

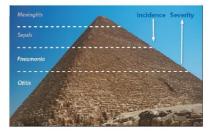
Objectives

- > Epidemiology of pneumococcal infections after PCV10
- Role of infant vaccinations for elderly
- Influence of the SARS-CoV2 pandemic on pneumococcal infections

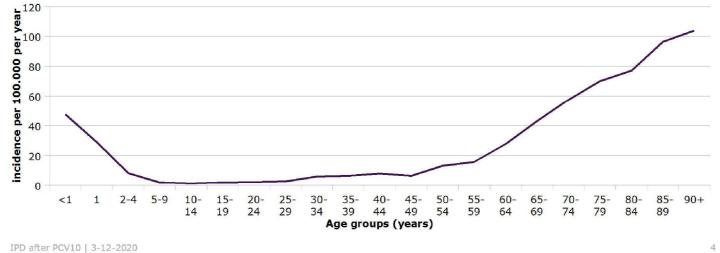
Pneumococcal disease

- > Streptococcus pneumoniae gram-positive bacterium
- › Polysaccharide capsule
 - Virulence factor
 - > 90 serotypes
- > Commensal upper respiratory tract
 - Carriage prevalence: Children 60-90%; elderly 5-10%
- > Disease
 - Invasive disease (IPD) \rightarrow meningitis, sepsis, invasive pneumonia
 - Non-invasive disease \rightarrow pneumonia, otitis media
- > High incidence in young children and elderly

IPD after PCV10 | 3-12-2020



IPD by age



Pneumococcal vaccination

POLYSACCHARIDE VACCINES

- Not immunogenic in children
- > No memory induced
- > No booster response
- > Short duration of protection
- > PPV23

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CONJUGATE VACCINES

- Polysaccharide conjugated to carrier protein
- > Immunogenic in children
- Memory induced and booster response
- > Longer duration of protection

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PCV7, PCV10, PCV13, (PCV15/20)

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Pneumococcal vaccines

Vaccine	Serotypes												
PCV7	4	6B	9V	14	18C	19F	23F						
PCV10	4	6B	9V	14	18C	19F	23F	1	5	7F			
PCV13	4	6B	9V	14	18C	19F	23F	1	5	7F	3	6A	19A

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Pneumococcal vaccination

	Honths											Years														
	2	3	4	Concession of the local division of the loca	6	10	u	12	13	14	15	18	23	2	3 PC	5	6	12	18	19	50	60	64	65	75	22
Austria		PCV	PC	.v		PCV			PCV ^s				icv		PC	v				_	_		PO	V13 ²		
Belgium	PCV		PCV					PCV													P	nc)			Pnc*	
Bulgaria	PGV		PCV					PCV ⁶																		
Creatia	PCV ⁴		PCV ⁴					PCV ⁴																		
Cyprus	PCV		PCV	1					PC	N ⁹								PPS	W23 ¹						PPSV23	
Czech Republic		PCV®		PCV ¹⁸				PCV ^{IB}													Pnc ⁸⁸				Pnc ¹³	
Denmark		PCV13		PCV13				PCV13																	PSV23 ¹	•
Estonia																										
Finland		PCV10		PCV10				PCV10																POV	13+191951	/2314
France	PCV		PCV				PCV														PCV ^{ca}					
Germany	PCV		PCV					P	ev.			PCV ^{ss}												PP5V23 ^s		
Greece	PCV13		PCV13		PCV18			PCV13					PC	/113			PEV	13+PP5V	/2318		PCV13	PP5V23		PCV	13+ PPS	V23
Hungary	PCV13		PCV13					POV13															PP	5V23		
Iceland		PCV10		PCV10				PCV10																PPSV23 ¹	1	
Ircland	PCV				PCV				PCV																PSV23	
Italy		- 100		nme			PCV																	POV	3+PP5	/23 ³¹
Latvia	pneur	mococcal	conjuga	ite vaccir	ne, 13-1	valent			P	DV.																
Liechtenste	in PCV13		PCV13					PCV13																		
Lithuania	PCV		PCV						PC	V11																
Luxembour	rg PCV		PCV					PCV								P	CV.					PPSV	23 ²⁸	POV	3+PP5V	/2328
Malta	PCV10		PCV10					PCV10																	PCV	
Netherland	la l	PCV		PCV			PCV																PPS	V23 ²⁴		

- 2+1 schedule
- PCV10 or PCV13

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IPD after PCV10 | 3-12-2020

ECDC Vaccine scheduler

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Pneumococcal vaccination in NL



- > Vaccination coverage PCV ~95% since introduction
- > No recommendation for elderly until 2020

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Herd effects due to PCV7

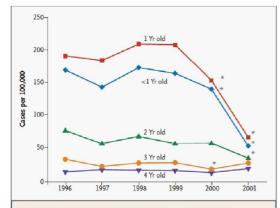
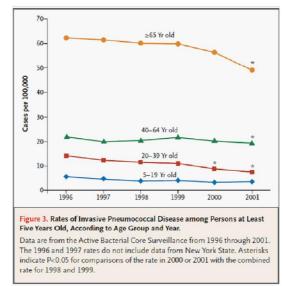


Figure 1. Rates of Invasive Pneumococcal Disease among Children under Five Years Old, According to Age and Year.

