

SUPPLEMENTARY MATERIAL

Burden of Invasive Pneumococcal Disease and Community-Acquired Pneumonia in Adults: Significant Adverse Outcomes and Costs Beyond Direct Treatment

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Supplementary Table S1. Serotype compositions of PCV13, PCV20, and PCV21.

	Serotype composition																															
PCV13	4	6B	9V	14	18C	19F	23F	1	3	5	6A	7F	19A																			
PCV20	4	6B	9V	14	18C	19F	23F	1	3	5	6A	7F	19A	22F	33F	8		10A	11A	12F	15B											
PCV21									3		6A	7F	19A	22F	33F	8	9N	10A	11A	12F	CR*	17F	20A	15A	15C**	16F	23A	23B	24F	31	35B	

PCV=pneumococcal conjugate vaccine

* PCV21 has demonstrated cross-reactivity to and protects against 15B. (Ref. [CAPVAXIVE, INN-Pneumococcal polysaccharide conjugate vaccine \(21-valent\)](#))

** PCV21 contains deOAc15B pneumococcal polysaccharide which has a molecular structure similar to 15C (referred to as 15C).

SupplementaryTable S2. Hazard ratios (HR) and 95% confidence intervals (95% CI) for recurrent IPD/CAP, admission to 24-h care and AMI in patients with IPD, inpatient or outpatient CAP compared to their matched controls by age group and overall.

Cohort/ Outcome	18–49 years of age		50–64 years of age		≥ 65 years of age		Overall	
	Events	HR (95% CI)	Events	HR (95% CI)	Events	HR (95% CI)	Events	HR (95% CI)
IPD								
Recurrent IPD/CAP	129	17.2 (10.8-27.4)	248	13.9 (10.2-18.9)	833	5.81 (5.05-6.69)	1210 ^c	7.48 (6.62-8.44)
Admission to 24-h care ^a	57	6.27 (3.61-10.9)	76	2.84 (1.81-4.45)	794	1.45 (1.24-1.70)	927	1.70 (1.48-1.95)
AMI	9	2.39 (0.64-8.88)	60	2.69 (1.62-4.46)	263	1.06 (0.81-1.40)	332	1.31 (1.04-1.66)
AMI ^b	n≥3	1.84 (0.44-7.67)	n≥3	2.11 (1.14-3.88)	162	1.15 (0.81-1.63)	213	1.33 (0.99-1.79)
Inpatient CAP								
Recurrent IPD/CAP	3449	19.8 (18.0-21.8)	7224	18.8 (17.7-20.0)	55,798	4.87 (4.79-4.95)	66,471 ^d	5.82 (5.73-5.92)
Admission to 24-h care ^a	1423	9.26 (8.23-10.4)	2747	9.14 (8.41-9.93)	68,763	2.02 (1.99-2.06)	72,933	2.21 (2.18-2.25)
AMI	239	3.45 (2.67-4.44)	1588	2.85 (2.58-3.15)	20,424	1.68 (1.63-1.73)	22,251	1.77 (1.72-1.81)
AMI ^b	220	3.29 (2.52-4.28)	1153	2.59 (2.30-2.91)	11,307	1.67 (1.61-1.74)	12,680	1.76 (1.70-1.83)
Outpatient CAP								
Recurrent IPD/CAP	6041	8.09 (7.65-8.56)	6798	10.1 (9.51-10.6)	25,740	4.64 (4.52-4.75)	38,579 ^e	5.63 (5.52-5.75)
Admission to 24-h care ^a	2362	2.92 (2.70-3.17)	1886	2.69 (2.46-2.95)	28,051	1.48 (1.44-1.52)	32,229	1.61 (1.57-1.65)
AMI	419	1.66 (1.36-2.03)	1757	1.72 (1.56-1.89)	9762	1.37 (1.31-1.43)	11,938	1.43 (1.37-1.48)
AMI ^b	378	1.59 (1.29-1.97)	1397	1.61 (1.44-1.80)	5865	1.35 (1.28-1.43)	7640	1.41 (1.34-1.48)

AMI=acute myocardial infarction, CAP=community-acquired pneumonia, IPD=invasive pneumococcal disease. n≥3=the exact value is omitted to prevent the identification of an individual when multiple results are combined.

