Full public health impact or cherry-picking?

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Disclosure

- The National Institute for Health and Welfare (THL) has received research funding from GlaxoSmithKline Biologicals SA for the **Fin**nish **I**nvasive **P**neumococcal disease vaccine trial (FinIP), a nationwide effectiveness trial of the 10-valent PCV
- No outside support for NVP evaluation

- A Palmu
  - A co-investigator in the FinIP trial
  - Has received honoraria and/or travel support from GSK, Merck and Sanofi-Pasteur
  - No support since 2011

Presentation contents

- **Full public health impact**:

Vaccine-preventable disease burden (VPDI) in children during the national vaccination programme

- **Cherry-picking:**

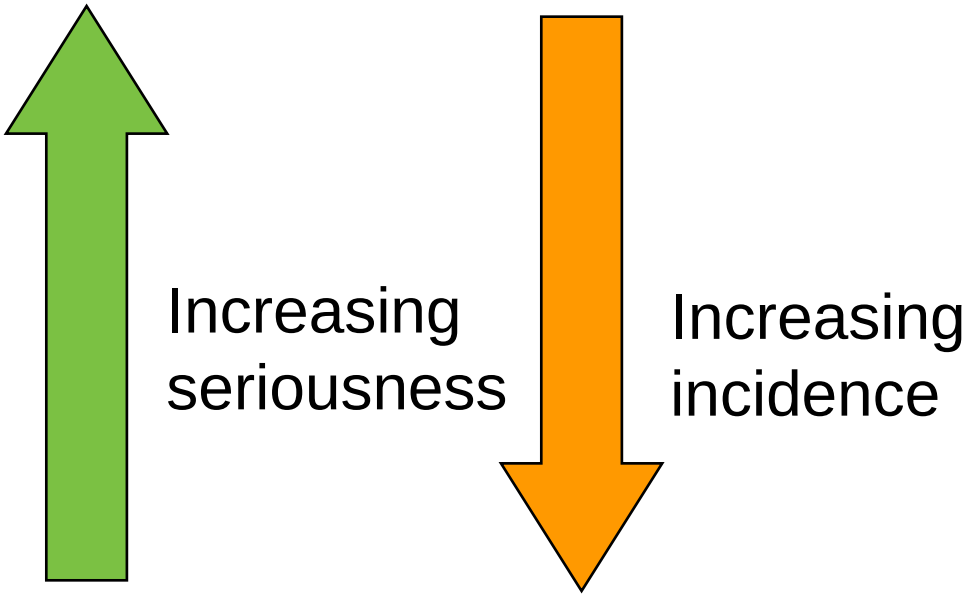
Serotype-specific changes in the elderly after infant NVP introductions

- **Full public health impact**:

Overall reductions in IPD and pneumonia in the elderly

Streptococcus pneumoniae (Pnc) causes a variety of clinical diseases

- IPD
  - Meningitis
  - Septicemia, bacteremia
  - Bacteremic pneumonia
- Non-bacteremic pneumonia
- Sinusitis
- Otitis media



- >90 serotypes
- Nasopharyngeal carriage important in transmission

PCV in the National Vaccination Programme (NVP)

- NVP started in Sep 2010 for children born June 2010 or later
  - 2+1 schedule: 3, 5, 12 mo of age
  - No catch-up, no previous PCV7
  - Since 2009 for high-risk groups under 5 y of age
- *Synflorix*™ (PCV10) selected based on public tender
- Coverage high based on vaccine consumption
  - National vaccination register being built-up
  - Survey on 1000 children born 2012: coverage 92%

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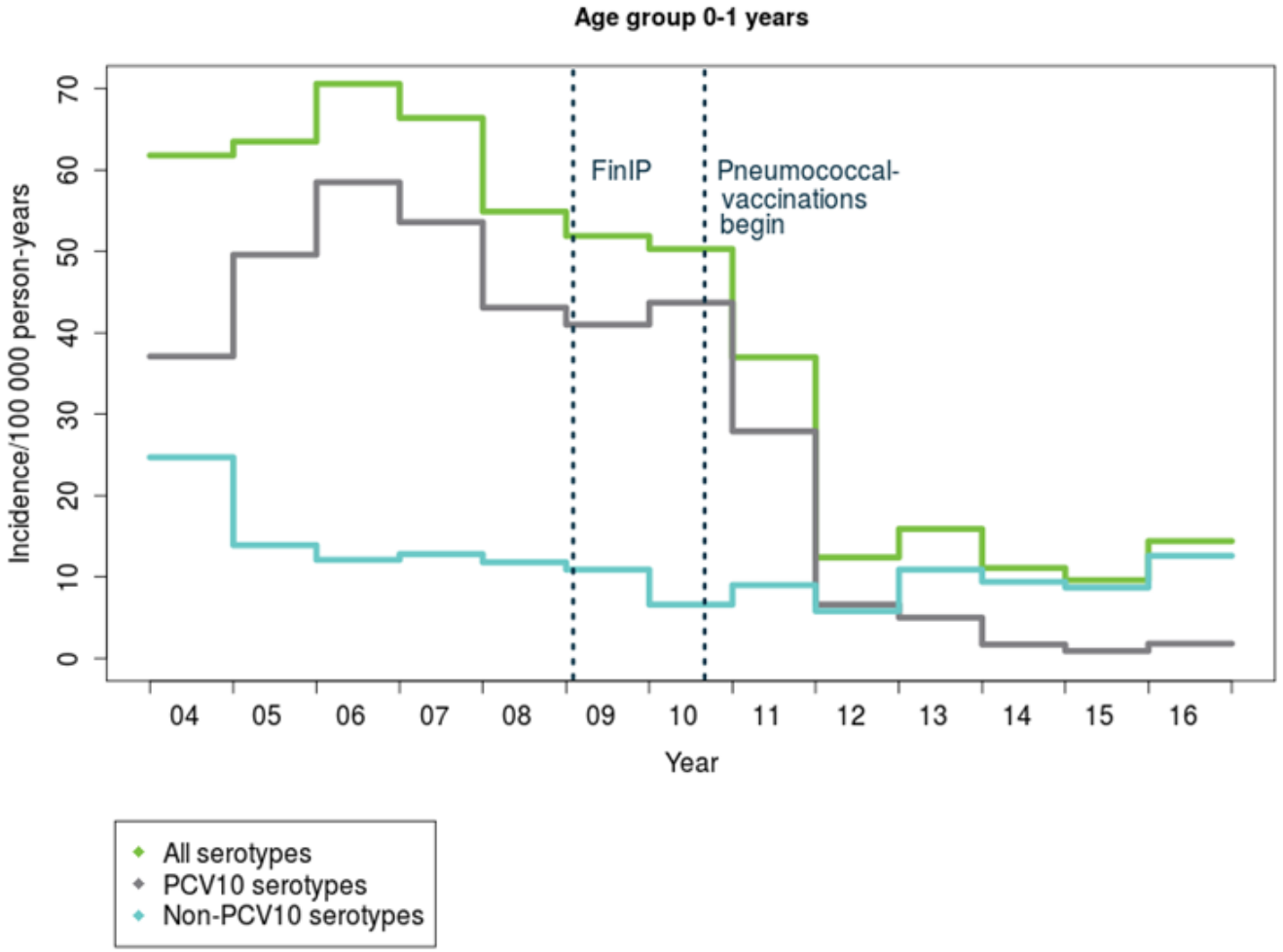
Incidence of invasive pneumococcal disease in children below 2 years of age in Finland



