

Supplementary material

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- **Figure S1.** Antibiotic index in different years stratified by patient years of age. Pedianet, 2012-2018
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- **Figure S3.** Treatment episodes with at least one switch stratified by diagnosis. Pedianet, 2012-2018
- **Figure S4.** Annual number of patients followed by the 140 FPs participating in Pedianet from 2012 to 2018.

Table S1. Population characteristics, antibiotic index and antibiotics prevalence rate stratified by calendar year. Pedianet 2012-2018

	2012	2013	2014	2015	2016	2017	2018	p value
Children 0-14 years of age, N	103684	106609	107316	107707	107516	106387	104877	
Sex, Male, N(%)	53743 (51.8)	55315 (51.9)	55681 (51.9)	55926 (51.9)	55835 (51.9)	55175 (51.9)	54291 (51.8)	0.991
Age, Years	6.54 (6.51, 6.56)	6.67 (6.65, 6.70)	6.83 (6.81, 6.86)	6.93 (6.91, 6.96)	6.99 (6.97, 7.02)	7.10 (7.08, 7.13)	7.28 (7.26, 7.30)	< 0.001
Geographical location								< 0.001
North, N(%)	54826 (52.9)	56205 (52.7)	56208 (52.4)	56154 (52.1)	56117 (52.2)	55597 (52.3)	54792 (52.2)	
Centre, N(%)	14816 (14.3)	14992 (14.1)	14960 (13.9)	14946 (13.9)	15061 (14.0)	14513 (13.6)	14132 (13.5)	
South with Islands, N(%)	34042 (32.8)	35412 (33.2)	36148 (33.7)	36607 (34.0)	36338 (33.8)	36277 (34.1)	35953 (34.3)	
Follow-up, Person-years								< 0.001
N	99276.49	102385.89	103786.27	103706.96	103560.21	102867.92	101618.68	
Mean (SD)	0.96 (0.16)	0.96 (0.16)	0.97 (0.14)	0.96 (0.16)	0.96 (0.15)	0.97 (0.14)	0.97 (0.14)	< 0.001
Antibiotic prescriptions								
N	78036	83085	76869	71539	70551	64846	61001	
Mean (SD)	0.75 (1.39)	0.78 (1.40)	0.72 (1.33)	0.66 (1.25)	0.66 (1.25)	0.61 (1.20)	0.58 (1.17)	
Antibiotic index, (95%CI)	0.80 (0.78, 0.81)	0.82 (0.81, 0.83)	0.75 (0.74, 0.76)	0.72 (0.71, 0.73)	0.71 (0.69, 0.72)	0.64 (0.63, 0.65)	0.62 (0.61, 0.63)	< 0.001
Total antibiotics, N	78036	83085	76869	71539	70551	64846	61001	
Co-amoxiclav, N(%)	24615 (32)	26120 (31)	25135 (33)	24062 (34)	23966 (34)	22005 (34)	24615 (32)	< 0.001
Amoxicillin, N(%)	17685 (23)	18094 (22)	15573 (20)	15191 (21)	16217 (23)	14692 (23)	17685 (23)	< 0.001
Macrolides, N(%)	15211 (19)	17309 (21)	17921 (23)	15177 (21)	14331 (20)	12781 (20)	15211 (19)	< 0.001
III-gen. Cephalosporins, N(%)	12273 (16)	13898 (17)	12212 (16)	11440 (16)	11302 (16)	10675 (16)	12273 (16)	< 0.001
II-gen. Cephalosporins, N(%)	5410 (7)	4518 (5)	3565 (5)	3403 (5)	2824 (4)	2441 (4)	5410 (7)	< 0.001
J01xx, N(%)	1092 (1)	1170 (1)	1104 (1)	1012 (1)	874 (1)	954 (1)	1092 (1)	< 0.001
Tiamphenicol, N(%)	135 (0)	302 (0)	160 (0)	96 (0)	77 (0)	80 (0)	135 (0)	< 0.001
Other aminoglycosides, N(%)	486 (1)	509 (1)	347 (0)	371 (1)	267 (0)	395 (1)	486 (1)	< 0.001
Fluoroquinolones, N(%)	108 (0)	122 (0)	68 (0)	80 (0)	92 (0)	114 (0)	108 (0)	0.136
Lincosamides, N(%)	45 (0)	53 (0)	56 (0)	34 (0)	26 (0)	38 (0)	45 (0)	0.065
Other, N(%)	976 (1)	990 (1)	728 (1)	673 (1)	575 (1)	671 (1)	976 (1)	< 0.001

