

Table S1. Socio-demographic and clinical characteristics of the cohorts. Pedianet 2009-2019.

		2009-2010 season				2010-2011 season			
		Unvaccinated		Vaccinated		Unvaccinated		Vaccinated	
		N=23,965				N=24,355			
		20465 (85.4)		3500 (14.6)		21955 (90.15)		2400 (9.85)	

		2011-2012 season				2012-2013 season				
		Unvaccinated		Vaccinated		Unvaccinated		Vaccinated		
		N=26,160				N=21,928				
		23940 (91.51)		2220 (8.49)		20300 (92.58)		1628 (7.42)		
Age in mo. - mean (std)		82.01	(39.21)	77.94	(35.86)	<0.0001	83.29	(39.48)	79.94	(36.39)
Follow-up in weks - mean (std)		29.37	(3.38)	29.78	(2.63)	<0.0001	28.75	(3.81)	29.59	(2.6)
Gender						<0.0001				
female		11682	(48.8)	985	(44.37)		9826	(48.4)	745	(45.76)
male		12258	(51.2)	1235	(55.63)		10474	(51.6)	883	(54.24)
Influenza vaccine in the previous year						<0.0001				
No		23190	(96.87)	566	(25.5)		19443	(95.78)	501	(30.77)
Yes		750	(3.13)	1654	(74.5)		857	(4.22)	1127	(69.23)
Influenza diagnosis in the previous year						<0.0001				
No		20934	(87.44)	2054	(92.52)		18695	(92.09)	1556	(95.58)
Yes		3006	(12.56)	166	(7.48)		1605	(7.91)	72	(4.42)
No. of Antibiotic Therapy						<0.0001				
0		14630	(61.11)	1047	(47.16)		12097	(59.59)	774	(47.54)
1		5191	(21.68)	504	(22.7)		4585	(22.59)	380	(23.34)
≥2		4119	(17.21)	669	(30.14)		3618	(17.82)	474	(29.12)
No. of Antibiotic Therapy in the previous year						<0.0001				
0		13017	(54.37)	886	(39.91)		12081	(59.51)	739	(45.39)
1		5539	(23.14)	484	(21.8)		4378	(21.57)	366	(22.48)
≥2		5384	(22.49)	850	(38.29)		3841	(18.92)	523	(32.13)
No. of Outpatient Visits						<0.0001				
0		4977	(20.79)	22	(0.99)		3956	(19.49)	24	(1.47)
1		5048	(21.09)	222	(10)		4167	(20.53)	161	(9.89)
2		4119	(17.21)	302	(13.6)		3514	(17.31)	252	(15.48)
≥3		9796	(40.92)	1674	(75.41)		8663	(42.67)	1191	(73.16)
No. of Outpatient Visits in the previous year						<0.0001				
0		3850	(16.08)	56	(2.52)		3762	(18.53)	77	(4.73)
1		4386	(18.32)	187	(8.42)		3891	(19.17)	151	(9.28)
2		3919	(16.37)	262	(11.8)		3352	(16.51)	199	(12.22)
≥3		11785	(49.23)	1715	(77.25)		9295	(45.79)	1201	(73.77)
Place of Birth						<0.0001				
North		10969	(46.3)	769	(34.84)		10096	(49.91)	731	(44.98)
Island		1249	(5.27)	460	(20.84)		930	(4.6)	299	(18.4)
Center		5045	(21.3)	256	(11.6)		3799	(18.78)	141	(8.68)
South		6427	(27.13)	722	(32.71)		5404	(26.71)	454	(27.94)
Influenza and/or influenza-like illness diagnosis						<0.0001				
No		22165	(92.59)	2126	(95.77)		17780	(87.59)	1548	(95.09)
Yes		1775	(7.41)	94	(4.23)		2520	(12.41)	80	(4.91)