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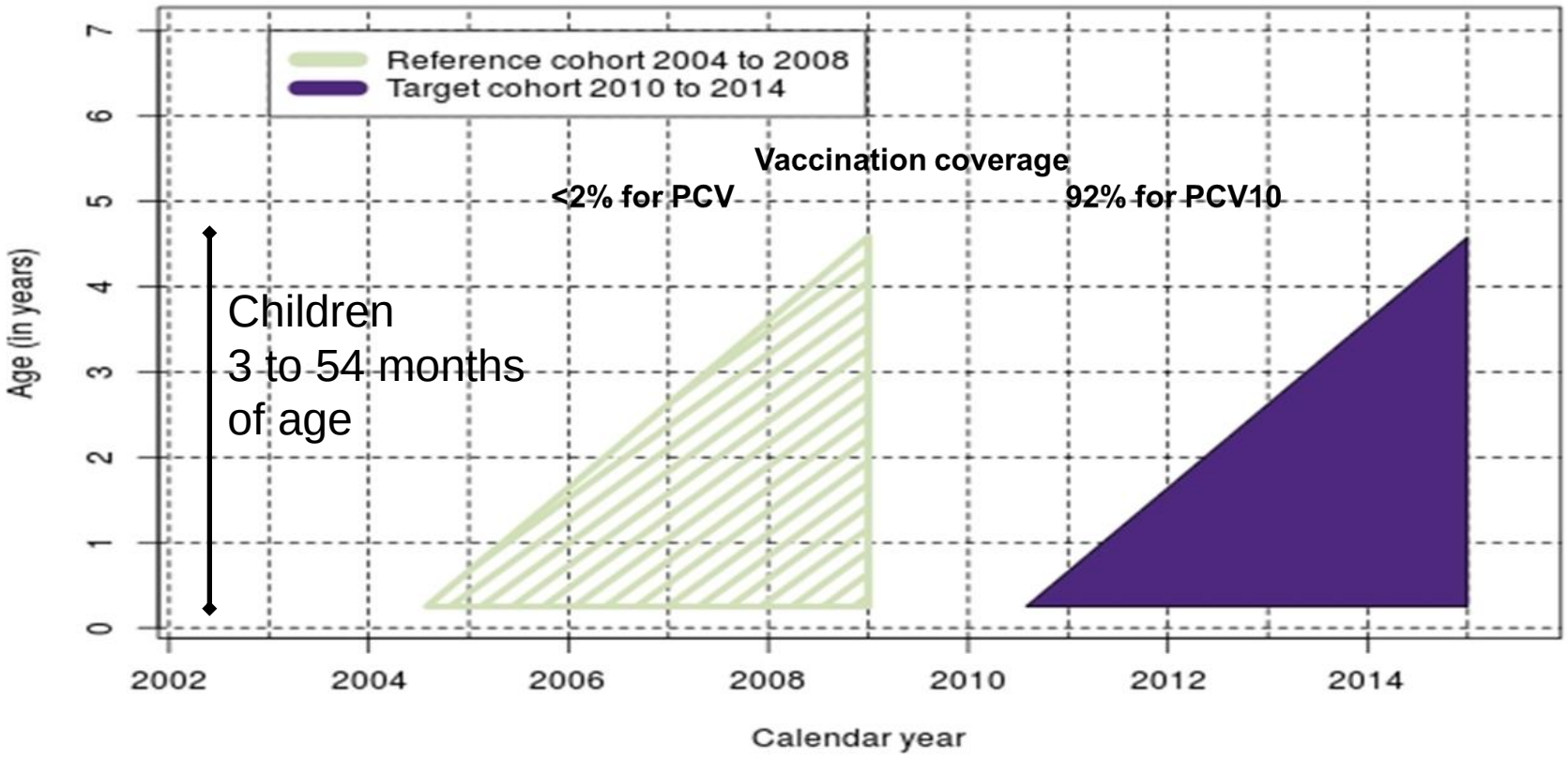
Before-after comparison of PCV10 target cohort 2010 to 2014 with a reference cohort 2004 to 2008



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Surveillance for impact

- **Nation-wide register-based surveillance based on routine diagnostics and treatment**
- **THL National Infectious Diseases Register**
  - Invasive pneumococcal disease (IPD)
- **THL Care register (hospital discharge register with in/outpatient hospitalizations and visits**
  - IPD diagnoses
  - Hospital-diagnosed pneumonia
  - Otitis media **surgery**
- **National Insurance Institution (KELA) registers**
  - Antimicrobial prescription (open care), surrogate for acute otitis media
  - Otitis media surgery

The disease burden caused by *S. pneumoniae* in infants and the vaccine preventable disease incidences (VPDI)