Table S2. Antibiotic index relative rate with 95% CI adjusted for patients age, sex and geographical location. Pedianet 2012-2018

	Relative rate	Lower CI	Higher CI	p.value
Time in years	0.96	0.96	0.96	<0.001
Patients age in years				
<1	ref	ref	ref	-
1	1.85	1.82	1.89	<0.001
2	1.94	1.91	1.98	<0.001
3	1.97	1.93	2.01	<0.001
4	1.97	1.93	2.01	<0.001
5	1.84	1.80	1.87	<0.001
6	1.37	1.34	1.40	<0.001
7	0.99	0.97	1.01	0.219
8	0.72	0.71	0.74	<0.001
9	0.64	0.62	0.65	<0.001
10	0.58	0.57	0.59	<0.001
11	0.50	0.49	0.52	<0.001
12	0.43	0.42	0.44	<0.001
13	0.40	0.39	0.41	<0.001
Male sex	1.05	1.04	1.05	<0.001
Geographical location				
North	ref	ref	ref	-
Centre	1.73	1.72	1.75	<0.001
South with Islands	1.74	1.73	1.75	<0.001

Table S3. Antibiotics prevalence rate stratified by antibiotic class, patients year of age and calendar year. Pedianet 2012-2018

	2012 N(%)	2013 N(%)	2014 N(%)	2015 N(%)	2016 N(%)	2017 N(%)	2018 N(%)	Grand Total N(%)
<i>Co-amoxiclav</i>	24615 (15)	26120 (16)	25135 (15)	24062 (14)	23966 (14)	22005 (13)	20731 (12)	166634 (100)
0	567 (17)	577 (17)	539 (16)	471 (14)	438 (13)	400 (12)	378 (11)	3370 (100)
1	2426 (16)	2602 (17)	2343 (15)	2099 (14)	2170 (14)	1978 (13)	1768 (11)	15386 (100)
2	2887 (15)	3060 (16)	2890 (15)	2633 (14)	2459 (13)	2538 (14)	2229 (12)	18696 (100)
3	3236 (16)	3014 (15)	3235 (16)	3030 (15)	2886 (14)	2489 (12)	2552 (12)	20442 (100)
4	3257 (15)	3580 (16)	3319 (15)	3220 (15)	3219 (15)	2888 (13)	2410 (11)	21893 (100)
5	2779 (15)	2768 (15)	2974 (16)	2662 (14)	2842 (15)	2507 (13)	2444 (13)	18976 (100)
6	2114 (14)	2314 (15)	2033 (14)	2142 (14)	2280 (15)	1988 (13)	2086 (14)	14957 (100)
7	1416 (13)	1678 (15)	1543 (14)	1578 (14)	1676 (15)	1535 (14)	1498 (14)	10924 (100)
8	1325 (14)	1460 (15)	1401 (14)	1402 (14)	1447 (15)	1349 (14)	1308 (13)	9692 (100)
9	1290 (15)	1256 (15)	1250 (15)	1216 (14)	1225 (14)	1168 (14)	1153 (13)	8558 (100)
10	1191 (16)	1321 (17)	1009 (13)	1043 (14)	1037 (14)	1034 (14)	914 (12)	7549 (100)
