Respiratory infections in the elderly: epidemiology and prevention strategies

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Conflicts of interest

• I have received a research grant from Sanofi Pasteur to estimate the incidence of disease due to respiratory syncytial virus in Washington State
Pathogens covered in this talk

- *Haemophilus influenzae* type b (Hib)
- Influenza
- Respiratory syncytial virus (RSV)
- *Streptococcus pneumoniae*
Haemophilus influenzae type b (Hib)


Source: Modified from MacNeil; *Clin Infect Dis* 2011; 53(12):1230-6
**Haemophilus influenzae** type b (Hib)

**Fig. 2.** Incidence of *Haemophilus influenzae* bacteraemia according to age and period, 1991–2008, Epibac Network, France.

Source: Modified from Georges et al; *Epidem Infect* 2013; 141:1787-96
1. Influenza infection causes non-specific clinical signs and symptoms
2. Influenza infection causes a variety of secondary complications
Influenza: surveillance challenges

Reported and estimated pediatric deaths due to laboratory-confirmed influenza – United States, 2010/11 through 2012/13 seasons

Incidence of severe influenza

Hospitalizations for pneumonia due to laboratory-confirmed influenza – Thailand

Source: Modified from Simmerman; *PloS One* 2009; 4(11):e7776
Incidence of severe influenza

Incidence of acute respiratory illness hospitalization due to influenza – northern India, 2010-2012

Source: Data from Hirve; J Infect 2015; 70:160-70
Incidence of severe influenza

Incidence of severe acute respiratory illness (SARI) due to influenza – Ghana, 2013-2015

Source: Data from Ntiri; BMC Infect Dis 2016; 16:757
Incidence of severe influenza

Incidence of presumptive influenza hospitalizations in adults aged ≥65 years – Five Central American Countries, 2009-2012

Source: Data from Descalzo; Influenza Other Resp Virus 2016; 10(4):340-5
Influenza vaccine effectiveness

Forest plot of studies included in meta-analysis: influenza vaccine effectiveness in elderly adults

Source: Data from Darvishian; *Lancet Infect Dis* 2014; 14:1228-39
Adjuvanted influenza vaccine

Odds ratio for laboratory-confirmed influenza
MF59-adjuvanted vs unadjuvanted vaccine

Source: Domnich; *Vaccine* 2017; 35:513-20
Intradermal vaccination in the elderly

Forest plots of the risk ratio of seroprotection for intradermal compared with intramuscular influenza vaccine administration

Source: Pileggi; Drugs Aging 2015; 32:857-69
Vaccinate schoolchildren to protect the elderly

Source: Modified from Reichert; NEJM 2001; 344(12):889-96
RSV incidence

Incidence of hospitalization for pneumonia due to laboratory-confirmed RSV infection by age group – Thailand, 2004-2007

Source: Fry; *PLoS One* 2010; 5(11):e15098
RSV incidence

Mortality attributed to influenza and RSV in seniors in various countries

Sources: (USA:) Matias; Influenza Other Resp Viruses 2014; 8(5):507-15  
(Netherlands:) Jansen; Eur Resp J 2007; 30:1158-66  
(South Africa:) Karstaedt; South Africa Med J 2009;99(10):750-4
RSV vaccine pipeline: vaccines aimed at adults aged ≥55 years

<table>
<thead>
<tr>
<th>Platform</th>
<th>Sponsor</th>
<th>Most advanced trial phase</th>
<th>Registration number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recombinant viral vector</td>
<td>Bavarian Nordic</td>
<td>Phase 2</td>
<td>NCT02873286</td>
</tr>
<tr>
<td></td>
<td>Janssen Vaccine</td>
<td>Phase 1</td>
<td>NCT02926430</td>
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<tr>
<td></td>
<td>Reithera</td>
<td>Phase 1</td>
<td>NCT01805921</td>
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<tr>
<td></td>
<td>Vaxart</td>
<td>Phase 1a</td>
<td>NCT02830932</td>
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<tr>
<td>Recombinant subunit</td>
<td>Dalhousie University</td>
<td>Phase 1a</td>
<td>NCT02472548</td>
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<tr>
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<td>Novavax</td>
<td>Phase 3</td>
<td>NCT02608502</td>
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<tr>
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<td>MedImmune</td>
<td>Phases 2b</td>
<td>NCT02508194</td>
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</table>

