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The effect of pneumococcal conjugate vaccines on the incidence of invasive pneumococcal disease caused by ten non-vaccine serotypes in Denmark

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ABSTRACT

Background: Surveillance data on invasive pneumococcal disease (IPD) in Denmark (1999–2014) was analysed regarding the incidence and age-distribution due to ten selected non-PCV serotypes (10-Non-PCV). The effect of PCV-7 and PCV-13 vaccines on the 10-Non-PCV IPD incidence was examined.
Methods: IPD cases caused by serotypes included in PCV-7, the additional six serotypes included in PCV-13 and 10-Non-PCV serotypes were identified (8, 9N, 11A, 12F, 15A, 22F, 24F, 20, 23B, 33F). The IPD incidence was stratified by three age groups: 0–4 years, 5–64 years and 65+ years.
Results: The predominant IPD cases were caused by serotypes that are not included in PCV-13 (71%), followed by the six additional PCV-13 serotypes. The IPD incidence of serotypes included in the PCV-7 decreased markedly after PCV-7 introduction but are still diagnosed at a low level. The IPD incidence for the 10-Non-PCV serotypes was low for age groups 0–4 years and 5–64 years but high for 65+ years.
Conclusion: Future vaccinations of the young age group alone with a vaccine targeting some of the 10-Non-PCV serotypes may not elicit the desired effect on herd protection since these serotypes are primarily causing IPD among the elderly. Future pneumococcal vaccination strategies in Denmark may therefore need carriage studies in order to identify among whom the pneumococcal serotypes causing IPD are carried.

1. Introduction

Infections by *Streptococcus pneumoniae* (pneumococci) are worldwide a cause of high morbidity and mortality among children and elderly [1]. Invasive pneumococcal disease (IPD) is one of the most frequent types of bacteraemia and meningitis in infants globally as well as in Denmark [2,3]. With the introduction and use of the pneumococcal conjugate vaccines (PCV) in children, an effective protection has been provided against IPD caused by the serotypes included in the vaccines [4,5]. The first pneumococcal conjugate vaccine was Prevnar 7 (PCV-7) (Pfizer Vaccines) which covered seven different serotypes and was licensed in USA in 2000 [5]. The PCV-7 has been followed by the 10-valent pneumococcal *Haemophilus influenza*e protein D conjugate vaccine (PCV-10) (Synflorix, GlaxoSmithKline Biologicals) and the Prevnar 13 (PCV-13) (Pfizer Vaccines) expanding the vaccine coverage to 10 and 13 serotypes, respectively [4,6].

In Denmark the PCV-7 was introduced into the childhood immunisation programme in October 2007 to be given at the ages of 3, 5 and 12 months [7]. Furthermore, a catch-up programme was introduced for children born after April 2006 [7]. In 2010 the PCV-7 was replaced with PCV-13 [7], and from 2013 and onwards the PCV-13 was approved for use in all age groups (http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/001104/human_med_001220.jsp&mid=WC0b01ac058001d124, accessed 12-09-2015).

In general, the coverage of the PCVs among Danish children has been stable and above 80% [8]. With the introduction of PCV-7 and PCV-13 in Denmark, the number of IPD cases in the population due to PCV serotypes declined markedly [7]. Moreover, a marked decline in IPD cases caused by PCV-7 serotypes among non-vaccinated age groups was observed three years after the PCV-7 introduction suggesting a herd protection effect [9]. This effect has also been observed in other countries, e.g. USA and United Kingdom, in particular among the elderly [10,11].

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Table 1
The total serotype distribution of IPD isolates by age groups in Denmark in 2014.

Serotype	Total IPD	The number of IPD isolates in 2014 by serotype and age group Age group (years)																						Serotype included in PCV-10 and PPV-23
	0–95+	0	1–4	5–9	10–14	15–19	20–24	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85–89	90–94	95+	
Serotypes included in PCV-7																							
4	11														1	1	4	2	1	1	1		PCV-10, PPV-23
6B	4															1	3						PCV-10, PPV-23
9V	3											1	1					1					PCV-10, PPV-23
14	0																						PCV-10, PPV-23
18C	1											1											PCV-10, PPV-23
19F	8														2		1	1	2	1	1		PCV-10, PPV-23
23F	1															1							PCV-10, PPV-23
Additional serotypes included in PCV-13																							
1	47		2	2	1				2	3	5	3	6	2	4	3	9	5					PCV-10, PPV-23
5	0																						PCV-10, PPV-23
7F	58	1				1		2		3	4	5	1	6	5	11	6	4	3	5	1		PCV-10, PPV-23
3	53							1		3		1	3	3	4	6	14	10	4	3	1		PPV-23
19A	21									2		1	1	2	1		5	2	4	3			PPV-23
6A	2																1			1			
The 10-Non-PCV serotypes selected in this study																							
8	126	1		1				2	2	3	4	7	7	14	12	18	16	17	10	7	3	2	PPV-23
9N	41		1							1		2	2	3	3	10	3	5	3	3	4	1	PPV-23
11A	16									1				1	3	2	4	3		2			PPV-23
12F	40	1	1							2	5	1	1	3	7	8	7	2	2				PPV-23
15A	27	1	1										1	1	2	4	4	1	1	6	4	1	Non-vaccine serotype
20	13												1	1	2	3	1		3	1	1		PPV-23
22F	44	1										1	1	3	5	7	8	7	1	5	1	4	PPV-23
23B	10														5	1	1		3				Non-vaccine serotype
24F	42	3	8			1									3	6	3	7	7	3	1		Non-vaccine serotype
33F	32		1		1						1		3		3	2	1	7	9	3	1		PPV-23
All other serotypes																							
NT	1													1									Non-vaccine serotype
10A	16	1	2	2									1	1	2	2	2			3			PPV-23
15B	3														1			1			1		PPV-23
17F	3										1				1		1						PPV-23
6C	13									1				2	3	1	2	3	1				Non-vaccine serotype
16F	10	1													1	3		2	1	2			Non-vaccine serotype
23A	14										1			2	2	2			2	3	1	1	Non-vaccine serotype
28F	1																	1					Non-vaccine serotype
21	4	1	2																1				Non-vaccine serotype
31	11													1	3	1	1	2	2	1			Non-vaccine serotype
35F	14												1	1	1	3	2	4	1		1		Non-vaccine serotype
35B	11												1		1	3	1	3	1	1			Non-vaccine serotype
15C	9		3										1	1	1	1	1	1					Non-vaccine serotype
10B	5	1												1	1	1	1						Non-vaccine serotype
34	1															1							Non-vaccine serotype
17A	1													1									Non-vaccine serotype
24B	1		1																				Non-vaccine serotype
25A	1										1												Non-vaccine serotype
29	3															1	2						Non-vaccine serotype
38	6	1												1			2	1		1			Non-vaccine serotype
g25	1											1											Non-vaccine serotype
g22	1																1						Non-vaccine serotype