^aIndividuals who lived in institutional (24-h) care at index date excluded. HR adjusted for age and sex.

^bIndividuals who had healthcare encounters with a diagnosis of ischemic heart disease (ICD-10 codes I20-I25) within 4 years preceding the index date or a valid entitlement to special reimbursement of medications costs due to coronary heart disease excluded. HR adjusted for age and sex.

^cOf the 827 events among patients with IPD, 22 (2.7%) were laboratory confirmed IPD.

^dOf the 41,929 events among patients with inpatient CAP, 164 (0.4%) were laboratory confirmed IPD.

^eOf the 24,580 events among patients with outpatient CAP, 136 (0.6%) were laboratory confirmed IPD.

Supplementary Table S3. Mortality in patients with IPD, inpatient or outpatient CAP and their matched population controls within 7 days, 30 days and 3 years after the index date by age group and overall.

Cohort/ Follow-up	18–49 years of age		50–64 years of age		≥ 65 years of age		Overall	
	Patient % (95% CI)	Control % (95% CI)	Patient % (95% CI)	Control % (95% CI)	Patient % (95% CI)	Control % (95% CI)	Patient % (95% CI)	Control % (95% CI)
IPD	<i>N</i> =524	<i>N</i> =1570	<i>N</i> =760	<i>N</i> =2281	<i>N</i> =1610	<i>N</i> =4810	<i>N</i> =2894	<i>N</i> =8661
7 days	1.9 (1.0-3.6)	0.0 (0.0-0.3)	4.3 (3.1-6.1)	0.0 (0.0-0.2)	8.3 (7.0-9.7)	0.1 (0.0-0.2)	6.1 (5.3-7.0)	0.1 (0.0-0.1)
30 days	3.1 (1.8-5.0)	n<3	6.7 (5.1-8.8)	0.0 (0.0-0.2)	12.8 (11.2-14.5)	0.5 (0.4-0.8)	9.4 (8.4-10.6)	n≥3
3 years	7.4 (5.4-10.1)	0.7 (0.4-1.3)	16.7 (14.2-19.6)	2.1 (1.5-2.8)	41.1 (38.7-43.6)	15.1 (14.1-16.1)	28.6 (27.0-30.3)	9.0 (8.4-9.7)
Inpatient CAP	<i>N</i> =13,185	<i>N</i> =39,415	<i>N</i> =18,715	<i>N</i> =55,850	<i>N</i> =97,303	<i>N</i> =282,532	<i>N</i> =129,203	<i>N</i> =377,797
7 days	0.5 (0.4-0.7)	0.0 (0.0-0.0)	2.0 (1.8-2.2)	0.0 (0.0-0.0)	4.9 (4.8-5.1)	0.1 (0.1-0.1)	4.1 (4.0-4.2)	0.1 (0.1-0.1)
30 days	1.3 (1.1-1.5)	0.0 (0.0-0.0)	5.0 (4.7-5.3)	0.0 (0.0-0.1)	12.4 (12.2-12.7)	0.5 (0.5-0.5)	10.2 (10.1-10.4)	0.4 (0.4-0.4)
3 years	7.1 (6.7-7.6)	0.4 (0.3-0.4)	23.9 (23.3-24.6)	1.9 (1.8-2.1)	52.6 (52.3-52.9)	20.2 (20.1-20.4)	43.8 (43.6-44.1)	15.4 (15.3-15.6)
Outpatient CAP	<i>N</i> =43,175	<i>N</i> =129,057	<i>N</i> =27,662	<i>N</i> =82,557	<i>N</i> =55,477	<i>N</i> =162,676	<i>N</i> =126,314	<i>N</i> =374,290
7 days	0.1 (0.1-0.1)	n<3	0.5 (0.4-0.6)	n≥3	3.8 (3.6-4.0)	0.1 (0.1-0.1)	1.8 (1.7-1.9)	0.0 (0.0-0.0)
30 days	0.2 (0.1- 0.2)	0.0 (0.0-0.0)	1.0 (0.9-1.1)	0.0 (0.0-0.1)	7.1 (6.9-7.3)	0.3 (0.3- 0.4)	3.4 (3.3-3.5)	0.2 (0.1-0.2)
3 years	1.2 (1.1-1.3)	0.3 (0.3-0.3)	7.3 (7.0-7.6)	1.7 (1.6-1.8)	33.2 (32.9-33.6)	15.3 (15.1-15.5)	16.6 (16.4-16.8)	7.1 (7.0-7.2)

