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National Institute for Health and Welfare, Finland



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Long-term population impact of infant 10-valent pneumococcal conjugate vaccination on adult invasive pneumococcal disease in Finland

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Adult Immunization Board
Helsinki, December 4, 2024



National Institute for Health and Welfare, Finland



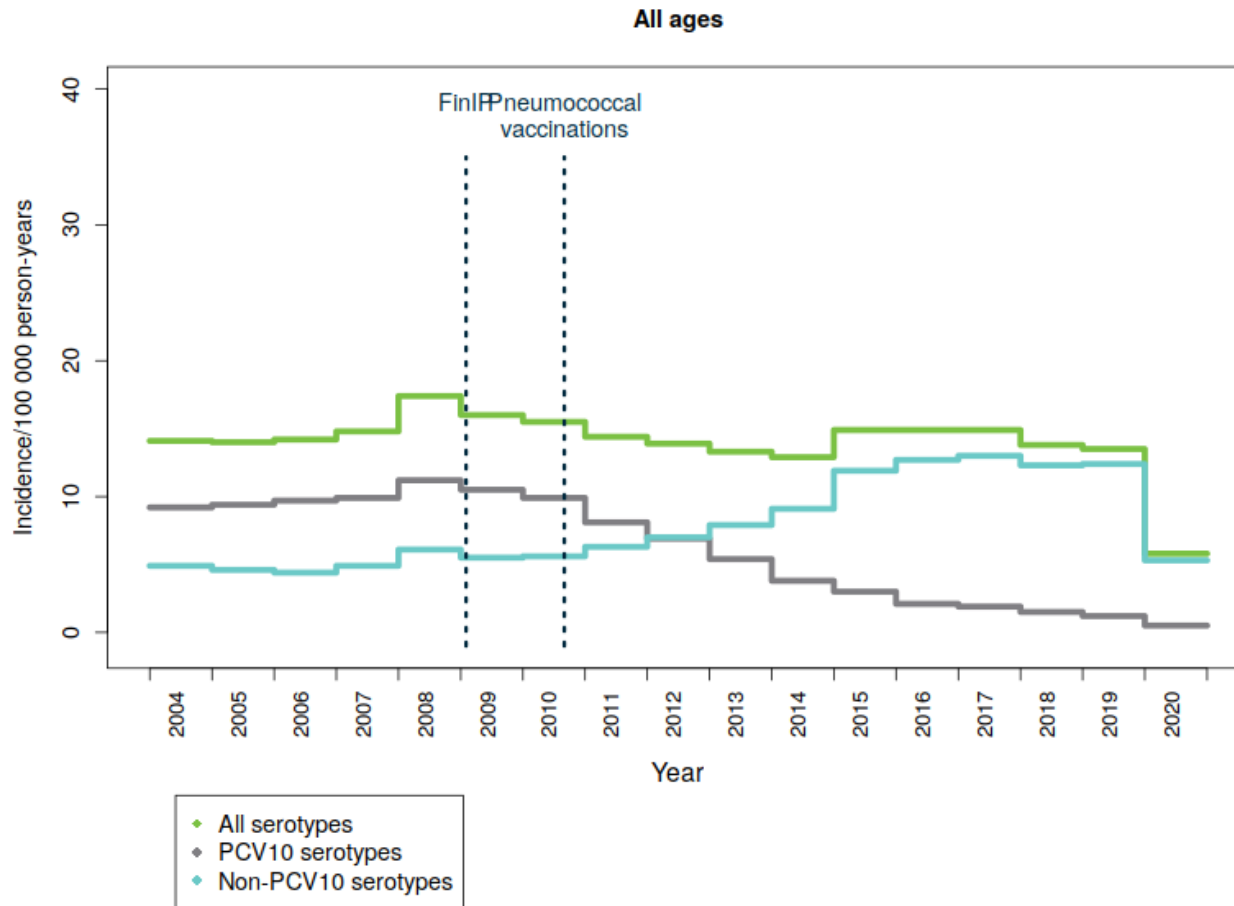
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Background

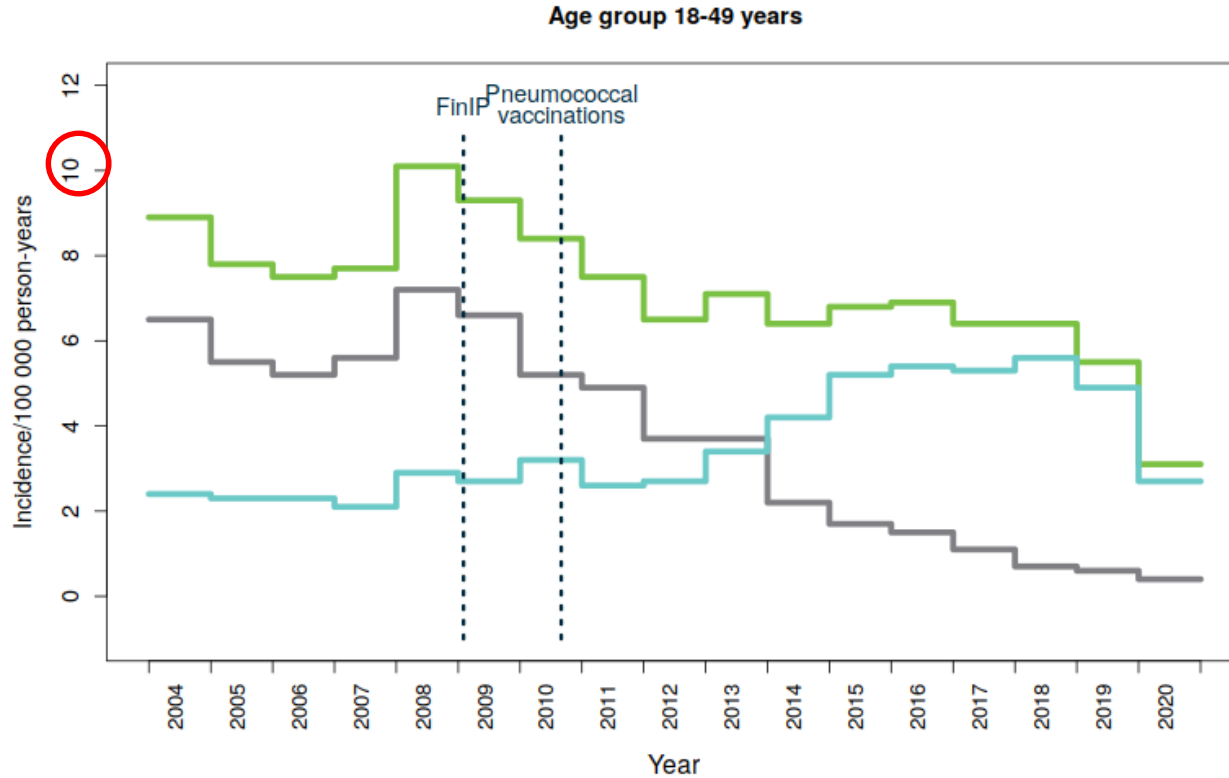
- Limited data are available on long-term indirect protection of infant PCV10 programs, particularly from settings without previous PCV use
- PCV10 introduced in the Finnish infant National Vaccine Program as first PCV in Sept 2010 (2+1 schedule)
- In earlier studies, estimates for reduction in PCV-type disease were reasonably consistent, but large differences have been reported for NVT replacement disease