11	866 (14)	1066 (17)	1070 (17)	898 (14)	863 (14)	853 (13)	763 (12)	6379 (100)
12	715 (14)	768 (15)	811 (16)	882 (17)	702 (13)	723 (14)	610 (12)	5211 (100)
13	546 (12)	656 (14)	718 (16)	786 (17)	722 (16)	555 (12)	618 (13)	4601 (100)
<i>Amoxicillin</i>	17685 (16)	18094 (16)	15573 (14)	15191 (14)	16217 (15)	14692 (13)	13964 (13)	111416 (100)
0	727 (19)	667 (18)	600 (16)	479 (13)	482 (13)	407 (11)	387 (10)	3749 (100)
1	2690 (17)	2814 (18)	2385 (15)	2054 (13)	2040 (13)	2008 (13)	1706 (11)	15697 (100)
2	2602 (17)	2475 (16)	2384 (15)	2261 (14)	2018 (13)	1950 (12)	1965 (13)	15655 (100)
3	2435 (16)	2527 (17)	2164 (14)	2183 (14)	2214 (14)	1822 (12)	1949 (13)	15294 (100)
4	2279 (15)	2321 (16)	2160 (15)	1981 (13)	2206 (15)	2103 (14)	1690 (11)	14740 (100)
5	1714 (15)	1742 (15)	1530 (13)	1617 (14)	1894 (16)	1575 (13)	1606 (14)	11678 (100)
6	1214 (15)	1220 (15)	1050 (13)	1127 (14)	1427 (17)	1171 (14)	1118 (13)	8327 (100)
7	810 (14)	902 (15)	714 (12)	757 (13)	991 (17)	919 (15)	842 (14)	5935 (100)
8	697 (15)	763 (16)	558 (12)	621 (13)	761 (16)	700 (15)	695 (14)	4795 (100)
9	752 (18)	646 (15)	498 (12)	527 (12)	596 (14)	594 (14)	617 (15)	4230 (100)
10	649 (18)	701 (19)	428 (12)	454 (12)	516 (14)	503 (14)	451 (12)	3702 (100)
11	478 (15)	567 (18)	479 (15)	404 (13)	404 (13)	396 (13)	381 (12)	3109 (100)
12	349 (15)	430 (18)	320 (13)	402 (17)	313 (13)	295 (12)	297 (12)	2406 (100)
13	289 (14)	319 (15)	303 (14)	324 (15)	355 (17)	249 (12)	260 (12)	2099 (100)
<i>Macrolides</i>	15211 (15)	17309 (17)	17921 (17)	15177 (14)	14331 (14)	12781 (12)	12011 (11)	104741 (100)
0	295 (15)	370 (19)	282 (14)	285 (14)	273 (14)	248 (13)	213 (11)	1966 (100)
1	1290 (16)	1406 (17)	1368 (16)	1086 (13)	1130 (14)	1132 (14)	902 (11)	8314 (100)
2	1545 (15)	1693 (16)	1624 (16)	1515 (15)	1393 (13)	1336 (13)	1225 (12)	10331 (100)
3	1984 (16)	2049 (16)	2077 (17)	1860 (15)	1661 (13)	1515 (12)	1310 (11)	12456 (100)
4	2010 (15)	2250 (17)	2258 (17)	2068 (15)	1865 (14)	1724 (13)	1455 (11)	13630 (100)