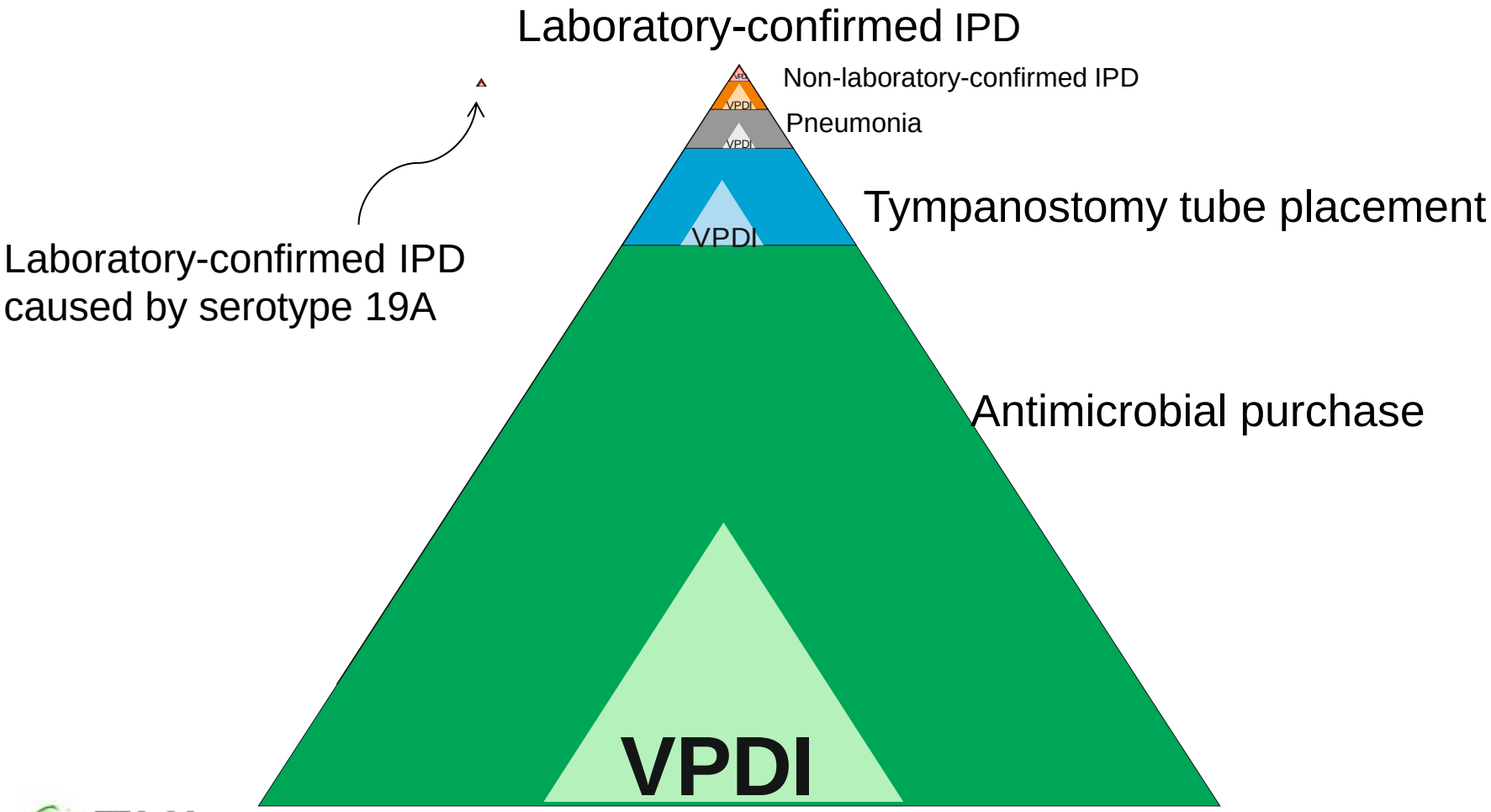
Outcomes	Incidence, per 10^5 person-years (py)		Reduction after PCV10 introduction		Proportion of the outcome out of total reduction, %	
	Reference cohort	Target cohort	Relative reduction, %	VPDI, per 10^5 py	Of all VPDI reduction	Of all cost reduction
Laboratory-confirmed IPD	54	11	80 (73-85)	43	0.2	2.4
Non-laboratory-confirmed IPD/sepsis	358	217	39 (35-44)	141	0.7	7.8
Hospital-diagnosed pneumonia	1036	898	13 (10-17)	138	0.7	5.4
Tympanostomy tube placements	5417	4590	15 (14-17)	827	4.0	23.0
Antimicrobial purchases	109084	89550	18 (18-18)	19534	94.4	61.4
Any outcome	115949	95226		20683	100	100

VE, Vaccine Effectiveness; CI, Confidence Interval; VPDI, Vaccine-Preventable Disease Incidence; IPD, Invasive Pneumococcal Disease; AOM, Acute Otitis Media.

Refs. Jokinen PlosOne2015, Palmu, Pediatrics2015, PlosOne2017, PIDJ2017 in press

The disease burden caused by *S. pneumoniae* in children and the VPDI during the Finnish NVP.

Graphics based on true incidences.



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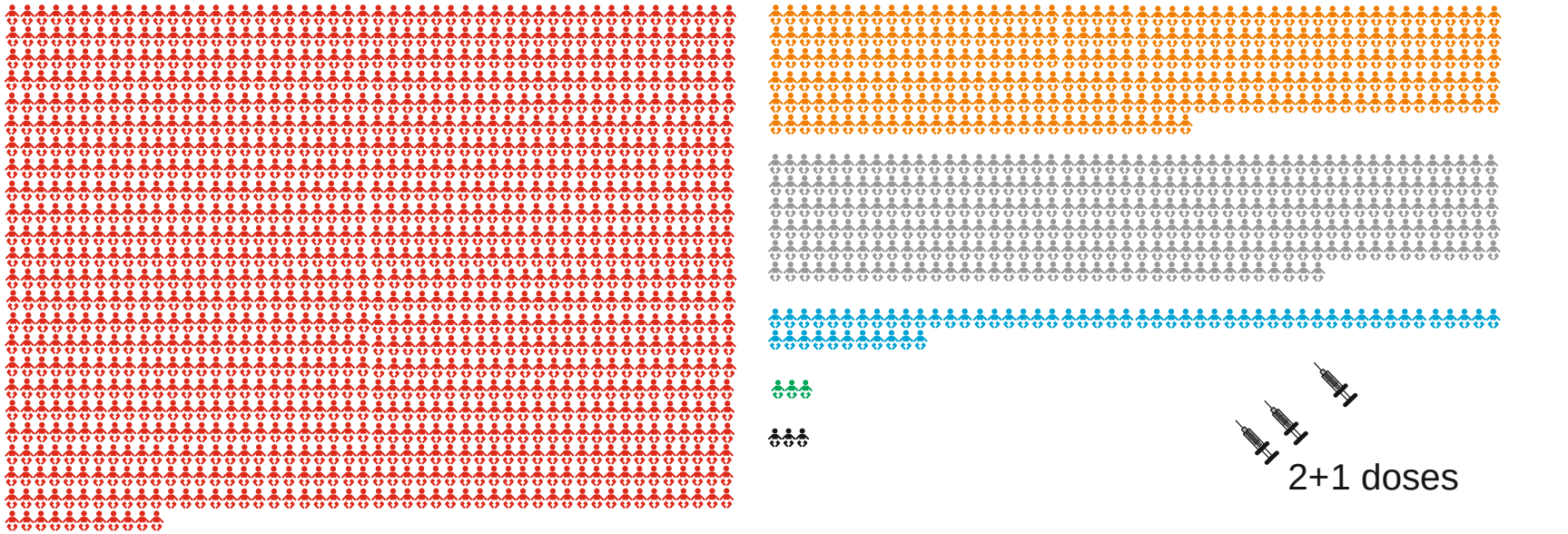
Number needed to vaccinate to prevent one event during two-year follow-up – Finnish NVP

Disease	NNV
Laboratory-confirmed IPD	1161
Suspected non-laboratory-confirmed IPD / sepsis	354
Pneumonia	363
Tympanostomy tube placement	61
Antimicrobial purchase	3
Any of the outcomes above	3