Incidence of Invasive Pneumococcal Disease (IPD) - ALL AGES, Finland 2004-2020

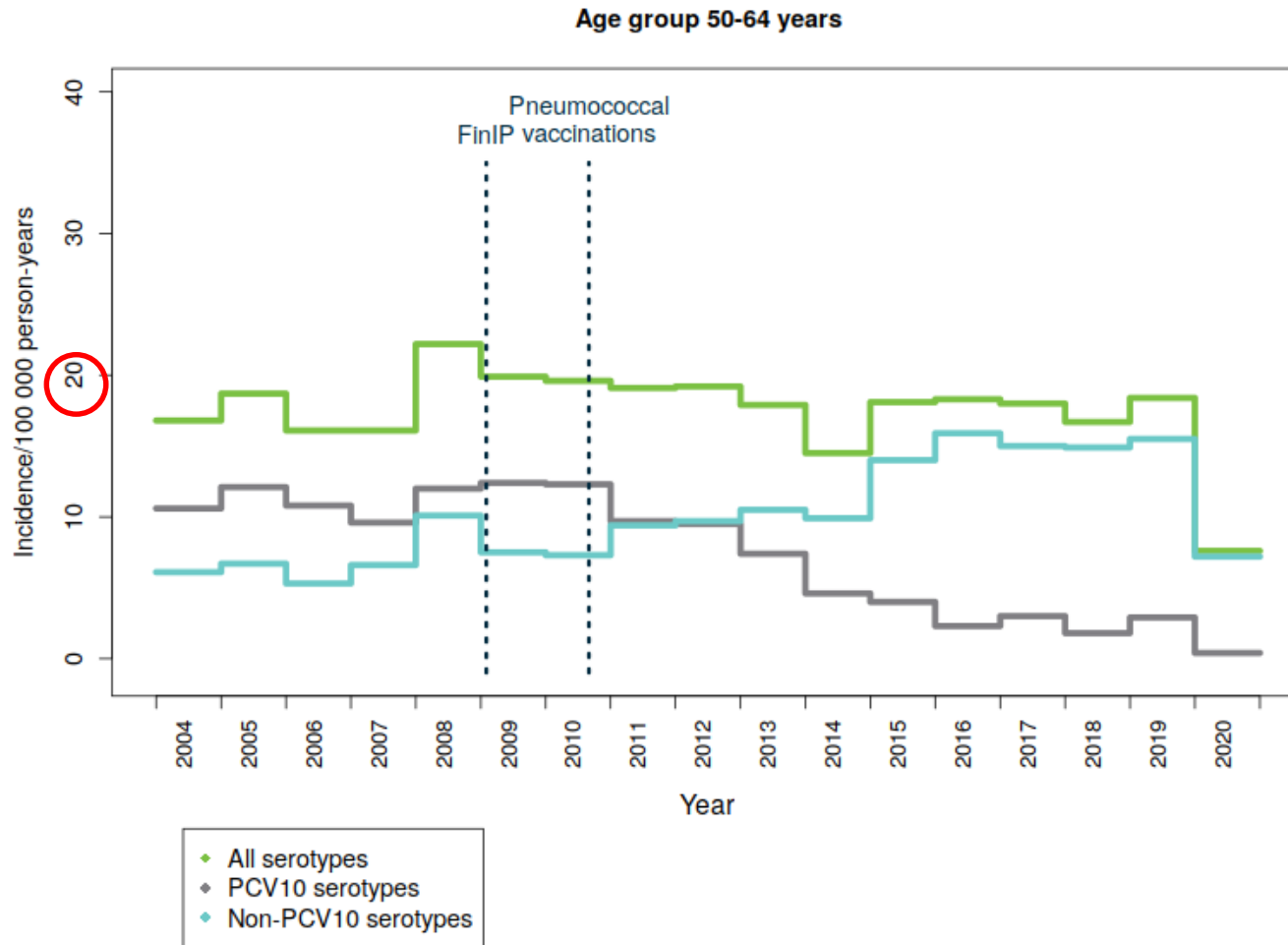


IPD incidence in adults 18-49 years by serotype group, NIDR Finland 2004-2020

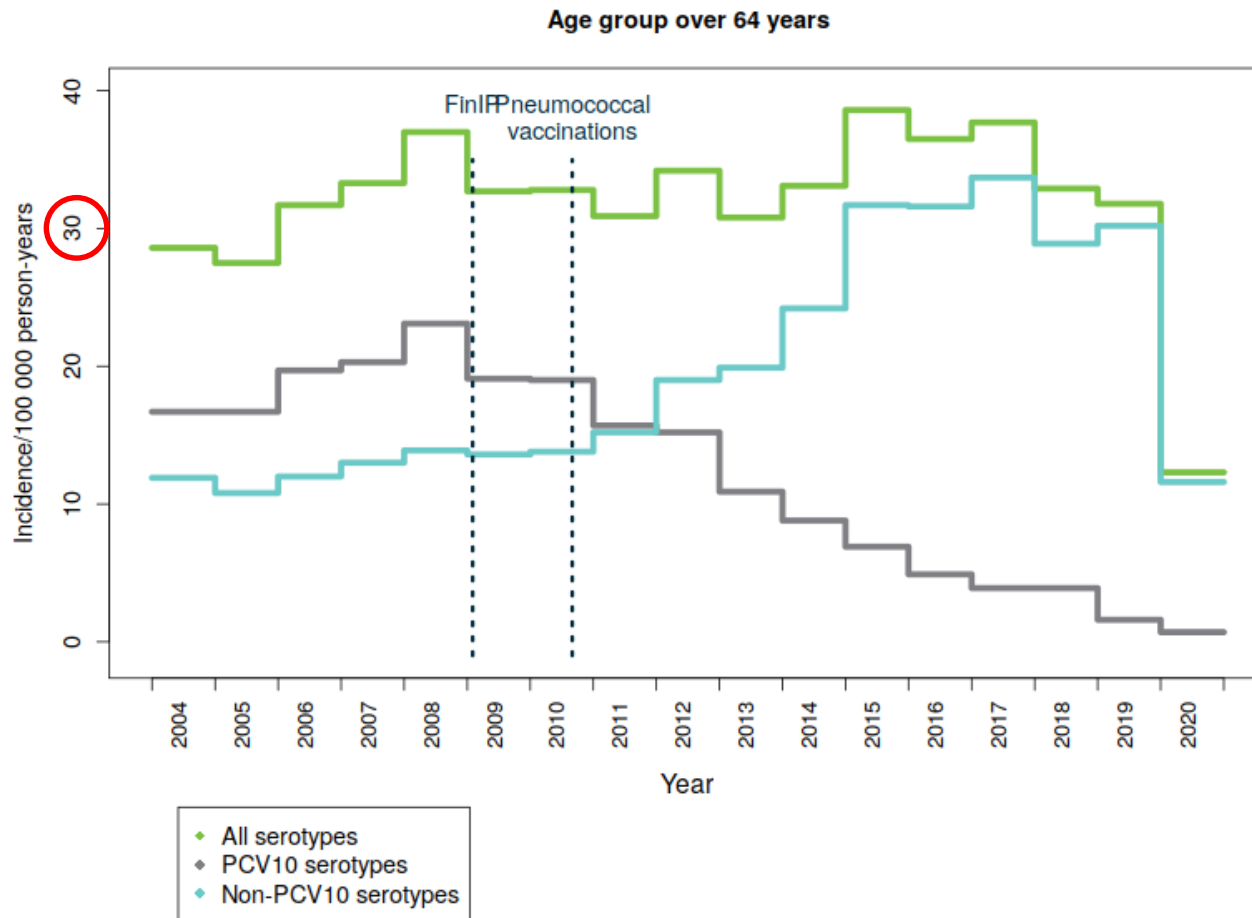


- ◆ All serotypes
- ◆ PCV10 serotypes
- ◆ Non-PCV10 serotypes

IPD incidence in adults 50-64 years by serotype group, NIDR Finland 2004-2020



IPD incidence in adults ≥ 65 years by serotype group, NIDR Finland 2004-2020



Objective

- We assessed long-term changes in invasive pneumococcal disease (IPD) incidence, mortality and serotype distribution in adults up to 9 years after infant PCV10 introduction
- A nationwide, population-based observational follow-up study