CAP=community-acquired pneumonia, IPD=invasive pneumococcal disease, N=sample size, n<3=individual level results (n=1 or 2) not reported. n≥3=the exact value is omitted to prevent the identification of an individual when multiple results are combined.

Supplementary Table S4. All-cause costs within 1 year before and all-cause and disease-specific costs within 1 year after the index date among patients with IPD, inpatient or outpatient CAP with no risk factors, by age group. Only direct healthcare costs are included.

Cohort /Costs	18–49 years of age			50–64 years of age			≥ 65 years of age		
	Before	After	Difference	Before	After	Difference	Before	After	Difference
	€/PY	€/PY	€/PY	€/PY	€/PY	€/PY	€/PY	€/PY	€/PY
IPD	<i>PY=425</i>	<i>PY=406</i>		<i>PY=426</i>	<i>PY=395</i>		<i>PY=602</i>	<i>PY=502</i>	
All-cause	5656	16,097	+10,441 ^a	4186	17,897	+13,711 ^a	7519	24,725	+17,206 ^a
Disease-specific	NA	8507	+1934 ^b	NA	11,842	+1869 ^b	NA	13,963	+3243 ^b
Inpatient CAP	<i>PY=10,018</i>	<i>PY=9842</i>		<i>PY=9398</i>	<i>PY=8618</i>		<i>PY=33,034</i>	<i>PY=24,584</i>	
All-cause	5022	12,210	+7188 ^a	6931	17,962	+11,281 ^a	12,712	25,789	+13,077 ^a
Disease-specific	NA	5723	+1465 ^b	NA	7975	+3306 ^b	NA	9644	+3433 ^b
Outpatient CAP	<i>PY=36,802</i>	<i>PY=36,699</i>		<i>PY=17,238</i>	<i>PY=16,962</i>		<i>PY=22,584</i>	<i>Py=19,936</i>	
All-cause	2355	2993	+638 ^a	2662	4067	+1405 ^a	6968	10,144	+3176 ^a
Disease-specific	NA	325	+313 ^b	NA	498	+907 ^b	NA	977	+2199 ^b

CAP=community-acquired pneumonia, IPD=invasive pneumococcal disease, NA=not applicable, PY=person years.