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Presentation contents 2

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Vaccine-preventable disease burden (VPDI) in children during the national vaccination programme

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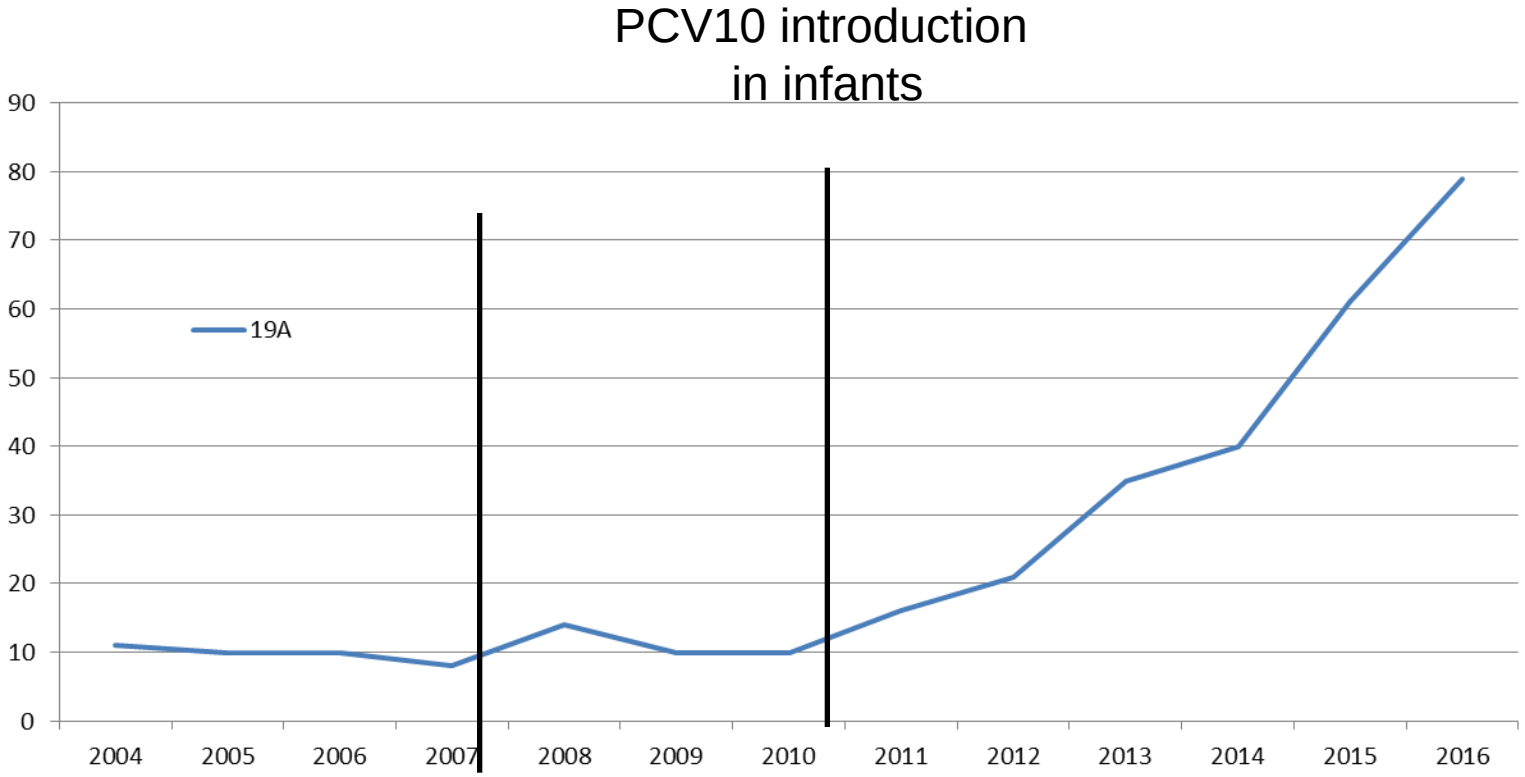
Serotype-specific changes in the elderly after infant NVP introductions

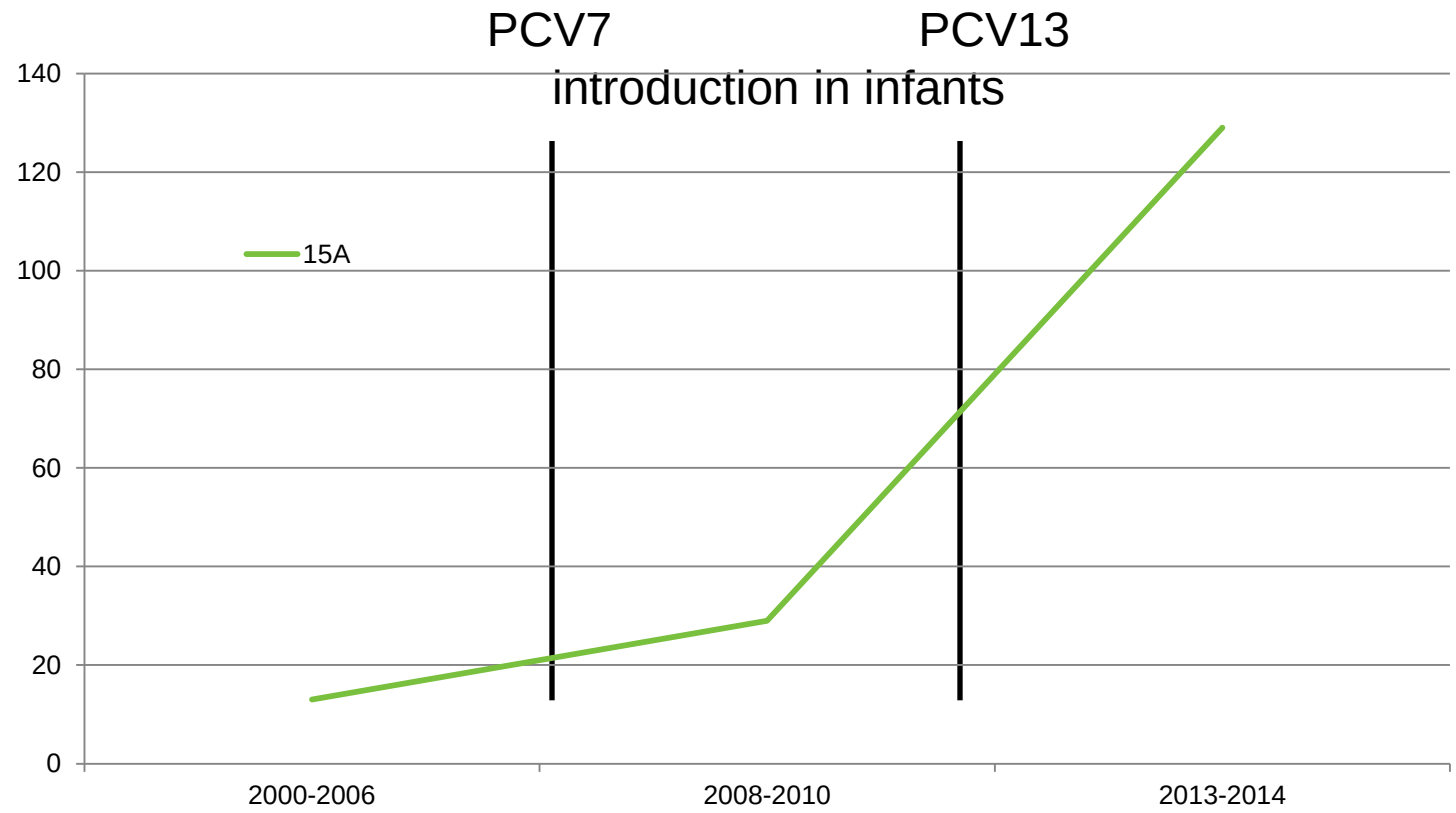
- **Full public health impact**:

Overall reduction in IPD and pneumonia in the elderly

Number of 19A IPD cases by calendar year in the elderly (>=65 years) in Finland after infant PCV10 introduction in 2010



Number of 15A IPD cases (adjusted) by epidemic year in the elderly (>=65 years) in England+Wales after infant PCV7/13 introduction in 2006/2010



Data sources UK: Miller et al LancetID2011, Waight et al, LancetID2015

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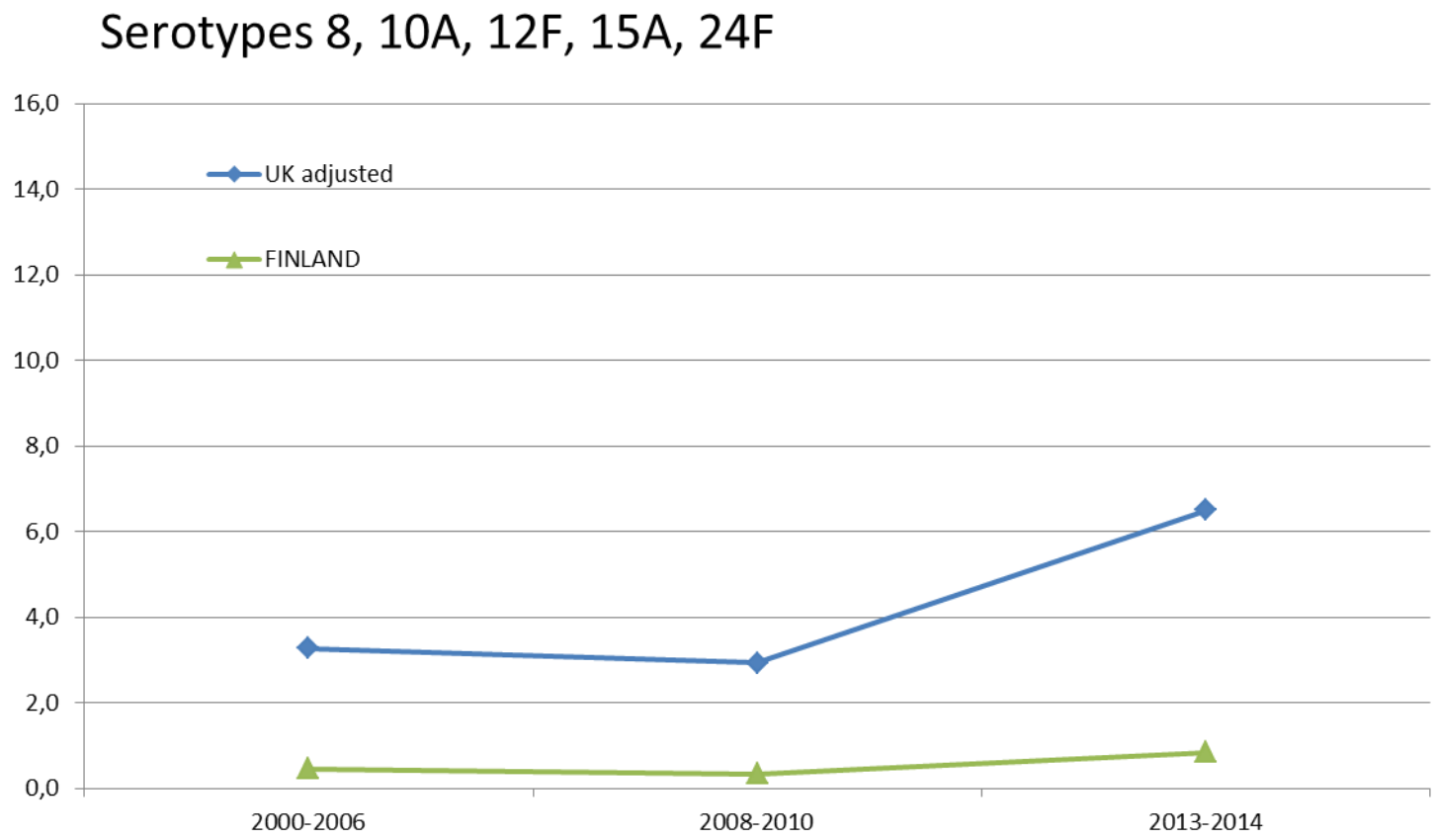
Incidence of IPD due to 5 most common replacement serotypes in UK by year in the elderly (>=65 years) in England and Wales and in Finland