		2013-2014 season				2014-2015 season					
		Unvaccinated		Vaccinated		Unvaccinated		Vaccinated			
		N=22,542				N=20,490					
		20832 (92.41)		1710 (7.59)		19139 (93.41)		1351 (6.59)			
Age in mo. - mean (std)		85.51	(39.77)	81.72	(36.47)	0.0001	87.69	(39.92)	83.86	(36.98)	0.0006
Follow-up in weks - mean (std)		29.66	(2.47)	29.9	(1.78)	<0.0001	28.98	(3.82)	29.67	(2.53)	<0.0001
Gender						0.0508					0.6944
female		10038	(48.19)	782	(45.73)		9144	(47.78)	638	(47.22)	
male		10794	(51.81)	928	(54.27)		9995	(52.22)	713	(52.78)	
Influenza vaccine in the previous year						<0.0001					<0.0001
No		20401	(97.93)	545	(31.87)		18505	(96.69)	339	(25.09)	
Yes		431	(2.07)	1165	(68.13)		634	(3.31)	1012	(74.91)	
Influenza diagnosis in the previous year						<0.0001					0.0003
No		18329	(87.98)	1573	(91.99)		18311	(95.67)	1320	(97.71)	
Yes		2503	(12.02)	137	(8.01)		828	(4.33)	31	(2.29)	
No. of Antibiotic Therapy						<0.0001					<0.0001
0		13303	(63.86)	781	(45.67)		12243	(63.97)	686	(50.78)	
1		4333	(20.8)	363	(21.23)		3969	(20.74)	308	(22.8)	
≥2		3196	(15.34)	566	(33.1)		2927	(15.29)	357	(26.42)	
No. of Antibiotic Therapy in the previous year						<0.0001					<0.0001
0		12294	(59.01)	721	(42.16)		11637	(60.8)	568	(42.04)	
1		4738	(22.74)	404	(23.63)		4101	(21.43)	285	(21.1)	
≥2		3800	(18.24)	585	(34.21)		3401	(17.77)	498	(36.86)	
No. of Outpatient Visits						<0.0001					<0.0001
0		4360	(20.93)	14	(0.82)		3944	(20.61)	6	(0.44)	
1		4486	(21.53)	175	(10.23)		3969	(20.74)	145	(10.73)	
2		3628	(17.42)	253	(14.8)		3224	(16.85)	204	(15.1)	
≥3		8358	(40.12)	1268	(74.15)		8002	(41.81)	996	(73.72)	
No. of Outpatient Visits in the previous year						<0.0001					<0.0001
0		3821	(18.34)	63	(3.68)		3558	(18.59)	42	(3.11)	
1		4165	(19.99)	157	(9.18)		3768	(19.69)	132	(9.77)	
2		3552	(17.05)	238	(13.92)		3214	(16.79)	186	(13.77)	
≥3		9294	(44.61)	1252	(73.22)		8599	(44.93)	991	(73.35)	
Place of Birth						<0.0001					<0.0001
North		10893	(52.55)	699	(40.93)		8619	(45.21)	550	(40.77)	
Island		1557	(7.51)	392	(22.95)		1720	(9.02)	271	(20.09)	
Center		3738	(18.03)	99	(5.8)		4317	(22.64)	102	(7.56)	
South		4539	(21.9)	518	(30.33)		4408	(23.12)	426	(31.58)	
Influenza and/or influenza-like illness diagnosis						<0.0001					<0.0001
No		19986	(95.94)	1676	(98.01)		17386	(90.84)	1300	(96.23)	
Yes		846	(4.06)	34	(1.99)		1753	(9.16)	51	(3.77)	

		2015-2106 season				2016-2017 season					
		Unvaccinated		Vaccinated		Unvaccinated		Vaccinated			
		N=17,106				N=19,110					
		15796 (92.34)		1310 (7.66)		17627 (92.24)		1483 (7.76)			
Age in mo. - mean (std)		89.16	(40.1)	83.6	(37.75)	<0.0001	92.22	(39.87)	85.35	(38.01)	<0.0001
Follow-up in weks - mean (std)		29.24	(3.35)	29.87	(2.15)	<0.0001	29.21	(3.75)	29.82	(2.26)	<0.0001
Gender						0.1728					0.1774
	female	7544	(47.76)	600	(45.8)		8344	(47.34)	675	(45.52)	
	male	8252	(52.24)	710	(54.2)		9283	(52.66)	808	(54.48)	
Influenza vaccine in the previous year						<0.0001					<0.0001
	No	15496	(98.1)	388	(29.62)		17367	(98.52)	516	(34.79)	
	Yes	300	(1.9)	922	(70.38)		260	(1.48)	967	(65.21)	
Influenza diagnosis in the previous year						0.0005					<0.0001
	No	14585	(92.33)	1244	(94.96)		15943	(90.45)	1391	(93.8)	
	Yes	1211	(7.67)	66	(5.04)		1684	(9.55)	92	(6.2)	
No. of Antibiotic Therapy						<0.0001					<0.0001
	0	10191	(64.52)	622	(47.48)		11975	(67.94)	719	(48.48)	
	1	3286	(20.8)	308	(23.51)		3477	(19.73)	348	(23.47)	
	≥2	2319	(14.68)	380	(29.01)		2175	(12.34)	416	(28.05)	
No. of Antibiotic Therapy in the previous year						<0.0001					<0.0001
	0	9664	(61.18)	600	(45.8)		11250	(63.82)	667	(44.98)	
	1	3423	(21.67)	291	(22.21)		3743	(21.23)	327	(22.05)	
	≥2	2709	(17.15)	419	(31.98)		2634	(14.94)	489	(32.97)	
No. of Outpatient Visits						<0.0001					<0.0001
	0	3263	(20.66)	9	(0.69)		3895	(22.1)	3	(0.2)	
	1	3351	(21.21)	129	(9.85)		4151	(23.55)	142	(9.58)	
	2	2711	(17.16)	178	(13.59)		3034	(17.21)	215	(14.5)	
	≥3	6471	(40.97)	994	(75.88)		6547	(37.14)	1123	(75.72)	
No. of Outpatient Visits in the previous year						<0.0001					<0.0001
	0	3002	(19)	40	(3.05)		3316	(18.81)	43	(2.9)	
	1	3146	(19.92)	135	(10.31)		3605	(20.45)	140	(9.44)	
	2	2541	(16.09)	183	(13.97)		3053	(17.32)	205	(13.82)	
	≥3	7107	(44.99)	952	(72.67)		7653	(43.42)	1095	(73.84)	
Place of Birth						<0.0001					<0.0001
	North	7168	(45.53)	490	(37.49)		8578	(48.81)	535	(36.1)	
	Island	1052	(6.68)	306	(23.41)		1598	(9.09)	378	(25.51)	
	Center	2719	(17.27)	60	(4.59)		3900	(22.19)	115	(7.76)	
	South	4804	(30.52)	451	(34.51)		3497	(19.9)	454	(30.63)	
Influenza and/or influenza-like illness diagnosis						<0.0001					<0.0001
	No	14207	(89.94)	1257	(95.95)		16510	(93.66)	1451	(97.84)	
	Yes	1589	(10.06)	53	(4.05)		1117	(6.34)	32	(2.16)	