^a Increase in all-cause costs from 1 year before to 1 year after the index date

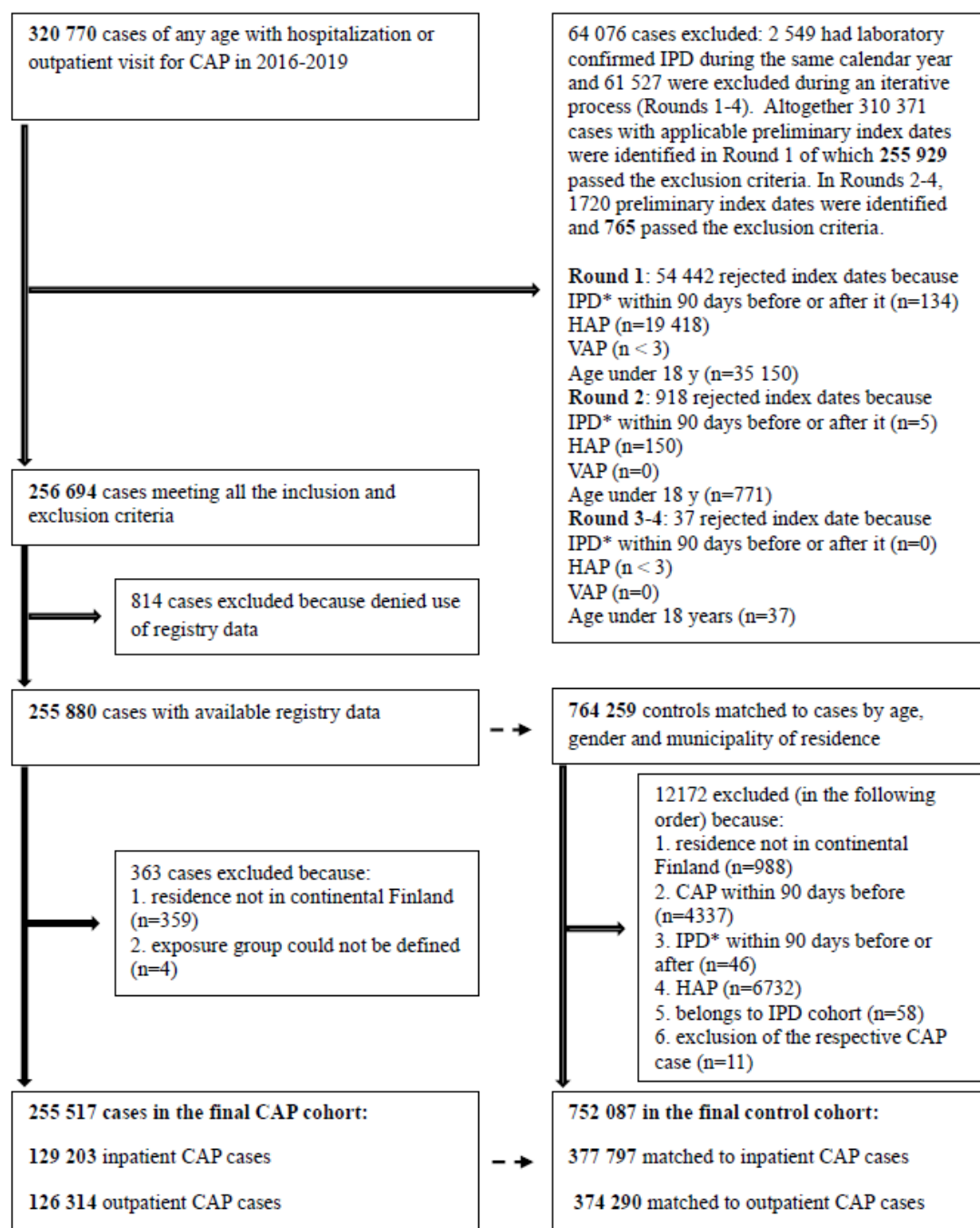
^b Increase in all-cause costs beyond disease-specific costs after the index date

Supplementary Table S5. Direct all-cause healthcare costs within 1 year before and after the index date among matched controls for patients with IPD, inpatient or outpatient CAP, by age group.