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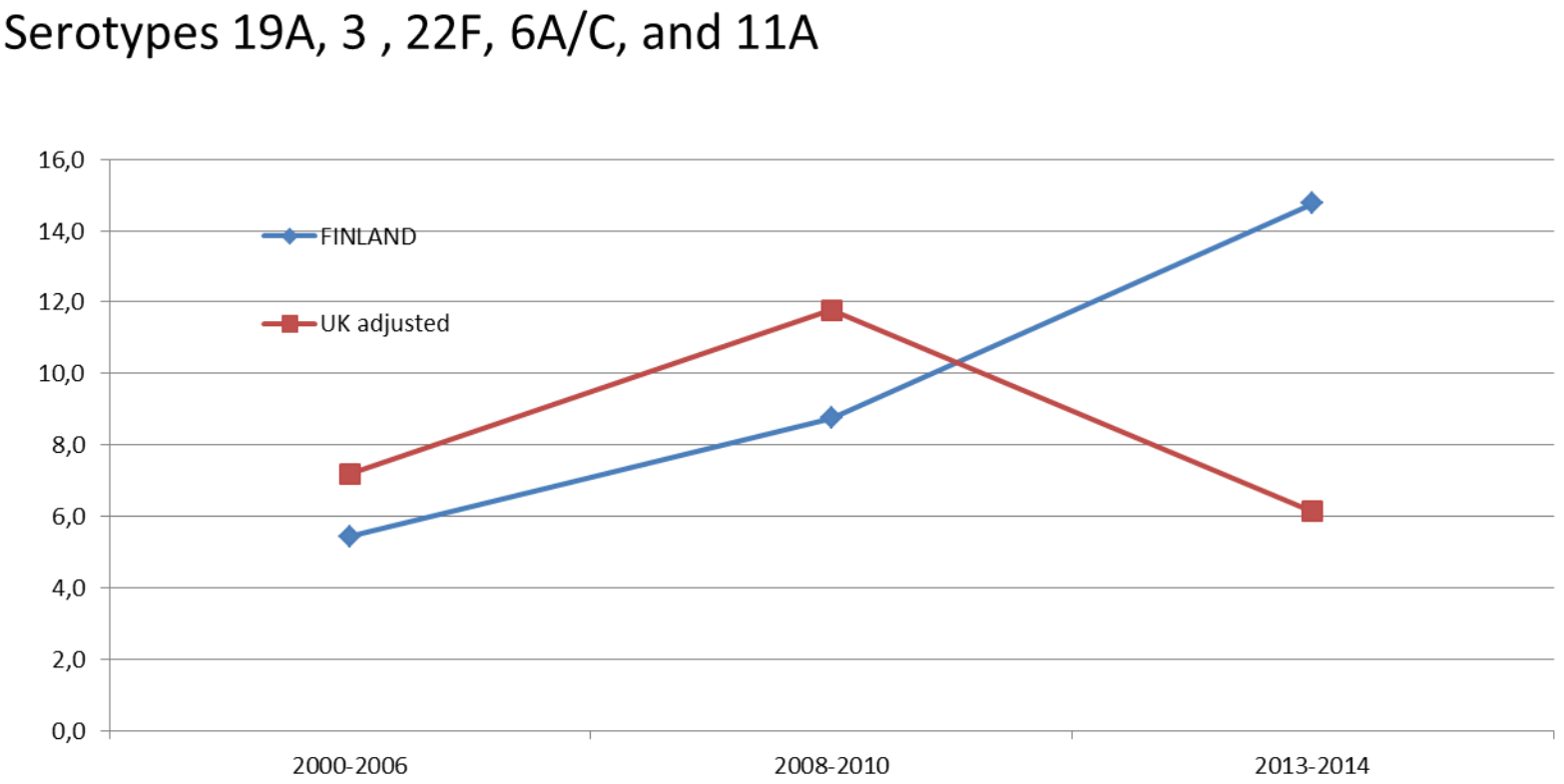

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Picking serotypes – up to >90 available

- The introduction of 7 or 10 or 13-valent vaccines have the potential to affect the ecology of all the serotypes
  - Adding any serotype in the vaccine, will affect the replament by the remaining serotypes
- Therefore, all disease needs to be evaluated, not only selected ones

- Public data available at www.thl.fi
  - data on individual serotypes by year and age groups
- Search for ”pneumococcal”
- You can pick your own!

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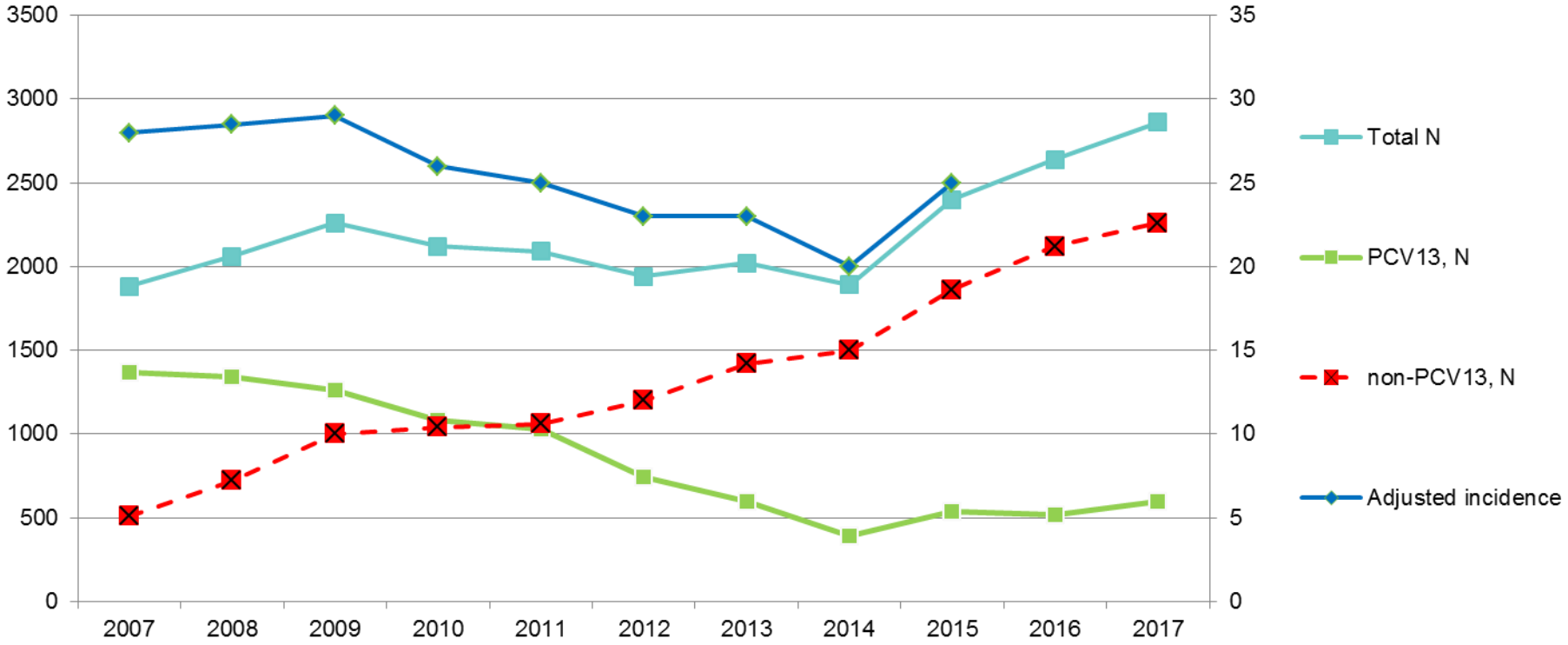
- **Full public health impact**:

Overall reductions in IPD and pneumonia in the elderly

Number of all IPD cases and adjusted incidence by epidemic year in the elderly (>=65 years) in England and Wales after infant PCV7/13 introduction in 2006/2010