Methods

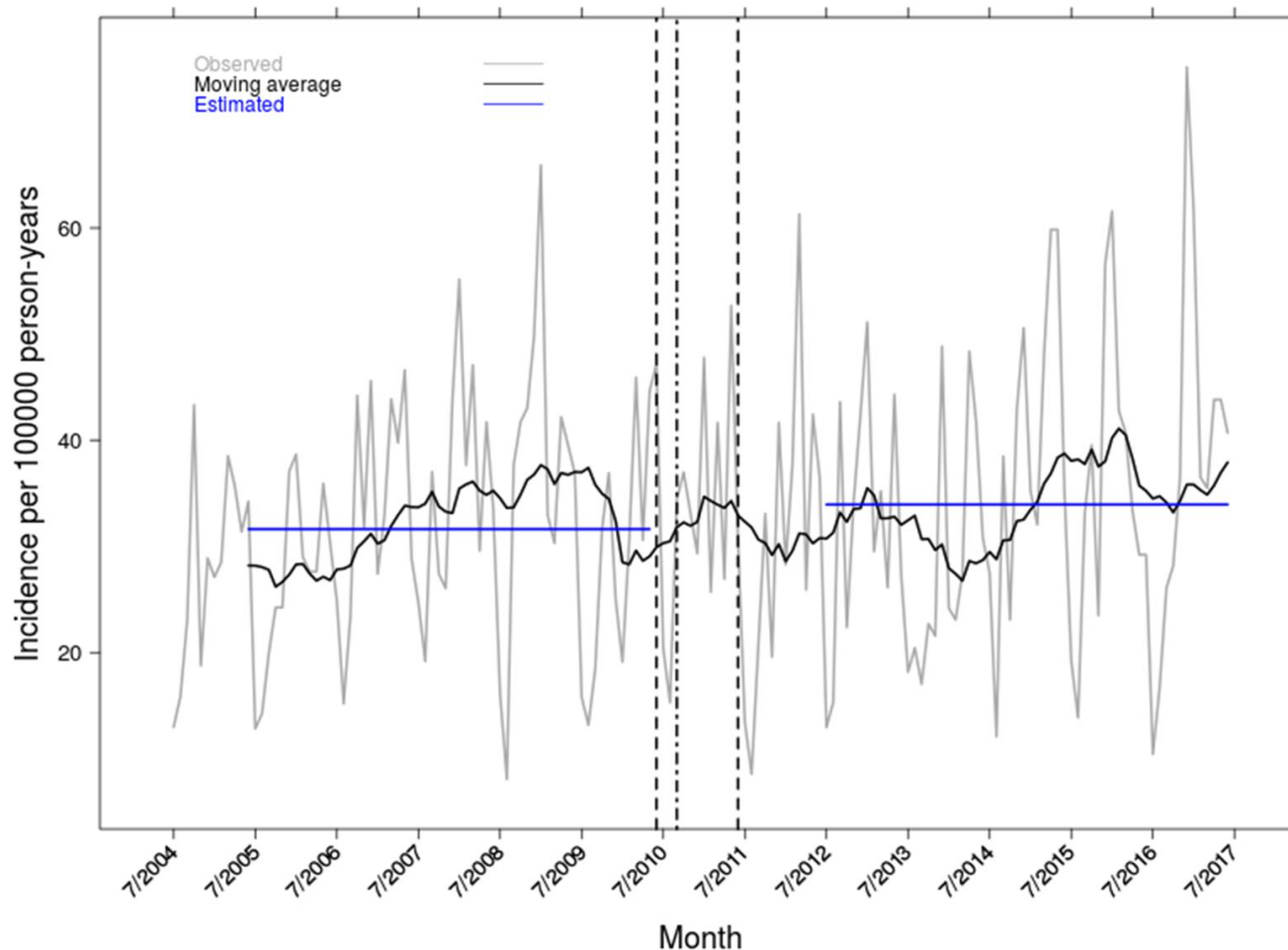
- **Case definition:** IPD case defined as *S. pneumoniae* isolated from blood or CSF.
- Culture dates from July 1, 2004 to June 30, 2019
- IPD cases ≥ 18 years were identified through national, population-based laboratory surveillance, the National Infectious Disease Register (NIDR)
- All clinical microbiology laboratories (n=22) report and submit isolates to THL reference laboratory for serotyping



Statistical analysis

- Surveillance data linked with the Population Information System (PIS) to conduct interrupted time-series analysis (ITSA)
- Denominators (person-years) from PIS were used to calculate age- and serotype group-specific rates
- We compared IPD incidence during **PCV10 period** (7/2011-6/2019) with **pre-PCV10 baseline** (7/2004-6/2010); transition period (7/2010-6/2011) was excluded
- **ITSA:** Negative binomial regression models adjusted for pre-PCV10 trend, seasonality, and changes in population size
- Model assumption: continuation of pre-vaccine trend after PCV10 introduction

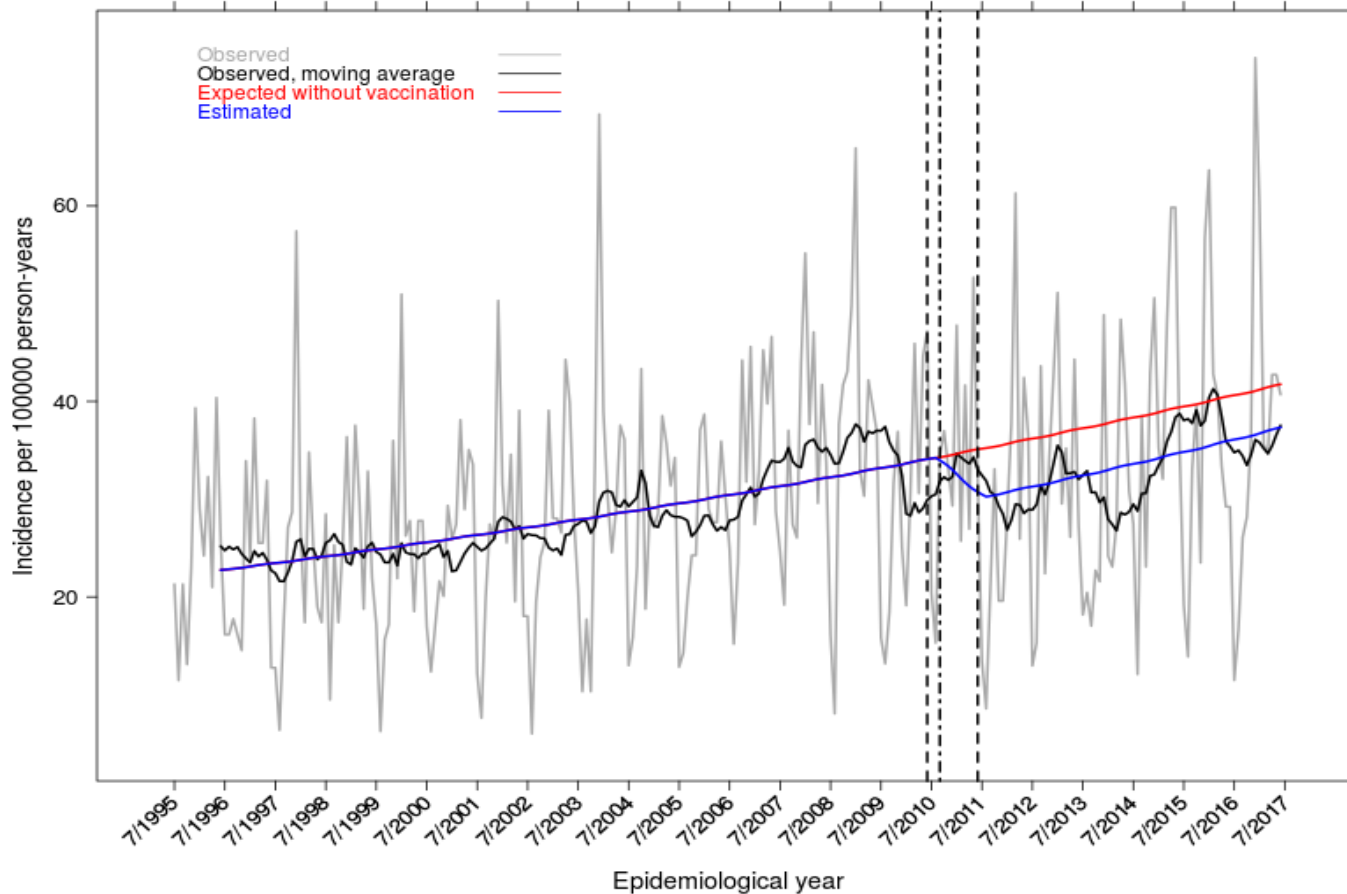
Estimated overall IPD incidence in persons ≥ 65 years before and after infant PCV10 introduction assuming constant incidence - NO adjustment for pre-PCV10 trend



Evidence supporting the long-term trend assumption:

Overall IPD incidence in adults ≥ 65 years by epidemiological year, Finland, 1995 – 2017 (ITSA)