5	1874 (16)	1835 (15)	2091 (17)	1715 (14)	1657 (14)	1442 (12)	1395 (12)	12009 (100)
6	1365 (15)	1632 (17)	1472 (16)	1333 (14)	1284 (14)	1128 (12)	1145 (12)	9359 (100)
7	896 (13)	1116 (17)	1153 (17)	913 (14)	924 (14)	860 (13)	820 (12)	6682 (100)
8	840 (14)	1040 (17)	1075 (17)	855 (14)	823 (13)	717 (12)	808 (13)	6158 (100)
9	913 (16)	902 (16)	1030 (18)	806 (14)	744 (13)	618 (11)	651 (11)	5664 (100)
10	747 (14)	965 (18)	964 (18)	742 (14)	716 (13)	610 (11)	594 (11)	5338 (100)
11	602 (13)	810 (17)	980 (21)	623 (13)	622 (13)	566 (12)	537 (11)	4740 (100)
12	466 (11)	678 (16)	823 (19)	782 (18)	556 (13)	460 (11)	502 (12)	4267 (100)
13	384 (10)	563 (15)	724 (19)	594 (16)	683 (18)	425 (11)	454 (12)	3827 (100)
<i>III-gen. cephalosporins</i>	12273 (15)	13898 (17)	12212 (15)	11440 (14)	11302 (14)	10675 (13)	9995 (12)	81795 (100)
0	231 (19)	242 (19)	191 (15)	179 (14)	161 (13)	133 (11)	111 (9)	1248 (100)
1	1142 (16)	1215 (17)	1110 (16)	1045 (15)	953 (13)	877 (12)	804 (11)	7146 (100)
2	1444 (15)	1667 (17)	1458 (15)	1354 (14)	1275 (13)	1240 (13)	1133 (12)	9571 (100)
3	1645 (16)	1744 (17)	1586 (15)	1476 (14)	1443 (14)	1315 (13)	1252 (12)	10461 (100)
4	1599 (15)	1910 (17)	1609 (15)	1552 (14)	1521 (14)	1483 (14)	1283 (12)	10957 (100)
5	1446 (16)	1494 (16)	1406 (15)	1254 (13)	1367 (15)	1189 (13)	1161 (12)	9317 (100)
6	1042 (14)	1194 (17)	1044 (15)	1044 (15)	994 (14)	986 (14)	895 (12)	7199 (100)
7	766 (14)	928 (17)	785 (15)	728 (14)	751 (14)	703 (13)	698 (13)	5359 (100)
8	603 (13)	765 (16)	704 (15)	624 (13)	655 (14)	655 (14)	643 (14)	4649 (100)
9	668 (16)	637 (15)	562 (14)	535 (13)	577 (14)	595 (14)	547 (13)	4121 (100)
10	656 (17)	748 (19)	509 (13)	480 (12)	500 (13)	496 (13)	485 (13)	3874 (100)
11	463 (14)	621 (19)	509 (16)	419 (13)	430 (13)	386 (12)	395 (12)	3223 (100)
12	314 (12)	432 (16)	431 (16)	415 (16)	347 (13)	365 (14)	324 (12)	2628 (100)
13	254 (12)	301 (15)	308 (15)	335 (16)	328 (16)	252 (12)	264 (13)	2042 (100)
<i>II-gen. cephalosporins</i>	5410 (22)	4518 (19)	3565 (15)	3403 (14)	2824 (12)	2441 (10)	2154 (9)	24315 (100)
0	106 (27)	78 (20)	48 (12)	53 (13)	31 (8)	52 (13)	29 (7)	397 (100)
1	621 (23)	491 (18)	388 (14)	395 (15)	292 (11)	275 (10)	241 (9)	2703 (100)
2	769 (22)	627 (18)	515 (15)	484 (14)	374 (11)	351 (10)	347 (10)	3467 (100)
3	955 (24)	679 (17)	581 (15)	573 (15)	463 (12)	374 (9)	321 (8)	3946 (100)
4	803 (21)	762 (20)	532 (14)	550 (15)	458 (12)	388 (10)	298 (8)	3791 (100)
5	674 (22)	521 (17)	470 (16)	411 (14)	379 (13)	301 (10)	262 (9)	3018 (100)
6	409 (20)	377 (18)	308 (15)	295 (14)	257 (12)	198 (10)	225 (11)	2069 (100)
7	309 (22)	263 (19)	191 (14)	185 (13)	175 (12)	155 (11)	135 (10)	1413 (100)
8	197 (20)	203 (21)	145 (15)	122 (13)	97 (10)	106 (11)	103 (11)	973 (100)
9	168 (22)	126 (17)	93 (12)	99 (13)	106 (14)	78 (10)	78 (10)	748 (100)
10	173 (26)	149 (23)	96 (15)	69 (10)	64 (10)	71 (11)	39 (6)	661 (100)
11	106 (20)	128 (24)	79 (15)	82 (16)	51 (10)	47 (9)	35 (7)	528 (100)
12	58 (17)	63 (19)	64 (19)	54 (16)	39 (12)	27 (8)	28 (8)	333 (100)
13	62 (23)	51 (19)	55 (21)	31 (12)	38 (14)	18 (7)	13 (5)	268 (100)