Data are from the Active Bacterial Core Surveillance from 1996 through 2001. The 1996 and 1997 rates do not include data from New York State. Asterisks indicate P<0.05 for comparisons of the rate in 2000 or 2001 with the combined rate for 1998 and 1999.

IPD after PCV10 | 3-12-2020

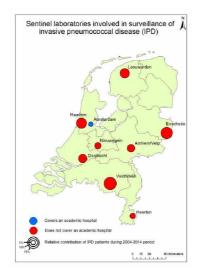


Whitney et al, NEJM 2003

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IPD surveillance

- Sentinel laboratory surveillance from 2004
 - Covering 25% of the Netherlands
 - Positive isolates from blood and/or CSF
 - Age, sex, date of material taken, serotype
- Nationwide laboratory surveillance for <5 year olds from 2008
- > Notification data for children born after 2006
 - Vaccination status, clinical presentation, outcome



Carriage IPD NL | 6-3-2018

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Evaluation of vaccination program

Impact

- > Before after analysis
- > By age group
- By serotype (vaccine types and non-vaccine types)
- Direct and indirect (herd) effects
- Dependent on vaccination coverage and effectiveness

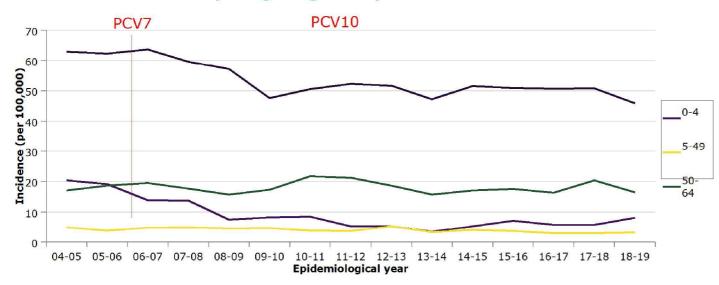
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Effectiveness

- > Vaccine eligible children
- Compare vaccination status in vaccine type IPD cases and non-vaccine type IPD cases
- > Direct effect of vaccination
- > Real world evidence

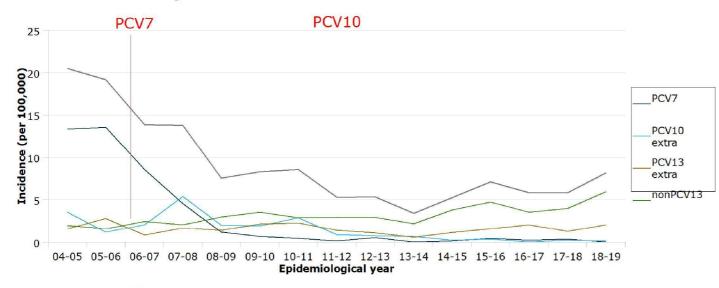


Overall IPD by age group



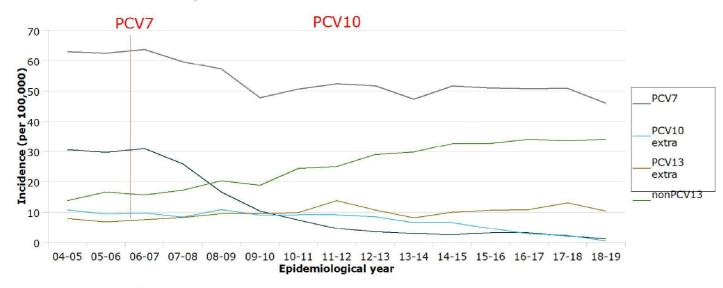
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IPD in <5 year olds



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IPD in 65+ year olds



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Vaccine effectiveness

Table 3

Number of invasive pneumococcal disease (IPD) cases and controls vaccinated and vaccines effectiveness (VE) of PCV10.

	Number of PCV10 cases vaccinated /total cases (%)	Number of non-PCV10 cases vaccinated /total controls (%)	OR (95%C)	VE % (95%CI)
Overall	8/13 (62)	206/218 (94)	0.09 [0.03; 0.32]	91 [67; 97]
Before October 2013 3 + 0/3 + 1 schedule	5/6 (83)	63/70 (90)*	0.24 [0.02; 2.73]	76[-173;98]
After October 2013 2 + 0/2 + 1 schedule	3/7 (43)	138/148 (93)*	0.05 [0.01; 0.25]	95 [75; 99]
Sex				
Male	4/7 (57)	122/126 (97)	0.04 [0.007; 0.26]	96 [74; 99]
Female	4/6 (67)	84/92 (91)	0.19 [0.03; 1.21]	81 [-21; 97]
Age (in year)				
0-1	2/4 (50)	150/157 (96)	0.05 [0.006; 0.38]	95 [62; 99]
2-4	6/9 (67)	56/61 (92)	0.18 [0.03; 0.94]	82 [6; 97]

* The comparison here is made between cases respecting the vaccine schedule and cases receiving no dose of IPD vaccine (dose = 0).