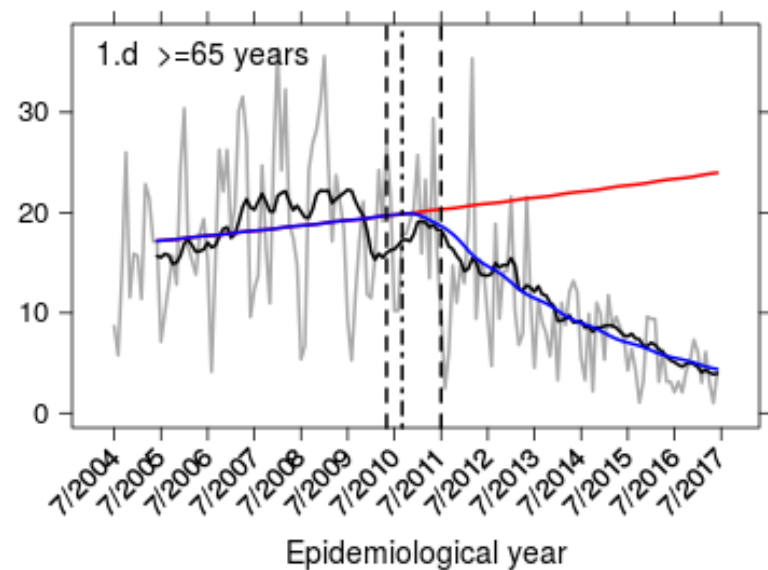
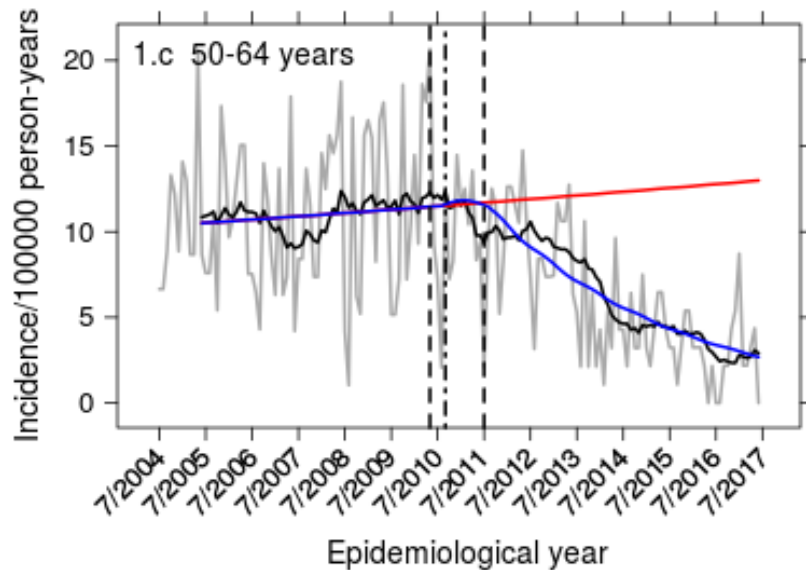
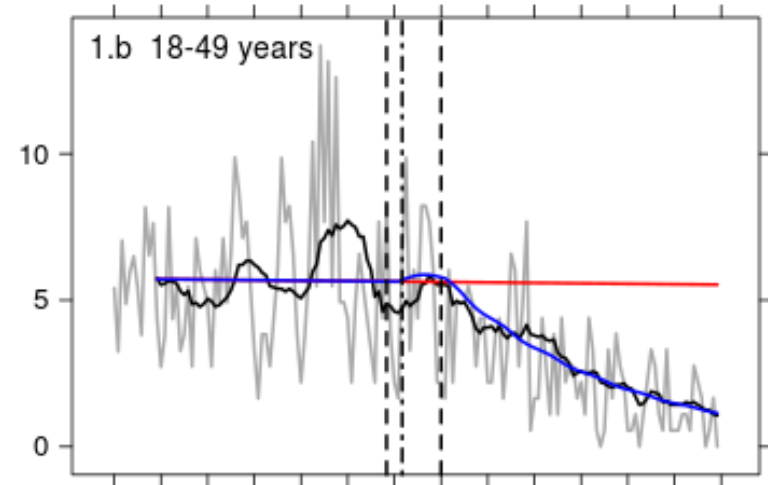
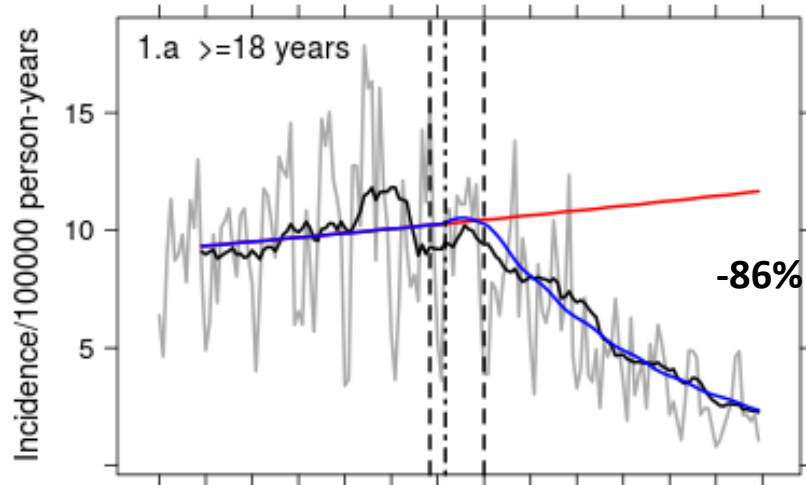
During pre-PCV10 period, adult IPD incidence increased yearly by **4.8%**



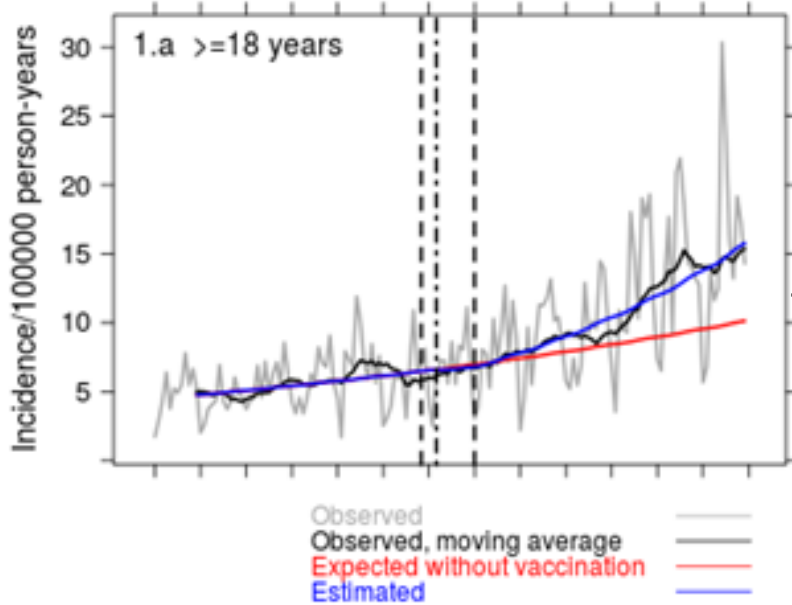
Results

- From 7/2004 to 6/2019
- 9833 total IPD cases in adults ≥ 18 years of age
- Median age, 64 years (IQR, 51-75 years)
- 85% were bacteremic pneumonia, 4.5% meningitis and 11.5% bacteremia or other

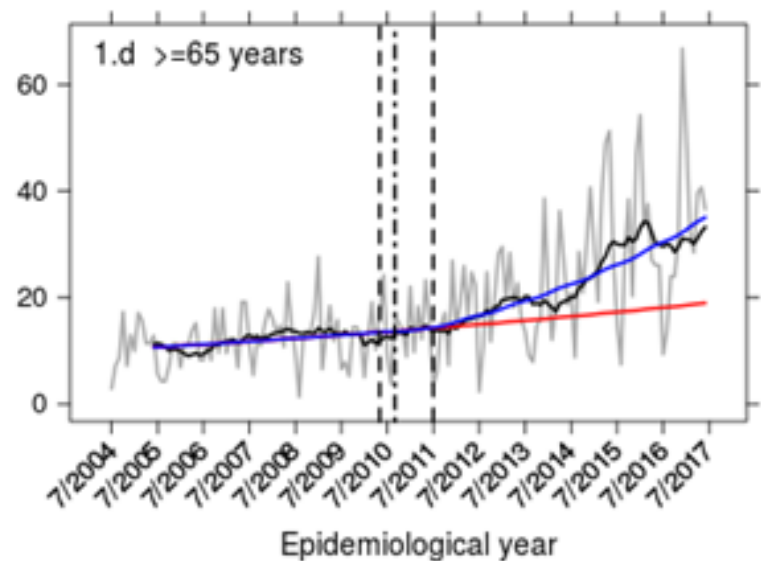
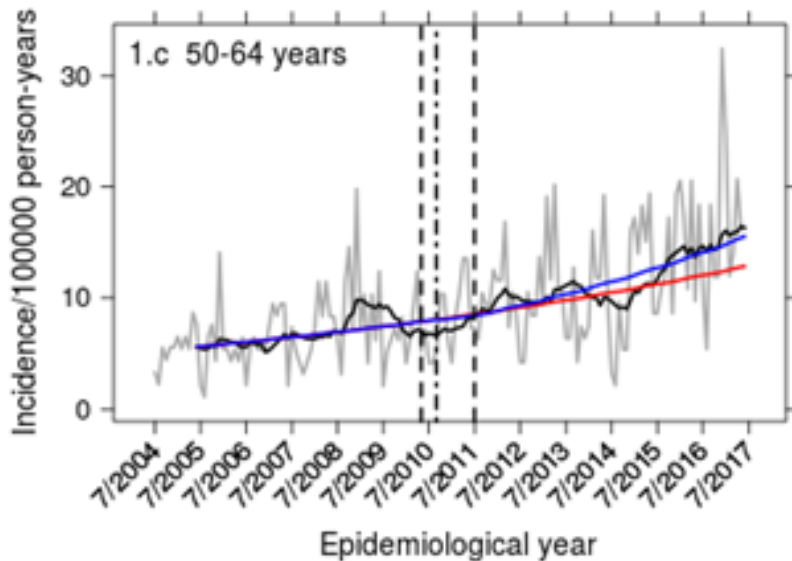
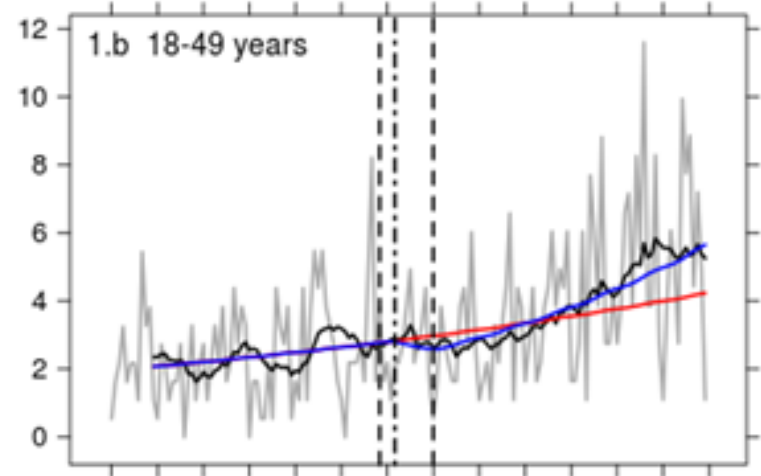
Observed and expected incidence of PCV10-type invasive pneumococcal disease in adults by age-group (ITSA with trend and seasonality adjustment)



