Experience with pneumococcal conjugate vaccines in New Zealand

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University of Auckland
• Some of the data in this presentation is from an investigator led study funded by GSK

• I have served on Advisory Groups to GSK, Merck, and Pfizer; any honorarium goes to the institution
Presentation overview

- Uptake of pneumococcal vaccines in NZ during three periods
- Impact on IPD, all-cause pneumonia, otitis media (through various lenses)
- Consideration of 19A
- Effect of pneumococcal vaccines on sociodemographic disparities
New Zealand

- 4.8m, ethnically heterogeneous
- Disparities in health
  - Ethnic and socioeconomic
- GDP rank 53rd, 2nd most prosperous
- Maori and Pacific ethnicities disproportionately higher deprivation
  - Economic, health, housing, education...
Infectious diseases in NZ and introduction of PCVs
New Zealand has a high burden of infectious diseases and major ethnic inequities

Rates of serious bacterial infections and respiratory diseases: International comparisons

<table>
<thead>
<tr>
<th>Disease</th>
<th>Other OECD countries: relative rate</th>
<th>NZ: relative rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatic fever</td>
<td>1 (OECD)</td>
<td>13.8</td>
</tr>
<tr>
<td>Serious skin infections</td>
<td>1 (USA, Australia)</td>
<td>2</td>
</tr>
<tr>
<td>Whooping cough</td>
<td>1 (UK, USA)</td>
<td>5–10</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>1 (USA)</td>
<td>5–10</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>1 (Finland)</td>
<td>7</td>
</tr>
</tbody>
</table>

In New Zealand, Maori and Pacifica children carry this burden

Hospitalisations for serious bacterial infections and respiratory diseases in children and young people; risk by *ethnicity*, 2010–2014

<table>
<thead>
<tr>
<th>Cause of hospital admission</th>
<th>European</th>
<th>Māori</th>
<th>Pacific</th>
<th>Asian/Indian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute rheumatic fever⁺</td>
<td>1</td>
<td>33.07</td>
<td>70.42</td>
<td>0.77</td>
</tr>
<tr>
<td>Serious skin infection*</td>
<td>1</td>
<td>2.74</td>
<td>4.68</td>
<td>1.09</td>
</tr>
<tr>
<td>Pertussis#</td>
<td>1</td>
<td>2.09</td>
<td>2.58</td>
<td>0.32</td>
</tr>
<tr>
<td>Pneumonia⁺</td>
<td>1</td>
<td>1.91</td>
<td>4.16</td>
<td>1.06</td>
</tr>
<tr>
<td>Bronchiectasis⁺</td>
<td>1</td>
<td>7.94</td>
<td>10.28</td>
<td>1.09</td>
</tr>
</tbody>
</table>

*0–14 years; *0–24 yr; *<1 year

Respiratory infections have increased since 2000 among poorer children, with the exception of bacterial pneumonia.

Hospital admissions for lower respiratory conditions with a social gradient in children aged 0–14 Years, New Zealand 2000–2013

Note: Acute and arranged admissions only
New Zealand has improved its vaccine coverage by ~150% since 1997: Disparities in coverage are now negligible
New Zealand introduced PCV7 in 2008

- PCV7 in 2008
- PCV10 in 2011
- PCV13 in 2014
- PCV10 in 2017

All in a 3+1 schedule

Concerns about 19A

Competitive tender

Hospitalisations pre-vaccine introduction

Hospitalisations during PCV7 period

Hospitalisations during PCV10 period

Hospitalisations during PCV13 period

Hospitalisations during PCV10 period


VS.

VS.

VS.

VS.