Data sources: www.gov.uk, Waight et al, LancetID2015, Collins et al ISPPD2016

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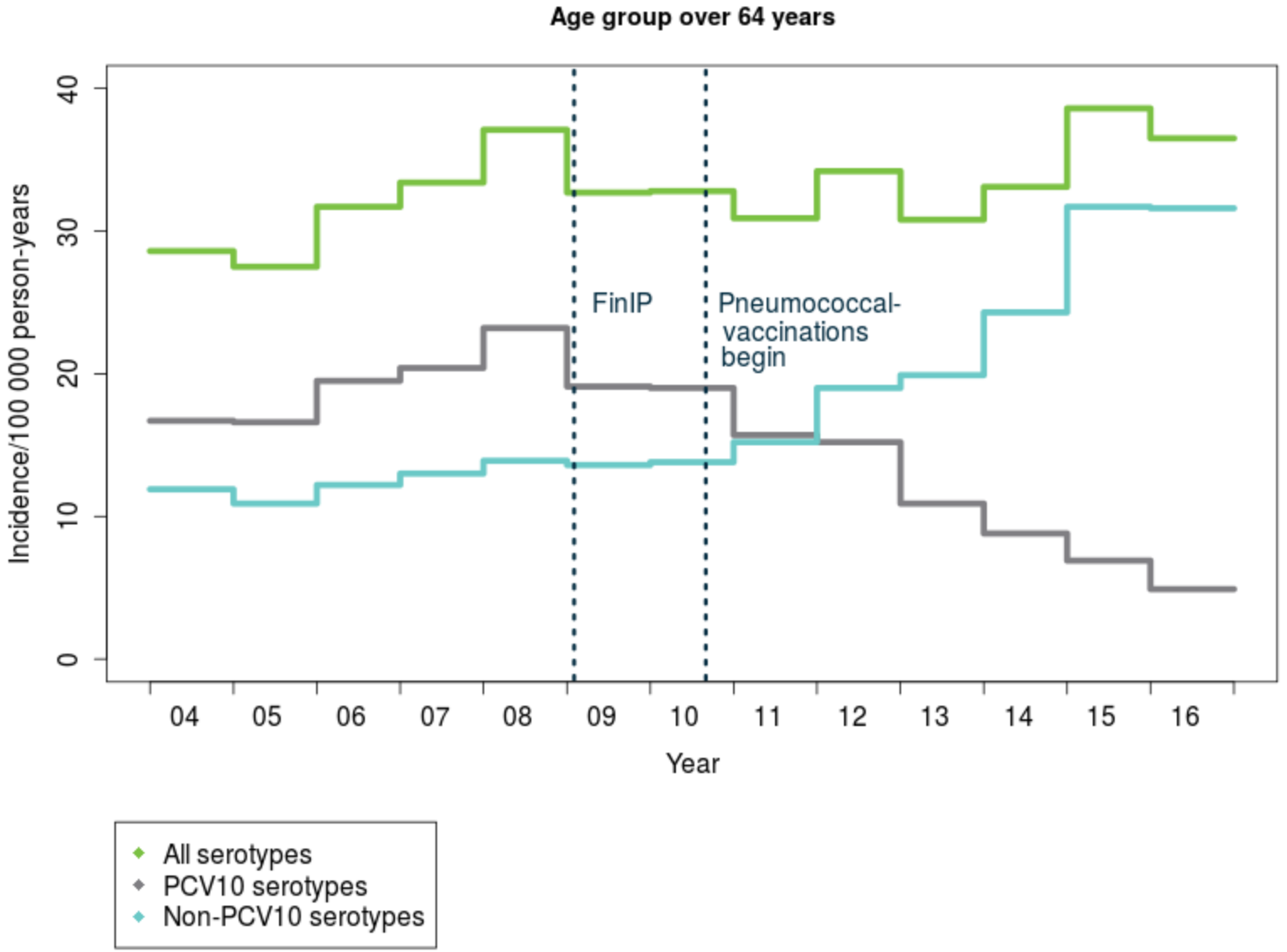
Incidence of all IPD cases by calendar year in the elderly (>=65 years) in Finland after infant PCV10 introduction in 2010



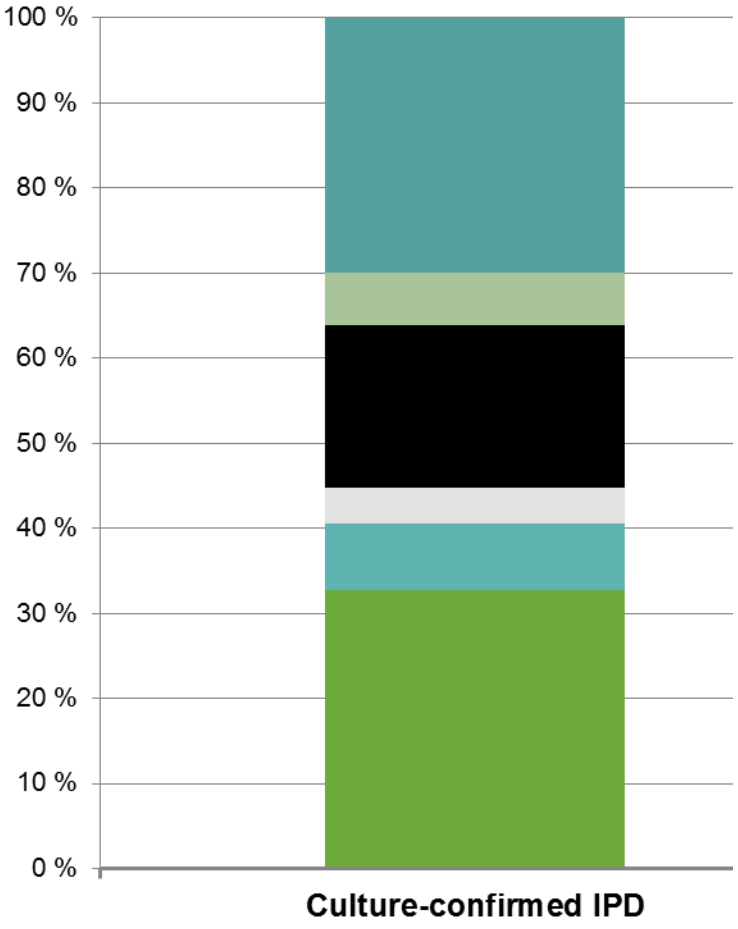
Reduction in the elderly population or not?