		2017-2018 season				2018-2019 season					
		Unvaccinated		Vaccinated		Unvaccinated		Vaccinated			
		N=15,203				N=18,589					
		13841 (91.04)		1362 (8.96)		16973 (91.31)		1616 (8.69)			
Age in mo. - mean (std)		94.4	(40.43)	86.48	(39.25)	<0.0001	94.54	(39.96)	84.67	(38.97)	<0.0001
Follow-up in weks - mean (std)		28.59	(4.41)	29.8	(2.11)	<0.0001	29.22	(3.39)	29.72	(2.33)	<0.0001
Gender						0.7508					0.3602
	female	6556	(47.37)	639	(46.92)		8085	(47.63)	789	(48.82)	
	male	7285	(52.63)	723	(53.08)		8888	(52.37)	827	(51.18)	
Influenza vaccine in the previous year						<0.0001					<0.0001
	No	13533	(97.77)	318	(23.35)		16695	(98.36)	540	(33.42)	
	Yes	308	(2.23)	1044	(76.65)		278	(1.64)	1076	(66.58)	
Influenza diagnosis in the previous year						<0.0001					<0.0001
	No	12879	(93.05)	1306	(95.89)		15088	(88.89)	1505	(93.13)	
	Yes	962	(6.95)	56	(4.11)		1885	(11.11)	111	(6.87)	
No. of Antibiotic Therapy						<0.0001					<0.0001
	0	9422	(68.07)	708	(51.98)		12014	(70.78)	808	(50)	
	1	2718	(19.64)	318	(23.35)		3088	(18.19)	355	(21.97)	
	≥2	1701	(12.29)	336	(24.67)		1871	(11.02)	453	(28.03)	
No. of Antibiotic Therapy in the previous year						<0.0001					<0.0001
	0	9007	(65.07)	616	(45.23)		11278	(66.45)	759	(46.97)	
	1	2867	(20.71)	305	(22.39)		3511	(20.69)	378	(23.39)	
	≥2	1967	(14.21)	441	(32.38)		2184	(12.87)	479	(29.64)	
No. of Outpatient Visits						<0.0001					<0.0001
	0	2993	(21.62)	0	(0)		4028	(23.73)	0	(0)	
	1	3371	(24.36)	153	(11.23)		4226	(24.9)	188	(11.63)	
	2	2431	(17.56)	236	(17.33)		2956	(17.42)	224	(13.86)	
	≥3	5046	(36.46)	973	(71.44)		5763	(33.95)	1204	(74.5)	
No. of Outpatient Visits in the previous year						<0.0001					<0.0001
	0	2665	(19.25)	28	(2.06)		3361	(19.8)	54	(3.34)	
	1	2984	(21.56)	123	(9.03)		3864	(22.77)	165	(10.21)	
	2	2314	(16.72)	177	(13)		2989	(17.61)	233	(14.42)	
	≥3	5878	(42.47)	1034	(75.92)		6759	(39.82)	1164	(72.03)	
Place of Birth						<0.0001					<0.0001
	North	6484	(47.02)	461	(33.87)		8687	(51.6)	566	(35.18)	
	Island	1074	(7.79)	362	(26.6)		1438	(8.54)	451	(28.03)	
	Center	3064	(22.22)	94	(6.91)		2848	(16.92)	106	(6.59)	
	South	3169	(22.98)	444	(32.62)		3863	(22.94)	486	(30.21)	
Influenza and/or influenza-like illness diagnosis						<0.0001					<0.0001
	No	12243	(88.45)	1326	(97.36)		15714	(92.58)	1562	(96.66)	
	Yes	1598	(11.55)	36	(2.64)		1259	(7.42)	54	(3.34)	