2015 Clinical review finds both vaccines suitable

Impact of the PCV programme in NZ
IPD among NZ children <5 years has declined dramatically 😊

Rate per 100,000 population of IPD by age group and year, 2006–2015

2018 < 2-years
- 1 case 1
- 1 case 19A
- 2 cases 3
- 21 cases non-PCV13

Note: Data presented for 2009 onwards is based on IPD notifications and data prior to 2009 is from ESR’s national laboratory-based surveillance of IPD.
Initial IPD hospitalisation: The most significant declines in <2s

All cause pneumonia hospitalisation: The most significant declines in <2s

Otitis media: Significant declines in <5s

Attempt at VE using indirect cohort method, IPD (2008–2013), aged <5 years

• VE was estimated as 1- (odds of vaccination in a VT case / odds of vaccination in a NVT case)¹

• Limitations: numbers of cases of IPD in NZ now very low
  – Only 169 cases in 2008–2011 for PCV7 analysis
  – Only 39 cases in 2012–2013 for PCV10 analysis

• Diminishing case numbers for future analysis

NVT, non-vaccine type; VE, vaccine effectiveness; VT, vaccine type
We measured VE, but ran out of IPD cases - a challenge for measuring PCV vaccine effects

<table>
<thead>
<tr>
<th>Serotype of infection</th>
<th>Vaccinated at time of infection (≥2 doses)</th>
<th>Unvaccinated at time of infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine serotype</td>
<td>11</td>
<td>44</td>
</tr>
<tr>
<td>Non-vaccine serotype</td>
<td>81</td>
<td>33</td>
</tr>
</tbody>
</table>

PCV7 vaccine effectiveness: 89.8% (77.9–95.3%)

<table>
<thead>
<tr>
<th>Serotype of infection</th>
<th>Vaccinated at time of infection (≥2 doses)</th>
<th>Unvaccinated at time of infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine serotype</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Non-vaccine serotype</td>
<td>21</td>
<td>10</td>
</tr>
</tbody>
</table>

PCV10 vaccine effectiveness: 84.1% (6.9–97.3%)

Unpublished data. H Petousis-Harris and J. Paynter
What about 19A?
Serotype 19A: A general trend upward in older adults (2006–2014)

Rate per 100,000 population of IPD due to serogroup 19A by age group and year, 2006–2014

Decline of 19A IPD occurred prior to change to PCV13 (2013–2018)

Number of IPD cases caused by 19A in children aged <5 years

Impact on sociodemographic inequities
IPD: significant reduction in ethnic disparities

IPD hospitalisation among children aged <6 years, by calendar year and ethnicity

All cause pneumonia: significant reductions in ethnic disparities

Otitis media related hospitalisations: significant reductions in ethnic disparities

PCV effectiveness against clinically suspected IPD

Petousis-Harris D, Best E, Palmu A, Turner N, Howe A
Retrospective cohort study using data-linkage of national administrative datasets

Population

Under 6-year-olds eligible for funded PCVs (2008–2015)

Primary exposure

Vaccinated ≥2 doses

CSIPD event

Not Vaccinated

CSIPD event

No CSIPD

Primary outcome

Vaccinated ≥2 doses

CSIPD event

No CSIPD

Not Vaccinated

No CSIPD

VE=1-OR, Adjusted for sex, deprivation, prioritised ethnicity, District Health Board; CSIPD, clinically suspected IPD
Main outcomes

- Primary outcome of interest is non-laboratory confirmed CSIPD before 6 years of age
- CSIPD is determined by ICD-10 codes used in the FinIP study

### Finnish study codes

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>G00</td>
<td>Bacterial meningitis, not elsewhere classified</td>
</tr>
<tr>
<td>G00.1</td>
<td>Pneumococcal meningitis</td>
</tr>
<tr>
<td>A40.3</td>
<td>Sepsis due to S pneumoniae</td>
</tr>
<tr>
<td>G00.9</td>
<td>Bacterial meningitis, unspecified</td>
</tr>
<tr>
<td>B95.3</td>
<td>S. pneumoniae as the cause of disease classified elsewhere</td>
</tr>
<tr>
<td>A419</td>
<td>Sepsis unspecified</td>
</tr>
<tr>
<td>A40.9</td>
<td>Streptococcal Septicaemia unspecified</td>
</tr>
<tr>
<td>A49.9</td>
<td>Bacterial infection, unspecified</td>
</tr>
<tr>
<td>M00</td>
<td>Pyogenic arthritis</td>
</tr>
<tr>
<td>M001</td>
<td>Pneumococcal arthritis</td>
</tr>
<tr>
<td>M00.9</td>
<td>Polygenic arthritis, unspecified</td>
</tr>
<tr>
<td>I30.1</td>
<td>Infective pericarditis</td>
</tr>
<tr>
<td>B95.5</td>
<td>Unspecified streptococcus as the cause of disease classified to other chapters</td>
</tr>
</tbody>
</table>