Source: http://www.who.int/immunization/research/vaccine_pipeline_tracker_spreadsheet/en/
Invasive pneumococcal disease

Fig. 1. Pneumococcal meningitis (■) and invasive pneumococcal disease (□), Czech Republic, 2000–2006, age-specific incidence. Pneumococcal meningitis = routine notification data (n = 411); invasive pneumococcal meningitis = laboratory-based data (n = 1236).

Source: Motlova; Epidem Infect 2009; 137:562-9
Invasive pneumococcal disease

Incidence of hospitalized pneumococcal bacteremia – rural Thailand, 2005-2010

Invasive pneumococcal disease – role of HIV infection


Pneumococcal pneumonia

Incidence of pneumococcal pneumonia hospitalizations by age group – rural Thailand, 2006–2011

Pneumococcal pneumonia


Source: Contreras; PLoS One 2015; 10(10):e0140939
Pneumococcal polysaccharide vaccine effectiveness

Forest plots of meta-analyses of randomized controlled trials of PPV23 against invasive pneumococcal disease (IPD) and pneumococcal pneumonia in seniors

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Events</th>
<th>Total</th>
<th>Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1.1.1 IPD (any serotype), RCTs</strong></td>
<td></td>
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<tr>
<td>Alfageme 2006</td>
<td>0</td>
<td>800</td>
<td>0</td>
<td>798</td>
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<tr>
<td>Honkanen 1999</td>
<td>2</td>
<td>19549</td>
<td>5</td>
<td>18488</td>
<td>52.9%</td>
<td>0.38 [0.07, 1.95]</td>
<td>0.38 [0.07, 1.95]</td>
</tr>
<tr>
<td>Maruyama 2010</td>
<td>0</td>
<td>1140</td>
<td>3</td>
<td>1149</td>
<td>16.2%</td>
<td>0.14 [0.01, 2.78]</td>
<td>0.14 [0.01, 2.78]</td>
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<tr>
<td>Örtqvist 1998</td>
<td>1</td>
<td>793</td>
<td>5</td>
<td>873</td>
<td>30.9%</td>
<td>0.22 [0.03, 1.88]</td>
<td>0.22 [0.03, 1.88]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>22282</td>
<td>21308</td>
<td>100.0%</td>
<td></td>
<td></td>
<td>0.27 [0.08, 0.90]</td>
<td>0.27 [0.08, 0.90]</td>
</tr>
<tr>
<td>Total events</td>
<td>3</td>
<td>13</td>
<td></td>
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<tr>
<td>Heterogeneity: Tau² = 0.00; Chi² = 0.37, df = 2 (P = 0.83); I² = 0%</td>
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<tr>
<td>Test for overall effect: Z = 2.13 (P = 0.03)</td>
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<tr>
<td><strong>1.1.2 PP, all RCTs</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Alfageme 2006</td>
<td>0</td>
<td>800</td>
<td>5</td>
<td>798</td>
<td>5.9%</td>
<td>0.09 [0.01, 1.64]</td>
<td>0.09 [0.01, 1.64]</td>
</tr>
<tr>
<td>Honkanen 1999</td>
<td>52</td>
<td>19549</td>
<td>40</td>
<td>18488</td>
<td>34.0%</td>
<td>1.23 [0.81, 1.86]</td>
<td>1.23 [0.81, 1.86]</td>
</tr>
<tr>
<td>Maruyama 2010</td>
<td>14</td>
<td>1140</td>
<td>37</td>
<td>1149</td>
<td>30.5%</td>
<td>0.38 [0.21, 0.70]</td>
<td>0.38 [0.21, 0.70]</td>
</tr>
<tr>
<td>Örtqvist 1998</td>
<td>19</td>
<td>793</td>
<td>16</td>
<td>873</td>
<td>29.5%</td>
<td>1.31 [0.68, 2.52]</td>
<td>1.31 [0.68, 2.52]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>22282</td>
<td>21308</td>
<td>100.0%</td>
<td></td>
<td></td>
<td>0.75 [0.35, 1.62]</td>
<td>0.75 [0.35, 1.62]</td>
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<tr>
<td>Total events</td>
<td>85</td>
<td>98</td>
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<tr>
<td>Heterogeneity: Tau² = 0.41; Chi² = 13.48, df = 3 (P = 0.004); I² = 78%</td>
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<tr>
<td>Test for overall effect: Z = 0.73 (P = 0.46)</td>
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<tr>
<td><strong>1.1.3 PP, RCTs with low risk-of-bias only</strong></td>
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<tr>
<td>Alfageme 2006</td>
<td>0</td>
<td>800</td>
<td>5</td>
<td>798</td>
<td>4.2%</td>
<td>0.09 [0.01, 1.64]</td>
<td>0.09 [0.01, 1.64]</td>
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<tr>
<td>Maruyama 2010</td>
<td>14</td>
<td>1140</td>
<td>37</td>
<td>1149</td>
<td>95.8%</td>
<td>0.38 [0.21, 0.70]</td>
<td>0.38 [0.21, 0.70]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>1940</td>
<td>1947</td>
<td>100.0%</td>
<td></td>
<td></td>
<td>0.36 [0.20, 0.65]</td>
<td>0.36 [0.20, 0.65]</td>
</tr>
<tr>
<td>Total events</td>
<td>14</td>
<td>42</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Heterogeneity: Tau² = 0.00; Chi² = 0.91, df = 1 (P = 0.34); I² = 0%</td>
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<tr>
<td>Test for overall effect: Z = 3.37 (P = 0.0008)</td>
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</tbody>
</table>