<i>Fluroquinolones</i>	108 (16)	122 (18)	68 (10)	80 (12)	92 (14)	114 (17)	94 (14)	678 (100)
0	3 (30)	0 (0)	0 (0)	0 (0)	4 (40)	1 (10)	2 (20)	10 (100)
1	5 (8)	13 (22)	2 (3)	9 (15)	11 (19)	4 (7)	15 (25)	59 (100)
2	15 (27)	3 (5)	5 (9)	4 (7)	12 (21)	9 (16)	8 (14)	56 (100)
3	11 (23)	10 (21)	1 (2)	2 (4)	3 (6)	18 (38)	2 (4)	47 (100)
4	6 (16)	2 (5)	11 (29)	2 (5)	3 (8)	3 (8)	11 (29)	38 (100)
5	2 (5)	6 (15)	3 (8)	7 (18)	11 (28)	6 (15)	5 (13)	40 (100)
6	7 (16)	4 (9)	7 (16)	2 (4)	7 (16)	16 (36)	2 (4)	45 (100)
7	1 (4)	6 (26)	2 (9)	8 (35)	0 (0)	2 (9)	4 (17)	23 (100)
8	9 (36)	1 (4)	3 (12)	2 (8)	1 (4)	3 (12)	6 (24)	25 (100)
9	12 (18)	33 (51)	1 (2)	5 (8)	3 (5)	5 (8)	6 (9)	65 (100)
10	10 (22)	12 (26)	3 (7)	2 (4)	7 (15)	10 (22)	2 (4)	46 (100)
11	11 (18)	8 (13)	12 (19)	13 (21)	2 (3)	11 (18)	5 (8)	62 (100)
12	8 (13)	10 (16)	4 (7)	14 (23)	5 (8)	6 (10)	14 (23)	61 (100)
13	8 (8)	14 (14)	14 (14)	10 (10)	23 (23)	20 (20)	12 (12)	101 (100)
<i>J01XX</i>	1092 (15)	1170 (16)	1104 (15)	1012 (14)	874 (12)	954 (13)	1045 (14)	7251 (100)
0	97 (17)	124 (21)	98 (17)	77 (13)	50 (9)	62 (11)	75 (13)	583 (100)
1	202 (16)	169 (14)	165 (13)	161 (13)	136 (11)	177 (14)	230 (19)	1240 (100)
2	114 (14)	119 (15)	101 (13)	94 (12)	94 (12)	118 (15)	149 (19)	789 (100)
3	97 (13)	123 (16)	122 (16)	106 (14)	96 (13)	106 (14)	103 (14)	753 (100)
4	116 (16)	145 (19)	115 (15)	112 (15)	78 (10)	92 (12)	86 (12)	744 (100)
5	95 (15)	104 (16)	124 (20)	87 (14)	79 (13)	75 (12)	68 (11)	632 (100)
6	73 (14)	69 (13)	87 (17)	88 (17)	63 (12)	73 (14)	72 (14)	525 (100)
7	63 (15)	64 (15)	57 (13)	66 (15)	57 (13)	57 (13)	70 (16)	434 (100)
8	57 (14)	66 (17)	61 (15)	57 (14)	59 (15)	50 (13)	45 (11)	395 (100)
9	52 (16)	48 (15)	46 (14)	43 (13)	43 (13)	42 (13)	57 (17)	331 (100)
10	53 (19)	50 (18)	37 (13)	40 (14)	34 (12)	39 (14)	32 (11)	285 (100)
11	32 (15)	41 (19)	36 (16)	32 (15)	37 (17)	23 (10)	19 (9)	220 (100)
12	19 (12)	26 (16)	30 (18)	21 (13)	22 (13)	26 (16)	19 (12)	163 (100)
13	22 (14)	22 (14)	25 (16)	28 (18)	26 (17)	14 (9)	20 (13)	157 (100)
<i>Lincosamides</i>	45 (17)	53 (20)	56 (21)	34 (13)	26 (10)	38 (14)	17 (6)	269 (100)
0	1 (20)	1 (20)	3 (60)	0 (0)	0 (0)	0 (0)	0 (0)	5 (100)
1	11 (85)	0 (0)	1 (8)	0 (0)	0 (0)	1 (8)	0 (0)	13 (100)
2	1 (10)	2 (20)	1 (10)	0 (0)	2 (20)	2 (20)	2 (20)	10 (100)
3	0 (0)	4 (17)	7 (29)	2 (8)	1 (4)	6 (25)	4 (17)	24 (100)
4	7 (18)	4 (11)	9 (24)	8 (21)	4 (11)	4 (11)	2 (5)	38 (100)
5	2 (8)	12 (46)	4 (15)	5 (19)	3 (12)	0 (0)	0 (0)	26 (100)
6	4 (17)	7 (30)	3 (13)	1 (4)	5 (22)	3 (13)	0 (0)	23 (100)
7	0 (0)	3 (17)	1 (6)	4 (22)	1 (6)	4 (22)	5 (28)	18 (100)