International statistical classification of diseases and related health problems, 10th revision, 2016. [apps.who.int/iris/bitstream/10665/246208/1/9789241549165-V1-eng.pdf](apps.who.int/iris/bitstream/10665/246208/1/9789241549165-V1-eng.pdf) (accessed April 2018)

Petousis-Harris D, Best E, Palmu A, Turner N, Howe A. PCV effectiveness against clinically suspected IPD. Poster. ISPPD. Melbourne. 2018
Cohort description, 2-dose definition. Reached most deprived the best

<table>
<thead>
<tr>
<th></th>
<th>Total sample</th>
<th>Vaccinated</th>
<th>Non-vaccinated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of individuals, n (%)</td>
<td>556,435</td>
<td>466,252 (84%)</td>
<td>90,183 (16%)</td>
</tr>
<tr>
<td>Sex, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>49%</td>
<td>84%</td>
<td>16%</td>
</tr>
<tr>
<td>Ethnicity, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maori</td>
<td>22%</td>
<td>89%</td>
<td>11%</td>
</tr>
<tr>
<td>Pacific</td>
<td>11%</td>
<td>85%</td>
<td>15%</td>
</tr>
<tr>
<td>Asian</td>
<td>14%</td>
<td>79%</td>
<td>21%</td>
</tr>
<tr>
<td>NZEO</td>
<td>53%</td>
<td>83%</td>
<td>17%</td>
</tr>
<tr>
<td>Other</td>
<td>2%</td>
<td>52%</td>
<td>48%</td>
</tr>
<tr>
<td>Deprivation, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 ( Least)</td>
<td>18%</td>
<td>82%</td>
<td>18%</td>
</tr>
<tr>
<td>2</td>
<td>17%</td>
<td>83%</td>
<td>17%</td>
</tr>
<tr>
<td>3</td>
<td>18%</td>
<td>83%</td>
<td>17%</td>
</tr>
<tr>
<td>4</td>
<td>20%</td>
<td>84%</td>
<td>16%</td>
</tr>
<tr>
<td>5 ( Most)</td>
<td>28%</td>
<td>85%</td>
<td>15%</td>
</tr>
</tbody>
</table>

Petousis-Harris D, Best E, Palmu A, Turner N, Howe A. PCV effectiveness against clinically suspected IPD. Poster. ISPPD. Melbourne. 2018
Results

Adjusted vaccine effectiveness:
64% (95% CI 60–68)

Controlled for sex, deprivation, prioritised ethnicity, District Health region, year of vaccination

In a Finnish retrospective cohort study, vaccine effectiveness was estimated to be about 34%¹

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¹ Petousis-Harris D, Best E, Palmu A, Turner N, Howe A. PCV effectiveness against clinically suspected IPD. Poster. ISPPD. Melbourne. 2018
VE varied by ethnicity and SES: higher in more deprived populations

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Number</th>
<th>Cases</th>
<th>VE (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maori</td>
<td>113,852</td>
<td>497</td>
<td>84% (81, 87)</td>
</tr>
<tr>
<td>Pacific</td>
<td>56,375</td>
<td>260</td>
<td>81% (75, 85)</td>
</tr>
<tr>
<td>NZEOA</td>
<td>346,284</td>
<td>617</td>
<td>54% (45, 62)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Socioeconomic status</th>
<th>Number</th>
<th>Cases</th>
<th>VE (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (least deprived)</td>
<td>91,469</td>
<td>156</td>
<td>46% (21, 63)</td>
</tr>
<tr>
<td>2</td>
<td>87,576</td>
<td>175</td>
<td>68% (56, 77)</td>
</tr>
<tr>
<td>3</td>
<td>91,268</td>
<td>205</td>
<td>62% (48, 72)</td>
</tr>
<tr>
<td>4</td>
<td>105,176</td>
<td>305</td>
<td>76% (69, 81)</td>
</tr>
<tr>
<td>5 (most deprived)</td>
<td>142,161</td>
<td>536</td>
<td>82% (79, 85)</td>
</tr>
</tbody>
</table>