Observed and expected incidence of **non-PCV10-type** IPD in adults by age-group (ITSA with trend and seasonality adjustment)

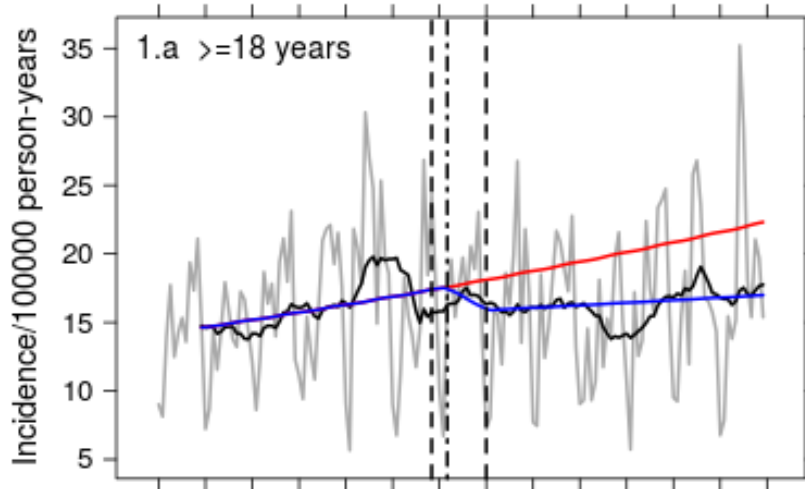


+40%
NS

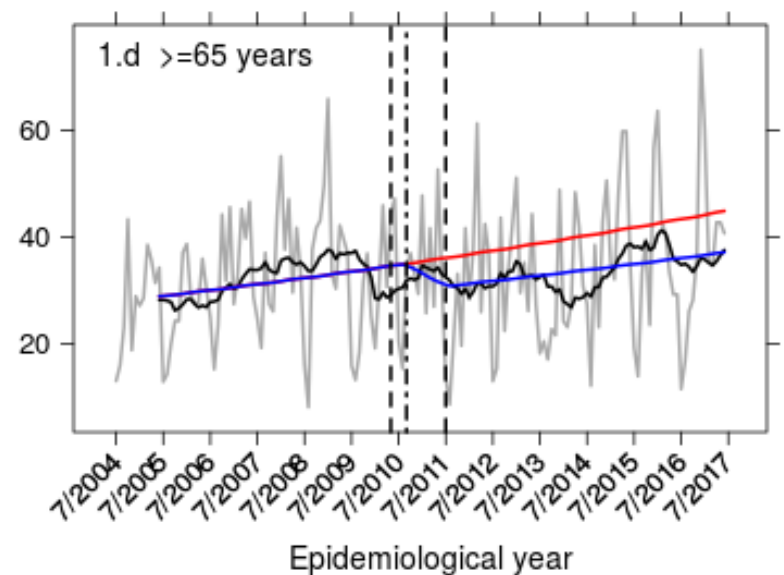
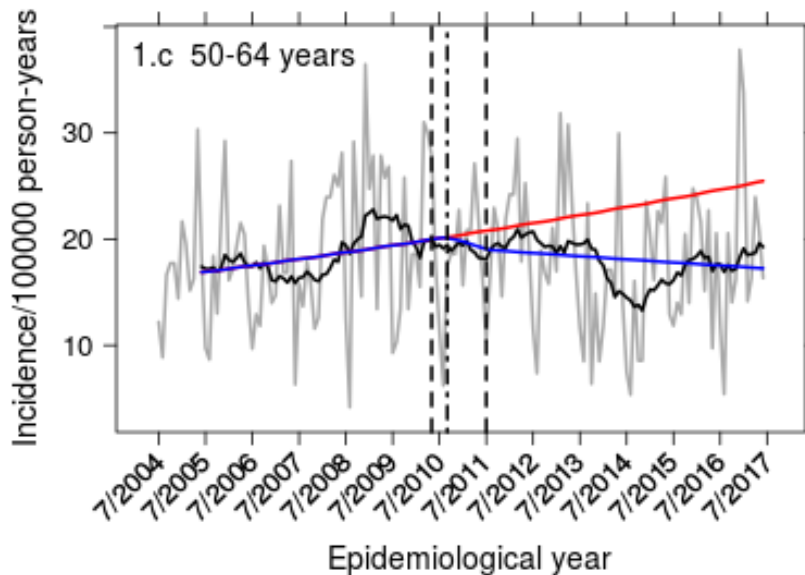
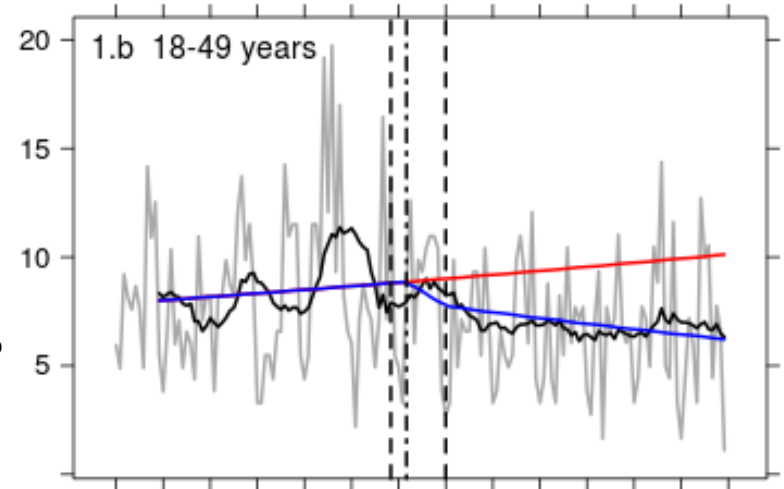


+70%
NS

Observed and expected incidence of **all IPD** in adults ≥ 18 years of age, interrupted time-series analysis (ITSA with trend and seasonality adjustment)