Pneumococcal conjugate vaccine effectiveness

Efficacy of PCV13 against vaccine-type pneumococcal disease in seniors

Source: Bonten; *NEJM* 2015; 372:1114-25
Impact of childhood PCV vaccination on IPD in seniors


Source: Active Bacterial Core surveillance; https://www.cdc.gov/abcs/reports-findings/survreports/spneu-types.html
Phase-out of PCV for seniors?

From the child immunization program, vaccination coverage among adults aged ≥65 years. In a setting of fully realized indirect protection coverage, the expected impact among this cohort will likely decline to IPD and 4,500 cases of community-acquired pneumonia among persons aged ≥65 years (14). Implementation and impact of the recommendations among adults aged ≥65 years, including PCV13 dosing and PPSV23, and impact of PCV13 on hospitalizations and community-acquired pneumonia. For non-receiving adults who do not receive PCV13 in adults aged ≥65 years, including the long-term utility of a single dose of PCV13 if they have not yet received it. A dose of PCV13 should be given ≥1 year after receipt of the most recent PPSV23 dose. For those for whom an additional dose of PPSV23 is indicated, this additional dose should be given 6–12 months after PCV13 and ≥5 years after the most recent dose of PPSV23 (15).

**Potential Time-Limited Utility of Routine PCV13 Use Among Adults ≥65 Years.** The recommendations for routine use of PCV13 among adults aged ≥65 years will be reevaluated in 2018 and revised as needed.

ACIP recommendations for routine use of PCV13 in adults aged ≥19 years with immunocompromising conditions, functional or anatomic asplenia, cerebrospinal fluid leak, or cochlear implants remain unchanged (6).

Source: Tomczyk; *Morb Mort Wkly Rep* 2014; 63(37):822-4
A potential complication: Reduced dose schedules for childhood PCV

Thank you!

Questions?