NZEOA, New Zealand European, Other, and Asian

Petousis-Harris D, Best E, Palmu A, Turner N, Howe A. PCV effectiveness against clinically suspected IPD. Poster. ISPPD. Melbourne. 2018
USA and Australia

- Lower effectiveness in indigenous peoples in USA and Australia
- Higher effectiveness in other ethnic minorities (people identifying as Black) USA
- Higher effectiveness in higher deprivation groups in the USA

New Zealand

- Higher effectiveness in Maori
- Higher effectiveness in other ethnic minorities (Pacific peoples)
- Higher effectiveness in higher deprivation groups


https://www.cdc.gov/abcs/reports-findings/surv-reports.html

Petousis-Harris D, Best E, Palmu A, Turner N, Howe A. PCV effectiveness against clinically suspected IPD. Poster. ISPPD. Melbourne. 2018
Are certain groups developing better immunity?

- This could be an effect of increased exposure in certain groups to pneumococcus younger in life, with the vaccines acting as a booster
  - This was seen to a small extent in the pre-licensure antibody titre studies¹

However, this doesn’t fully explain the high disease rates and lower VE in international indigenous groups...

New Zealand has switched vaccine brand three times

- PCV7 in 2008
- PCV10 in 2011
- PCV13 in 2014
- PCV10 in 2017

All in a 3+1 schedule

Change in brand administered was phased in as stock of predecessor exhausted – resulted in a lag

Schedule changes dates and actual administration

- **PCV10**: July 2011 – Oct 2011
- **PCV13**: July 2014 – Dec 2014
- **PCV10**: July 2017 – ?

Data source: National Immunisation Register
Exposure determined using batch #

- N=~30,000 each period
- Can do head-to-head VE for ACP, OM and CSIPD
Conclusion

• PCVs have had a dramatic impact in New Zealand and have reduced sociodemographic disparities

• Not possible to draw conclusions about 19A, however considerable health gains expected through expansion of the NIP

Next steps

• Head-to-head VE study of vaccines using the PCV7-PCV10-PCV13-PCV10 transition periods
  – Pneumonia, OM, CSIPD
Thank you!
### New Zealand National Immunisation Schedule from 1 April 2018

<table>
<thead>
<tr>
<th></th>
<th>RV</th>
<th>DTaP-IPV-HepB/Hib</th>
<th>PCV</th>
<th>Hib</th>
<th>VV</th>
<th>MMR</th>
<th>DTaP-IPV</th>
<th>Tdap</th>
<th>HPV</th>
<th>Td</th>
<th>Influenza</th>
<th>HZV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Every pregnancy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>6 weeks</td>
<td></td>
<td>Rotarix&lt;sup&gt;®&lt;/sup&gt;</td>
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<tr>
<td>3 months</td>
<td></td>
<td>Rotarix&lt;sup&gt;®&lt;/sup&gt;</td>
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<td></td>
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<tr>
<td>5 months</td>
<td></td>
<td>Infarrix&lt;sup&gt;®&lt;/sup&gt;-hexa</td>
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<td>15 months</td>
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<td>Synflorix&lt;sup&gt;®&lt;/sup&gt;</td>
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<tr>
<td>4 years</td>
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<td>Priorix&lt;sup&gt;®&lt;/sup&gt;</td>
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<tr>
<td>11 years</td>
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<td>12 years</td>
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<td>45 years</td>
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<td>65 years</td>
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</tbody>
</table>

**Vaccine Key**
- RV: Rotavirus
- DTaP-IPV: diphtheria, tetanus, acellular pertussis, polio, hepatitis B, Haemophilus influenzae type b
- PCV: Pneumococcal conjugate vaccine
- Hib: Haemophilus influenzae type b
- VV: Varicella (chickenpox) vaccine
- MMR: measles, mumps, rubella
- DTaP-IPV: diphtheria, tetanus, acellular pertussis, polio
- Tdap: tetanus, diphtheria, acellular pertussis
- HPV: human papillomavirus
- Td: tetanus, diphtheria
- HZV: herpes zoster (shingles) vaccine

