyping. This database allowed us to prospectively identify all cases of invasive pneumococcal disease in Northern Alberta.

### Clinical Data Collection

From 2000 to 2014, data were collected on all patients in Northern Alberta with invasive pneumococcal disease (approximate population 2,060,039). For each case, research nurses collected sociodemographic, clinical, functional, and laboratory data using a standardized case report form. The research nurses received training on data collection before the start of the study. Underlying illnesses were recorded according to the attending physician's documentation in the medical record. Definitions of comorbidities and complications are as previously reported.<sup>7</sup> This study received approval from the institutional research review committees of the Alberta Health Regions as well as the University of Alberta ethics review board.

## Identification and Serotyping of *S. pneumoniae* Isolates

*Streptococcus pneumoniae* isolates were received at the Provincial Laboratory from acute diagnostic laboratories in Alberta as per requirements of provincial notifiable disease regulations. These isolates were confirmed as *S. pneumoniae* on the basis of characteristic pneumococcal morphology and optochin susceptibility before serotyping.<sup>8</sup> All pneumococcal isolates that exhibited a positive Quellung reaction using commercial type-specific antisera obtained from Statens Serum Institute (Copenhagen, Denmark) were assigned a serotype designation.<sup>9</sup> Strains that were susceptible to optochin but that failed to serotype using the Quellung assay were assayed further using the AccuProbe *S. pneumoniae* culture identification test (GenProbe, San Diego, Calif) to confirm the species identification.

### Data Analysis

Sociodemographic variables, clinical characteristics, and invasive pneumococcal disease-related outcomes were compared according to age groups using Student's *t* test or  $\chi^2$  tests, or Fischer's exact test, as appropriate. For our age groups, we divided the adult population, those aged 17 years and older, into the following age groups: 17-54, 55-64, 65-74, and  $\geq 75$  years. In addition, for some analyses we further subdivided the 17-54 year age group into 17-26, 27-36, 37-46, and 47-54 years of age. Incidence rates of invasive pneumococcal disease per 100,000 were calculated yearly from 2000 to 2014 across the age groups, as well as stratified within age groups by males and females. Specific comparisons between invasive pneumococcal disease rates across age and sex groups over time were evaluated using generalized linear models. Invasive pneumococcal disease serotypes were also identified and summarized according to age groups. We also further explored serotypes according to whether the invasive pneumococcal disease serotypes were included in the protein conjugate vaccine 7 and protein conjugate vaccine 13. All analyses were performed with Stata MP, version 14.2 (StataCorp, College Station, Tex).

## RESULTS

Overall, 2435 incident cases of invasive pneumococcal disease in adults occurred from 2000 to 2014. **Table 1** shows the demographic features for the 4 age groups. There were major demographic changes from the youngest to the oldest groups. These included a significant decrease in the percentage of

### CLINICAL SIGNIFICANCE

- In adults with invasive pneumococcal disease the mortality rate increases with increasing age, from 9.6% to 31.7% for those in the 17-54 years and  $\geq 75$  years age groups.
- Symptoms of pneumonia as a manifestation of invasive pneumococcal disease, such as cough, sputum, and hemoptysis, decrease with increasing age.
- Some of the processes of care, such as admission to intensive care and mechanical ventilation, also decrease with increasing age.
- Changes in pneumococcal serotypes, especially in the very elderly, necessitate changes to current vaccination strategies.

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