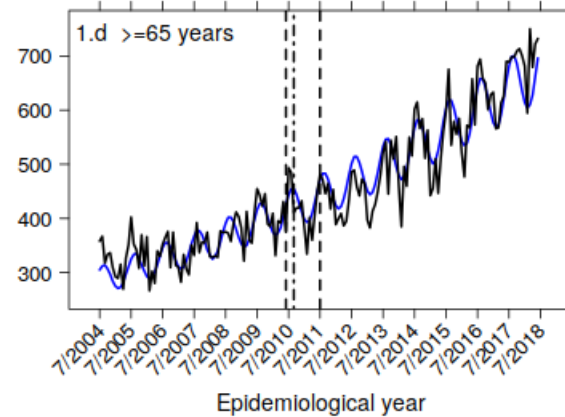
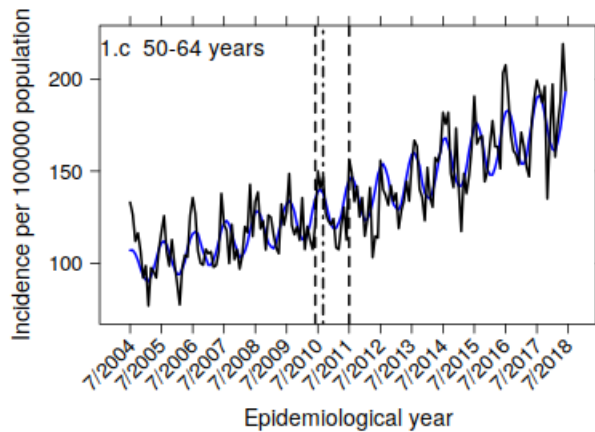
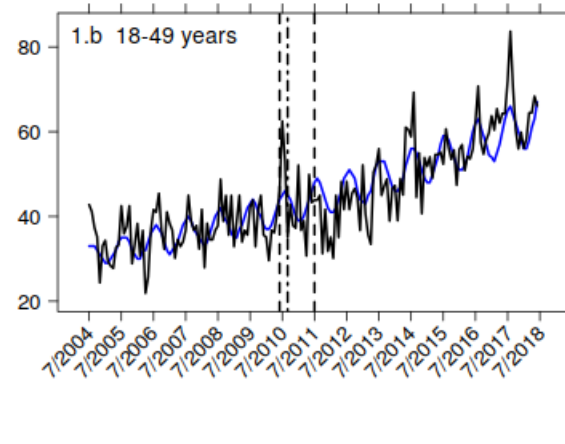
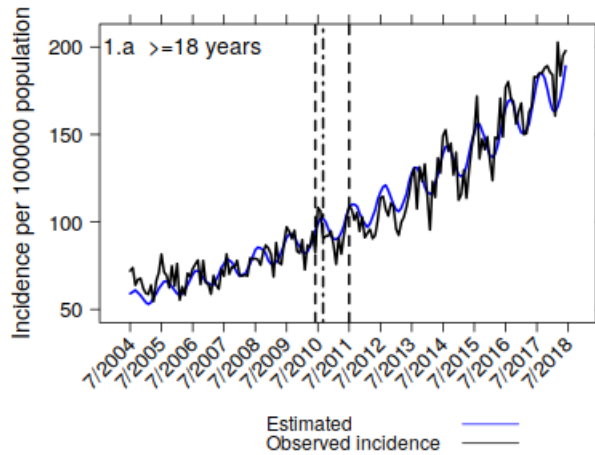


-33%

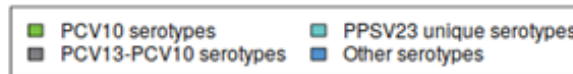
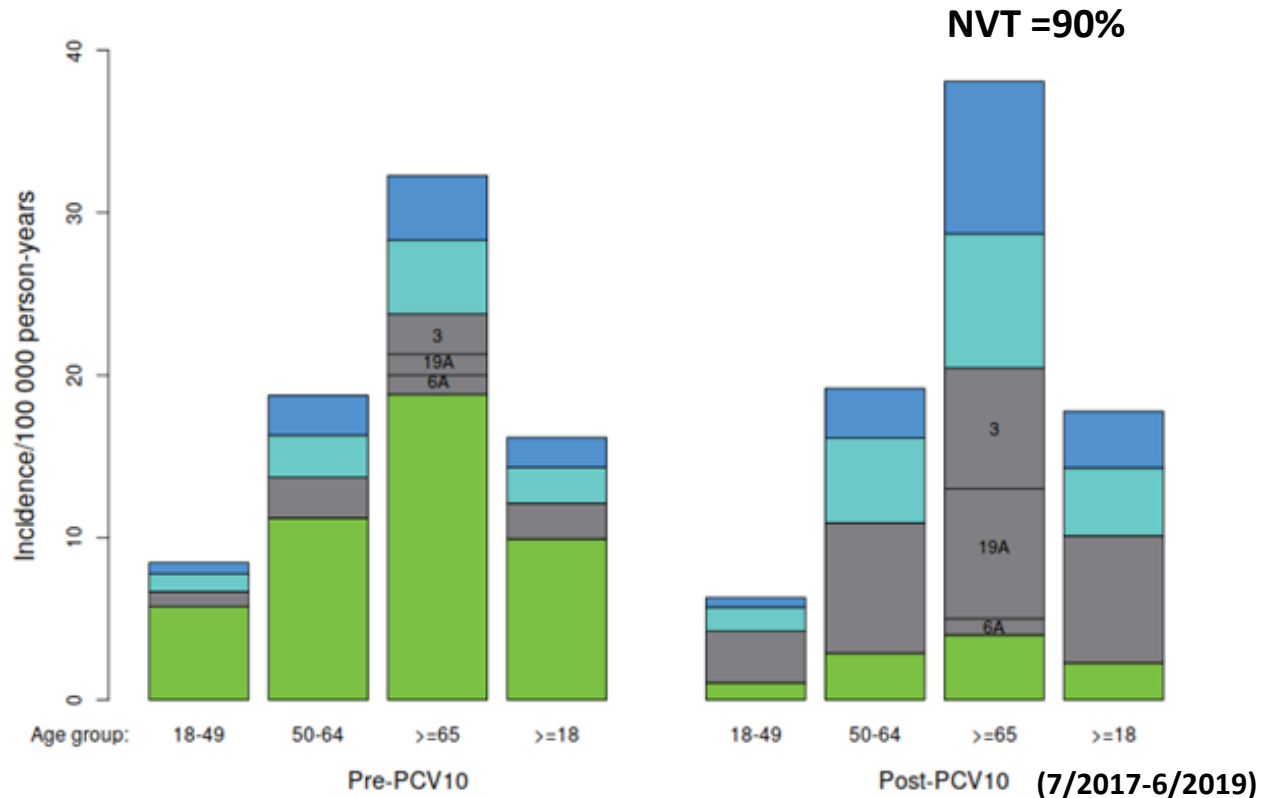


-31%

CONTROL CONDITIONS: Incidence of non-pneumococcal invasive bacterial infections reported to NIDR July/2004 – June/2018 – ITSA



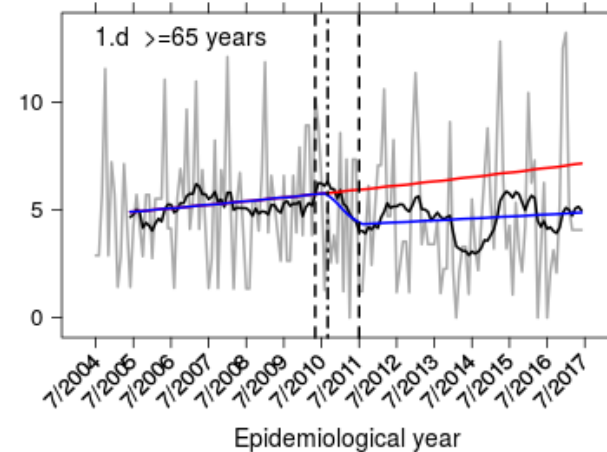
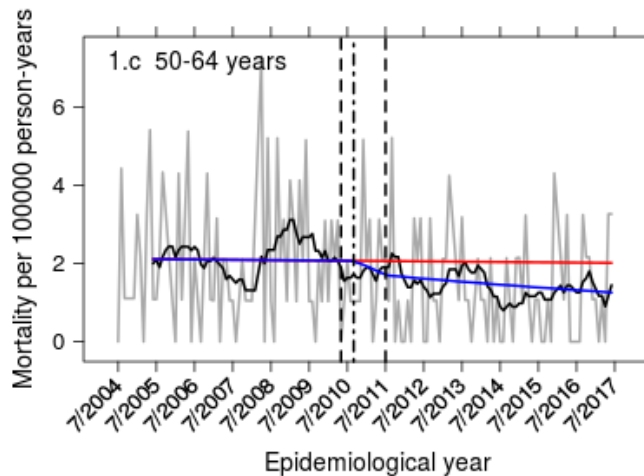
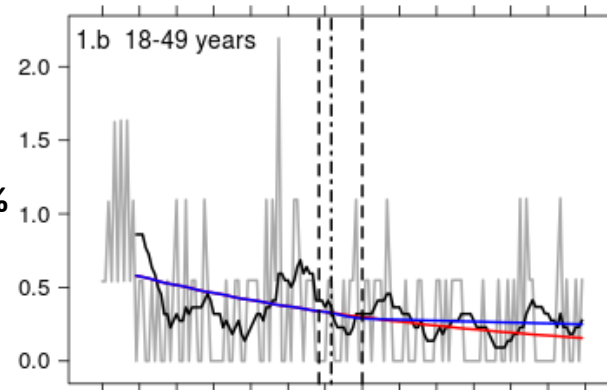
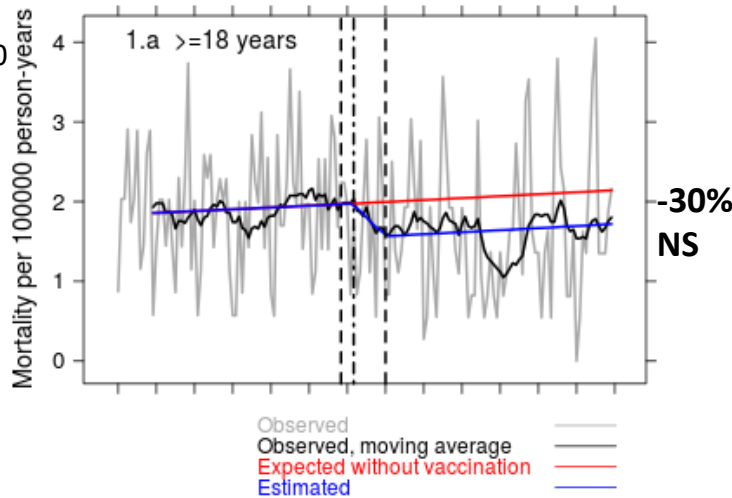
Changes in *absolute* IPD incidence rates in adults before PCV10 introduction and last two study years (2017-2019)