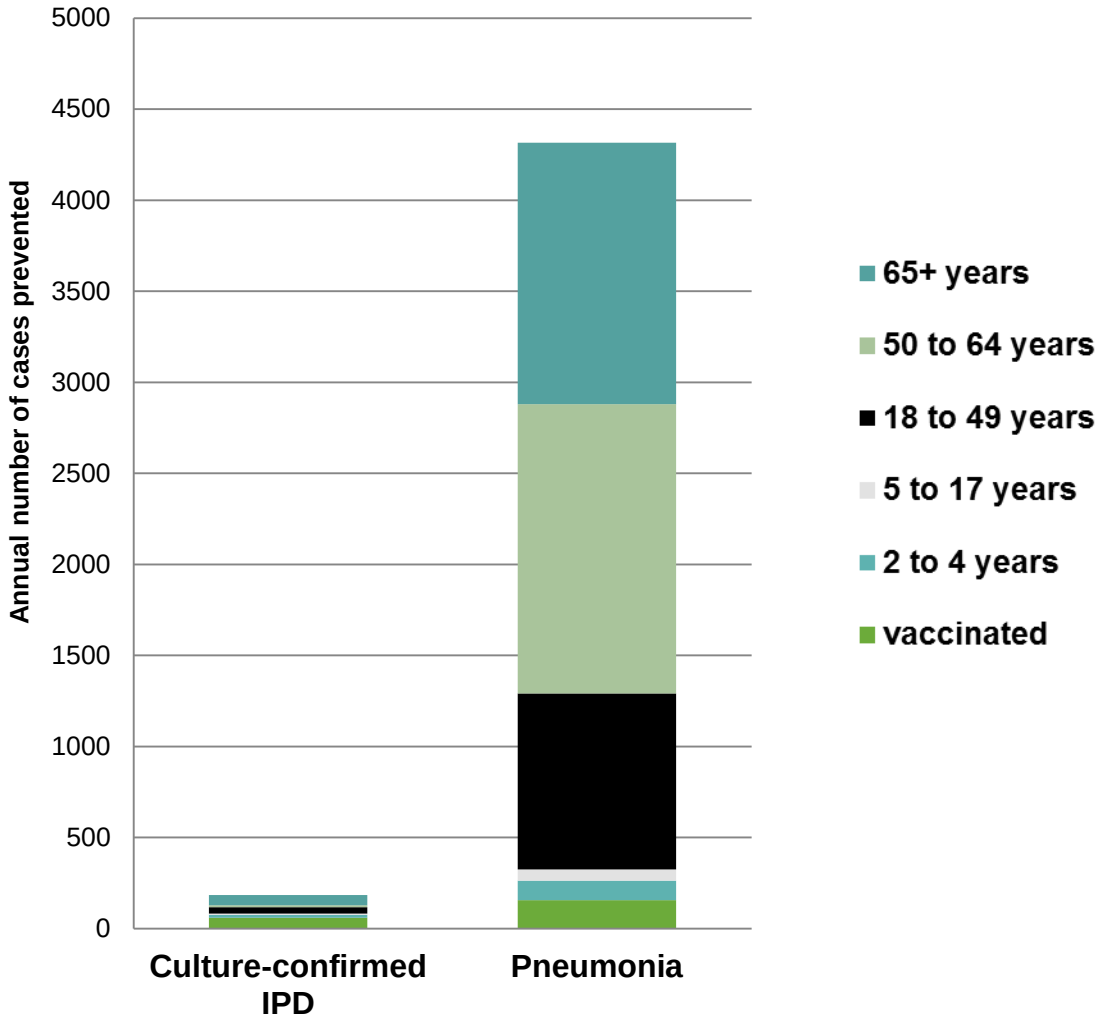
- Finland
  - No reduction in pre-post comparison, increase in 2015-2016
  - After adjustment for the baseline trend, 16% (ns.) reduction post PCV10

- England and Wales
  - After adjustment for the baseline trend, 19% reduction post PCV7 and further 25% reduction post PCV13 (2013-2014), but back to pre-PCV13 levels in 2015-2016

- Sweden, both PCV10 and PCV13 used in different counties (N=21)
  - No reduction in overall IPD observed (pre-PCV7 2005 compared to 2016)
  - However, 10-20% reduction comparing 2007-09 to 2013-16 (Naucler CID2017)
  - No reduction in Sweden/Stockholm with infant PCV13 (Galanis EurRespJ2016)

PCV10 impact on IPD and pneumonia by age group, proportion of number of prevented cases in Finland, with adjusted analyses for the elderly





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Public Health Perspective on the Impact Evaluation

- What's needed (=public health perspective)
  - **All disease syndromes** related to the pathogen, not only the severe ones
  - **Sensitive** case definitions relevant clinically and/or in public health
  - Effects on the **total population**, including indirect impact
  - **Long follow-up** times
  - **Effectiveness** studies and trials
  - **Absolute** incidences
  - **Adjustment** for baseline factors and trends where appropriate
- Useful, but not adequate
  - Coverage data, immunology, surrogates like carriage
- What's not needed (=cherry-picking)
  - Selected specific (microbiological) outcomes (only)
  - Focus on rare outcomes
  - Short per protocol follow-up periods, selected populations
  - Changes in proportions

ESSENTIAL FOR DECISION-MAKING
Question: How much disease will reduce due to the intervention?

LIMITED RELEVANCE FOR PUBLIC HEALTH OR CLINICAL DECISION-MAKING
Question: Does it work (in optimal conditions)?

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Acknowledgements

- Working group for the evaluation of the effectiveness of pneumococcal conjugate vaccination in the Finnish national vaccination programme
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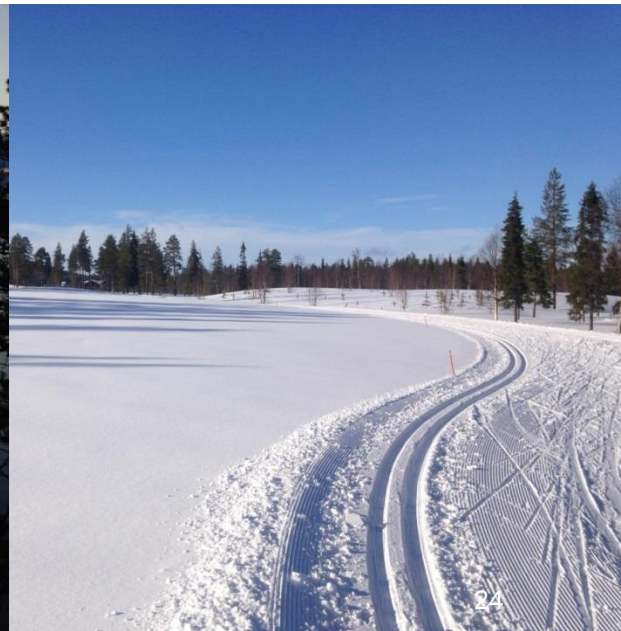
  - Heta Nieminen for animations





Nordic Vaccine Meeting 2018 in Helsinki

- **14-15 June 2018, Helsinki, Finland**
- Scandic Park Hotel

- https://www.thl.fi/en/web/vaccination/nordic-vaccine-meeting-2018

- WELCOME!