Epidemiology and burden of illness of seasonal influenza among the elderly in Japan: a systematic literature review and vaccine effectiveness analysis

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INTRODUCTION

- Seasonal influenza causes considerable healthcare burden. Morbidity and mortality are concentrated among older adults, the very young, and people with chronic diseases.
- In Japan, the influenza-associated respiratory mortality rate per 100,000 people has been estimated at 2.3, 5.1, and 27.5 among individuals aged <65 years, 65–74 years, and ≥75 years, respectively.
- The population is aging and the burden in the elderly is therefore likely to increase.
- Detailed epidemiological data have been generated from individual studies with different methods and populations, but never synthesized.
- Annual vaccination is recommended for elderly and other high-risk Japanese population groups. Vaccine effectiveness (VE) is affected by virus type/subtype, antigenic match, age and health status of vaccine recipients and vaccination timing.
- To describe the available evidence on influenza epidemiology and VE in adults in Japan, we conducted a systematic review and meta-analysis of VE, stratified by study characteristics.

METHODS

Literature review
- Systematic literature review of articles published in English or Japanese between January 1, 1997 and November 30, 2018 from PubMed, EMBASE, and ICHUSHI, and grey literature.
- Search criteria:
  - Influenza(A)/H1N1 and selection of epidemiological and/or health economic terms and/or elderly OR adult AND Japan published 1997–2018 AND English/angl OR Japan/angl
- Included: systematic reviews, prospective or retrospective observational studies (evaluating at least 10 patients), randomized controlled trials and economic studies describing populations aged ≥18 years.
- Excluded: animal studies, in vitro/ex vivo studies, gene expression/protein expression studies, laboratory studies, editorials, non-systematic reviews, conference minutes, and case studies/case series evaluating fewer than 10 patients.

Meta-analysis

- Age-specific (three categories: <65 years; mixed ages: 65–69 and ≥70 years) VE estimates or incidence rates of respiratory outcomes were extracted from a predefined data extraction template and converted to relative risks (RR).
- Random-effects meta-analysis estimated RR of outcomes in influenza vaccine recipients vs unvaccinated groups, and explored whether a) subject age; b) study setting, c) design or d) circulating influenza virus types were explanatory variables.
- RR estimates were presented as a forest plot and used to estimate VE using the formula RR = 1 / (V1 / V0 + 1).

RESULTS

Epidemiology

- Reported incidence rates varied considerably depending on study design, season, study setting and, most importantly, case definitions.
- Studies conducted at Long Term Care Facilities (LTCF) reported incidence rate ranging from 5% to 24%.
- From national surveillance data, 14,580,000 influenza cases were estimated in 2017/18 season, in which 9% were aged >70 years-old (overall attack rate: 28.60%).
- Mild episodes of non-specific endpoints such as Influenza-Like Illness (ILI) were much more common than hospitalized or laboratory-confirmed cases.
- Influenza A virus subtypes were the most common type (comprising 41.7-100% of isolates) in 21 of 24 publications between the 1998/1999 and 2017/2018 seasons.

Methods

- VE analysis confirmed the value of influenza vaccination. The rather low overall VE due to the high proportion of studies conducted in the elderly population in whom VE was lowest. This suggests better vaccines are needed for this group.
- Limitations: Studies were not excluded based on assessment of their methodological quality.

DISCUSSIONS

- The highest burden of influenza hospitalization in Japan is in the elderly population and while influenza vaccines are effective, VE is suboptimal in the elderly who are most at risk. In order to assess the burden of influenza more precisely, further study will be necessary.

REFERENCES


Figure 1: Forest plot of VE estimates included in the review and meta-analysis

Figure 2: Forest plot of VE estimates and the overall pooled estimate from a random effects model without adjustments. Lines are 95% CIs and boxes are weighted by the inverse of the variance of each point estimate.

Figure 3: Forest plot of VE estimates stratified by age

Table 1: Characteristics of studies included in the review and meta-analysis

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Setting</th>
<th>Population</th>
<th>Disease</th>
<th>Vaccine Type</th>
<th>Isolation</th>
<th>Age Group</th>
<th>Incidence Rate</th>
<th>Risk Ratio</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 1</td>
<td>2000</td>
<td>Hospital</td>
<td>Elderly</td>
<td>Hospitalized</td>
<td>Influenza A</td>
<td>Yes</td>
<td>65-74 yrs</td>
<td>10.0</td>
<td>0.96</td>
<td>0.85, 1.08</td>
<td>0.23</td>
</tr>
<tr>
<td>Study 2</td>
<td>2001</td>
<td>Outpatient</td>
<td>General</td>
<td>PCR-positive</td>
<td>Influenza A</td>
<td>Yes</td>
<td>&lt;65 yrs</td>
<td>5.0</td>
<td>1.13</td>
<td>0.96, 1.32</td>
<td>0.85</td>
</tr>
<tr>
<td>Study 3</td>
<td>2002</td>
<td>Community</td>
<td>Elderly</td>
<td>Hospitalized</td>
<td>Influenza B</td>
<td>Yes</td>
<td>&gt;75 yrs</td>
<td>15.0</td>
<td>0.64</td>
<td>0.42, 1.00</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Note: All p-values were derived through ORs. Sample size data for each study were estimated from the text in the publication. No meta-analysis was performed due to the heterogeneity observed in the studies.