NVT: 3, 19A, 22F, 6C

Observed and expected 30-day mortality rates for ALL IPD-associated deaths (n=1042) by age group (ITSA)

CFP: 11.9 vs. 10.0
P<0.01



CFP: 16.7 vs. 13.7
P<0.01

Conclusions

- PCV10 serotype IPD: significant reductions in in all adult age groups
- With pre-vaccine trend adjustment, estimated reduction in overall adult IPD incidence was 33%.
- Young and working age adults
 - indirect effects appear to have reversed the increasing pre-PCV10 IPD trend – substantial relative rate reductions
- CFP declined, particularly in older adults
- Older adults
 - after initial level decline, IPD incidence continued to increase following PCV10 introduction
- NVT replacement (3, 19A, 22F and 6C) in all age groups, mostly in older
 - leveled off after first 5 years
 - steady state where NVT accounted for 90% of IPD
- Considerable remaining burden of pneumococcal bacteremia and pneumonia in older adults

Discussion 1

- Estimates of indirect vaccine impact may differ depending on the analytic method, particularly whether long-term secular trends in incidence are accounted for
- Adjusting for the pre-vaccine trend in the ITSA model resulted in larger point estimates for relative reductions in overall IPD and smaller point estimates for non-PCV10 serotype increases than before-after analysis (data not shown)

Discussion 2

- In the presence of increasing pre-vaccine trend, ignoring the trend in analysis may underestimate indirect effects and overestimate replacement
- However, the assumption of continuing pre-PCV trend during PCV period cannot always be verified
- Analysis of control outcomes supported the assumption
- Comparability of reported indirect PCV effects from different study sites might be improved if similar analytic methods were used





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Long-term population impact of infant 10-valent pneumococcal conjugate vaccination on invasive pneumococcal disease in adults in Finland

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ABSTRACT

Background: Limited data are available on long-term indirect effects of ten-valent pneumococcal conjugate vaccine (PCV10) programmes. We evaluated changes in invasive pneumococcal disease (IPD) incidence, mortality, and serotype distribution in adults up to 9 years after infant PCV10 introduction.

Methods: Culture-confirmed IPD cases ≥ 18 years ($n = 5610$; 85% were pneumonia) were identified through national, population-based laboratory surveillance; data were linked with population registry to conduct nationwide follow-up study. In a time-series model, we compared serotype-specific IPD incidence and associated 30-day mortality rates before and after PCV10 by using negative binomial regression models.

Results: During pre-PCV10 period (7/2004–6/2010), overall IPD incidence in adults ≥ 18 years increased yearly by 4.8%. After adjusting for trend and seasonality, the observed PCV10 serotype IPD incidence in 7/2018–6/2019 was 90% (12/100,000 person-years) lower than the expected rate without PCV10 program. Non-PCV10 serotype incidence was 40% (4.4/100,000 person-years) higher than expected; serotypes 3, 19A, 22F, and 6C accounted for most of the rate increase. However, incidence of non-PCV10 IPD levelled off by end of follow-up. The observed-expected incidence rate-ratio (IRR) was 0.7 (95 %CI 0.5–0.8) for all IPD and 0.7 (95 %CI 0.3–1.3) for IPD-associated 30-day mortality. Case-fatality proportion decreased from 11.9% to 10.0% ($p < 0.01$). In persons ≥ 65 years, the IRR was 0.7 (95 %CI 0.5–0.95).

Conclusions: Significant indirect effects were seen for vaccine-serotype IPD and for overall IPD in all adult age groups. For non-vaccine IPD, the incidence stabilized 5 years after infant PCV10 program introduction, resulting in a steady state in which non-vaccine IPD accounted for nearly 90% of overall IPD. Substantial pneumococcal disease burden remains in older adults.

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Backup slides



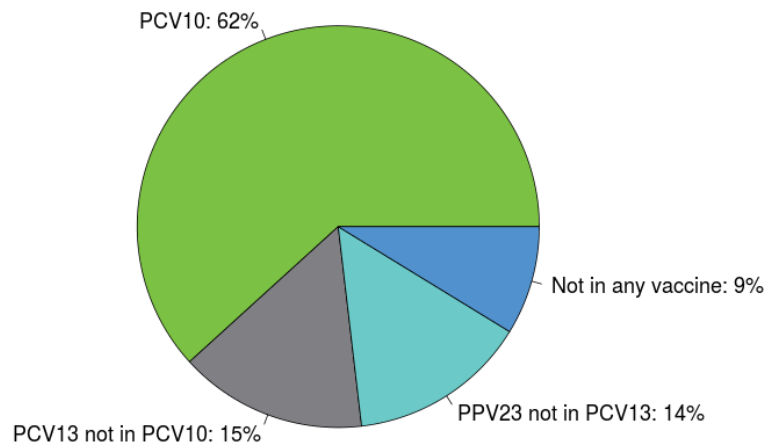
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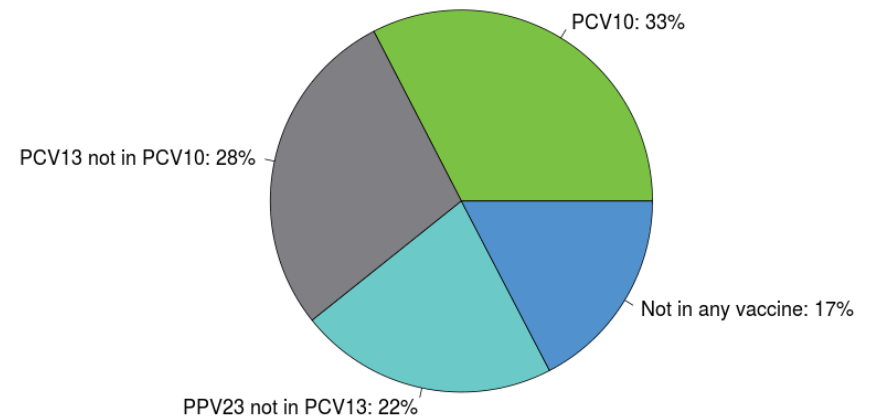
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Proportion of IPD cases in persons ≥ 65 years of age with chronic medical conditions by serotype group before and after PCV10