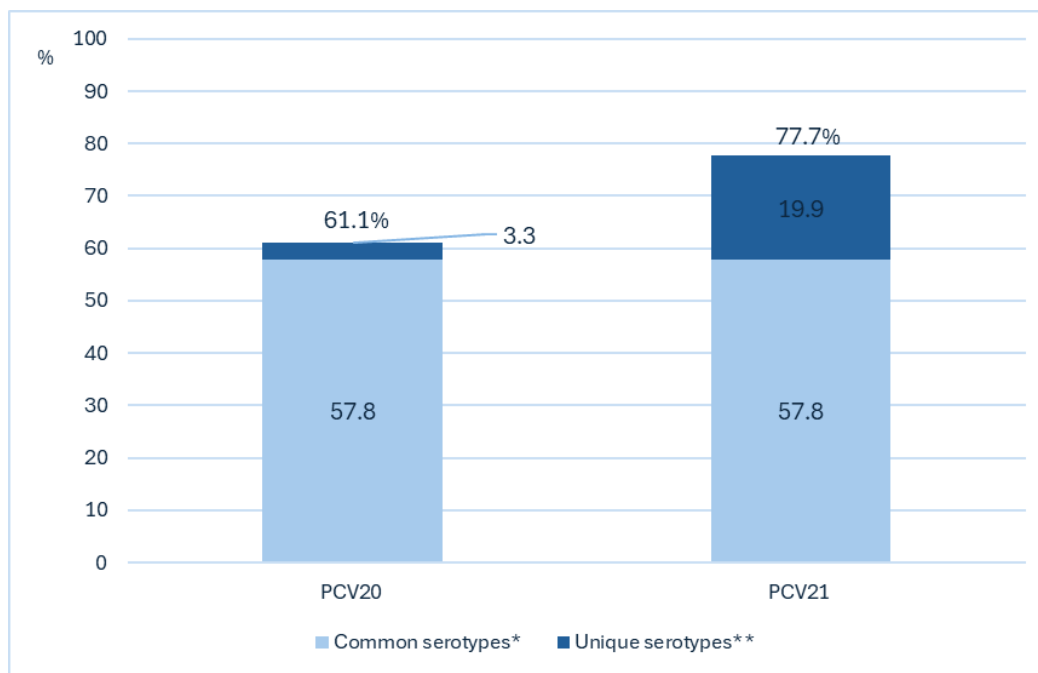
Controls for patients with/Costs	18–49 years of age			50–64 years of age			≥ 65 years of age		
	Before	After	Difference	Before	After	Difference	Before	After	Difference
	€/PY	€/PY	€/PY	€/PY	€/PY	€/PY	€/PY	€/PY	€/PY
IPD	<i>PY=1570</i>	<i>PY=1567</i>		<i>PY=2281</i>	<i>PY=2274</i>		<i>PY=4810</i>	<i>PY=4679</i>	
All-cause	1439	1471	+32 ^a	1551	1742	+191 ^a	4643	5169	+526 ^a
Inpatient CAP	<i>PY=39,415</i>	<i>PY=39,344</i>		<i>PY=55,850</i>	<i>PY=55,681</i>		<i>PY=282,532</i>	<i>PY=273,168</i>	
All-cause	1254	1256	+2 ^a	1477	1592	+115 ^a	5082	5916	+834 ^a
Outpatient CAP	<i>PY=129,057</i>	<i>PY=128,844</i>		<i>PY=82,557</i>	<i>PY=82,320</i>		<i>PY=162,676</i>	<i>PY=158,783</i>	
All-cause	1321	1303	-18 ^a	1474	1603	+129 ^a	4179	4866	+687 ^a

CAP=community-acquired pneumonia, IPD=invasive pneumococcal disease, PY=person years.

^a Increase in all-cause costs from 1 year before to 1 year after the index date



Supplementary Fig. S1. Flowchart of formation of CAP cohorts. HAP=hospital-acquired pneumonia, CAP=community acquired pneumonia, IPD=invasive pneumococcal disease, n=number, VAP=ventilator-associated pneumonia. *Laboratory confirmed IPD or healthcare encounters compatible with IPD diagnosis.



Supplementary Fig. S2. Serotype coverage of invasive pneumococcal disease episodes of common and unique serotypes of PCV20 and PCV21 in 65-year-olds and older (N=637) in Finland 2023-2024. *Common serotypes to PCV20 and PCV21: 3, 6A, 7F, 8, 10A, 11A, 12 F, 19A, 22F, 33F, 15B; **Unique to PCV20: 1, 4, 5, 6B, 9V, 14, 18C, 19F, 23F; **Unique to PCV21: 9N, 17F, 20A, 15A, 15C, 16F, 23A, 23B, 24F, 31, 35B. PCV=pneumococcal conjugate vaccine