### Additional Immunisations
- **High risk**
  - Meningococcal, BCG, PCV13
  - Maternal pertussis and flu

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### Immunisation Advisory Centre
For more details, visit immune.org.nz
How did New Zealand decide to switch?
New Zealand Decision to switch

- The Pharmacology and Therapeutics Advisory Committee (PTAC) Immunisation Subcommittee considered submissions received by the Pharmaceuticals Management Agency (PHARMAC) from GSK and Pfizer for both pneumococcal vaccines in 2015.¹
  - The Subcommittee considered that both of the submissions were of good quality, providing solid data which showed that the vaccines were efficacious.
  - The Subcommittee considered that both PCV10 and PCV13 are suitable for inclusion on the National Immunisation Schedule but that if PCV10 were listed for universal vaccination it may be necessary to continue to list PCV13 for vaccination of high risk groups.
  - GSK won the tender following which:²
    - Synflorix will have Sole Supply Status in both the community and DHB hospital settings from 1 July 2017 until 30 June 2020.
    - Prevenar 13 (pneumococcal 13-valent protein conjugate vaccine (PCV13)) will remain funded for high risk patients only.

1. PTAC. Immunisation Subcommittee of PTAC, meeting minutes. 28 October 2015. Available at: https://www.pharmac.govt.nz/assets/ptac immunisation-subcommittee-minutes-2015-10.pdf [accessed December 2018];
A competitive tender can result in savings that can be used to fund other health care priorities

New Zealand switched from PCV10 to PCV13 in 2014¹

- Concerns about serotype 19A??²

In 2015 a clinical review found that PCV10 and PCV13 are both suitable for inclusion in the national immunisation schedule but that if PCV10 were listed for universal vaccination it may be necessary to continue to list PCV13 for vaccination of high risk groups³

In 2016 PCV10 won the tender⁴

- Through a competitive procurement process and bundling of multiple vaccines⁴
- Program savings meant New Zealand was able to also introduce universal varicella vaccination and widen HPV vaccination access to people up to the age of 26⁴

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New Zealand public consultation (June 2016)

• PHARMAC acknowledges that there may be a small loss in health benefit from the change to PCV 10. However, the savings gained from this change and the health benefits gained from the widening of access to varicella and HPV vaccines are significant.

• The Immunisation Subcommittee of PTAC reviewed conjugated pneumococcal vaccines at its October 2015 and May 2016 (unpublished) meetings and considered that both PCV10 and PCV13 are suitable for inclusion on the National Immunisation Schedule. If PCV10 was listed, the Subcommittee recommended that PCV13 be listed for vaccination of high risk groups.

• Medsafe has recently approved an indication update for PCV10 (Synflorix), recognising protection against invasive pneumococcal disease (IPD) caused by serotype 19A pneumococcus. This indication has also recently been approved by the European Medicines Agency. The additional 19A indication is based on two post marketing studies on IPD in infants in Brazil (Domingues et al. Lancet Respir Med 2014;2:464-71) and Finland. Data from Quebec (Deceuninck et al (Vaccine 2015;33:2684-89) and clinical trials reporting on the immunogenicity of Synflorix also supported the change in indication.

• PHARMAC and the Immunisation Subcommittee also intends to monitor the incidence of serotype 19A.
PHARMAC (Pharmaceutical management agency)

Decides (on behalf of the district health boards) which medicines and pharmaceutical products are subsidised for community and hospital use

To secure for eligible people in need of pharmaceuticals, the best health outcomes that are reasonably achievable from pharmaceutical treatment and from within the amount of funding provided

Since July 2012 took over the management of immunisation schedule and assessment of new vaccines

Allows for savings to be spent elsewhere

Advised by Technical Sub Committee
Serotype 19A: Rate per 100,000 2004-2018 in under 2-years

Rate per 100,000

PCV13

PCV10

<2 cases rate not calculated
Through competitive procurement and bundling of several vaccines NZ added varicella and extended the HPV programme

- Universal varicella programme
- Extension of HPV programme to include males
  - Gardasil 9 for all up to age 26 years