IPD after PCV10 | 3-12-2020

Peckeu et al, Vaccine 2020

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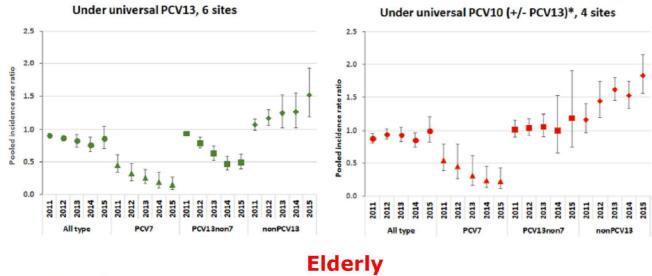
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Summary IPD after PCV10

- > Good effectiveness of PCV10
- > Reduction in IPD in children <5 yrs and elderly</p>
- > IPD caused by serotypes included in PCV10 nearly disappeared
 - Also in carriage
- Increasing IPD incidence due to serotypes not included in PCV10
- > Impact on overall IPD is decreasing due to replacement
 - Higher valent vaccines?

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PCV10 or PCV13?

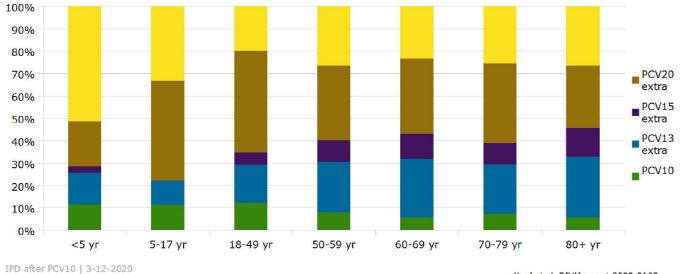


IPD after PCV10 | 3-12-2020

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Hanquet et al, Thorax 2019

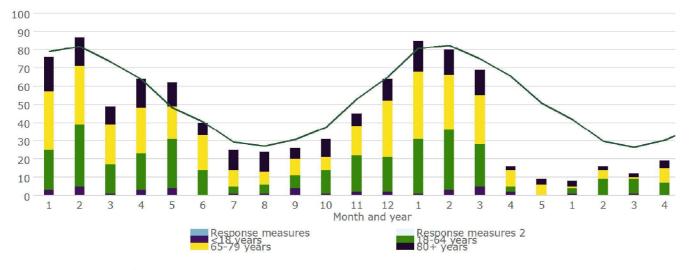
PCV15/PCV20?



Knol et al, RIVM report 2020-0168

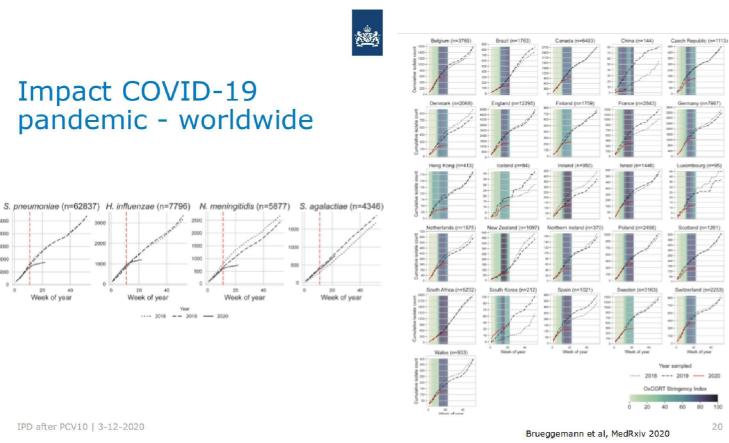
Impact COVID-19 pandemic

Q2: 80% reduction Q3: 40% reduction



IPD after PCV10 | 3-12-2020

Middeldorp et al, submitted



Week of year

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Impact COVID-19 pandemic

- > Currently reduction in IPD
 - Less transmission due to measures (social distancing, hand hygiene, school closure)
 - Less health care seeking behaviour, less diagnostics, less reporting
- > COVID-19 risk factor for IPD?
 - Bacterial superinfection \rightarrow antibiotic use
 - Increased susceptibility due to lung damage
- » Rebound effect?
- > Vaccination coverage?

Take home message

- > PCV7/PCV10 have reduced overall IPD in children and elderly
- > Maximum vaccine effects have been reached
- > Overall impact is reduced by ongoing serotype replacement
- > Higher valent PCV may be the solution
- > Currently reduced IPD incidence due to COVID-19 measures
- > Ongoing surveillance essential to monitor long term trends