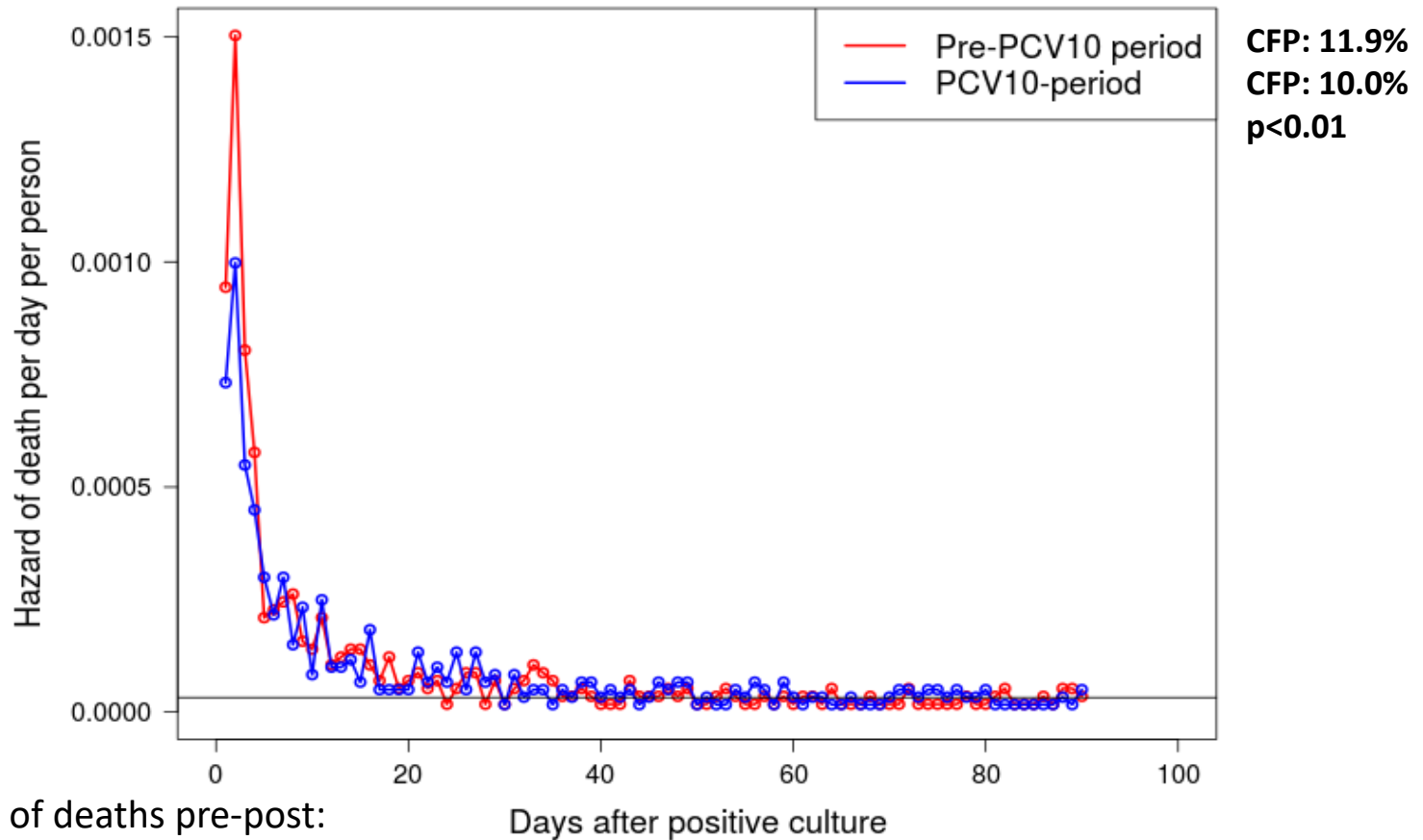
Pre-PCV10 period



PCV10 period

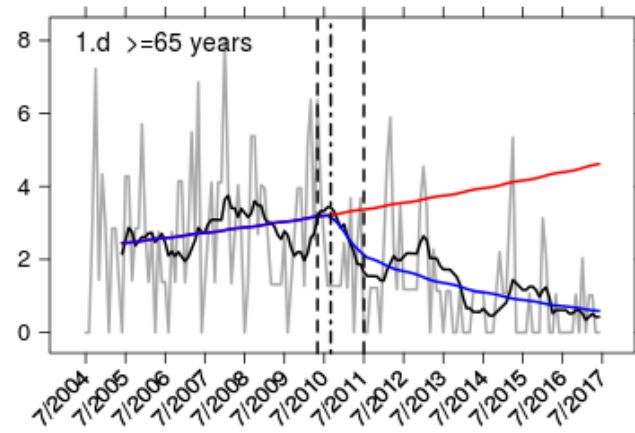
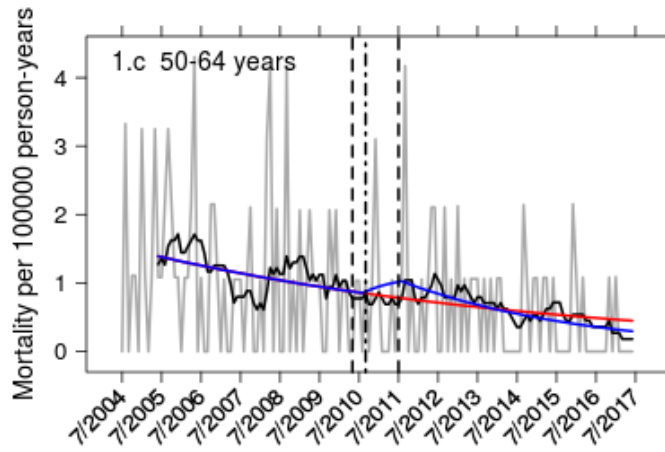
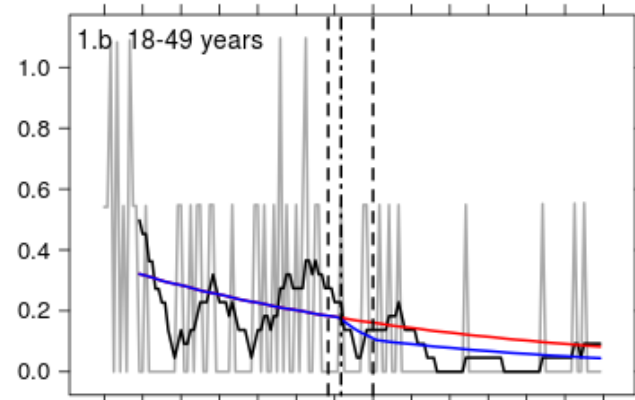
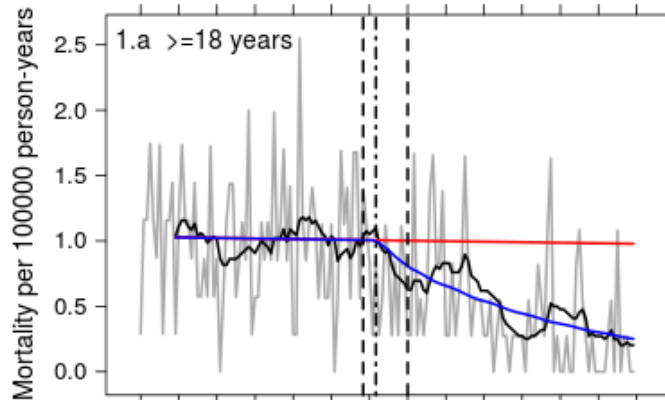


The daily hazard of death observed among adult IPD cases during 90 days after first positive culture and in the general population ≥ 18 years, Finland



Proportion of deaths pre-post:
0-2 days: 46% and 38% ($p=0.01$)
0-7 days: 67% and 63%

Observed and expected 30-day mortality rates for PCV10 type IPD-associated deaths by age group

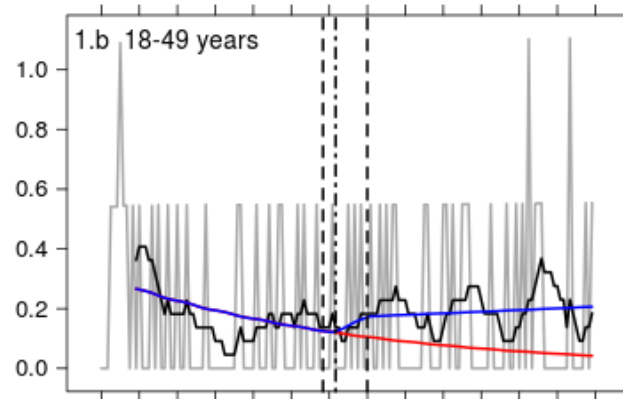
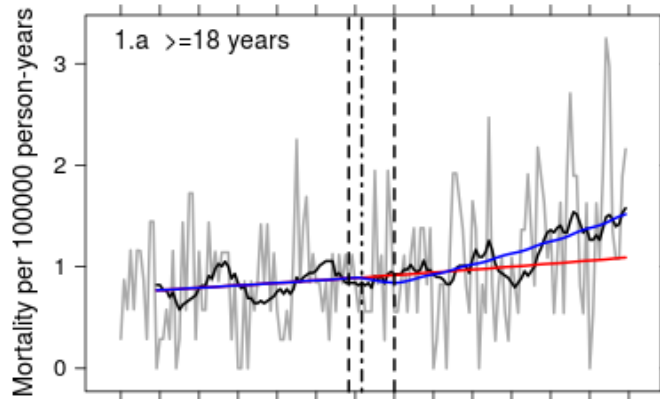


Observed —
Observed, moving average —
Expected without vaccination —
Estimated —

Epidemiological year

Epidemiological year

Observed and expected 30-day mortality rates for **non-PCV10 type IPD** -associated deaths by age group



Observed —
Observed, moving average —
Expected without vaccination —
Estimated —