8	6 (40)	2 (13)	1 (7)	1 (7)	2 (13)	3 (20)	0 (0)	15 (100)
9	1 (3)	8 (27)	5 (17)	4 (13)	1 (3)	9 (30)	2 (7)	30 (100)
10	1 (6)	2 (13)	8 (50)	1 (6)	1 (6)	2 (13)	1 (6)	16 (100)
11	4 (27)	2 (13)	1 (7)	6 (40)	2 (13)	0 (0)	0 (0)	15 (100)
12	1 (5)	6 (30)	4 (20)	2 (10)	4 (20)	2 (10)	1 (5)	20 (100)
13	6 (38)	0 (0)	8 (50)	0 (0)	0 (0)	2 (13)	0 (0)	16 (100)
<i>Other</i>	976 (19)	990 (19)	728 (14)	673 (13)	575 (11)	671 (13)	590 (11)	5203 (100)
0	7 (20)	8 (23)	6 (17)	3 (9)	5 (14)	1 (3)	5 (14)	35 (100)
1	48 (24)	36 (18)	26 (13)	22 (11)	26 (13)	16 (8)	29 (14)	203 (100)
2	71 (22)	47 (14)	54 (16)	36 (11)	39 (12)	51 (15)	32 (10)	330 (100)
3	84 (18)	103 (22)	56 (12)	73 (16)	52 (11)	56 (12)	39 (8)	463 (100)
4	108 (17)	128 (20)	93 (14)	78 (12)	68 (11)	96 (15)	71 (11)	642 (100)
5	91 (16)	104 (18)	86 (15)	72 (13)	67 (12)	87 (15)	66 (12)	573 (100)
6	96 (20)	88 (18)	59 (12)	66 (14)	50 (10)	63 (13)	64 (13)	486 (100)
7	75 (19)	83 (21)	35 (9)	51 (13)	38 (10)	55 (14)	53 (14)	390 (100)
8	77 (22)	60 (17)	44 (12)	44 (12)	41 (12)	45 (13)	42 (12)	353 (100)
9	61 (19)	64 (20)	38 (12)	31 (10)	22 (7)	54 (17)	44 (14)	314 (100)
10	59 (18)	61 (19)	59 (18)	46 (14)	29 (9)	35 (11)	32 (10)	321 (100)
11	69 (20)	65 (19)	45 (13)	53 (16)	27 (8)	42 (12)	39 (11)	340 (100)
12	74 (21)	75 (21)	48 (14)	36 (10)	51 (15)	28 (8)	37 (11)	349 (100)
13	56 (14)	68 (17)	79 (20)	62 (15)	60 (15)	42 (10)	37 (9)	404 (100)
<i>Other aminoglycosides</i>	135 (15)	302 (34)	160 (18)	96 (11)	77 (9)	80 (9)	50 (6)	900 (100)
0	0 (0)	0 (0)	2 (100)	0 (0)	0 (0)	0 (0)	0 (0)	2 (100)
1	8 (30)	14 (52)	1 (4)	1 (4)	2 (7)	0 (0)	1 (4)	27 (100)
2	3 (5)	35 (58)	9 (15)	2 (3)	7 (12)	3 (5)	1 (2)	60 (100)
3	8 (8)	40 (40)	20 (20)	8 (8)	7 (7)	12 (12)	4 (4)	99 (100)
4	15 (10)	38 (24)	28 (18)	32 (21)	14 (9)	22 (14)	7 (4)	156 (100)
5	17 (12)	52 (36)	28 (19)	19 (13)	15 (10)	8 (5)	7 (5)	146 (100)
6	11 (10)	42 (38)	22 (20)	7 (6)	10 (9)	14 (13)	6 (5)	112 (100)
7	8 (13)	15 (25)	13 (21)	7 (11)	3 (5)	6 (10)	9 (15)	61 (100)
8	11 (22)	7 (14)	7 (14)	10 (20)	10 (20)	4 (8)	0 (0)	49 (100)
9	5 (13)	10 (26)	4 (11)	2 (5)	5 (13)	7 (18)	5 (13)	38 (100)
10	18 (42)	10 (23)	5 (12)	2 (5)	2 (5)	2 (5)	4 (9)	43 (100)
11	16 (41)	18 (46)	2 (5)	0 (0)	1 (3)	0 (0)	2 (5)	39 (100)
12	4 (13)	15 (50)	3 (10)	4 (13)	0 (0)	2 (7)	2 (7)	30 (100)
13	11 (29)	6 (16)	16 (42)	2 (5)	1 (3)	0 (0)	2 (5)	38 (100)
<i>Tiamphenicol</i>	486 (18)	509 (19)	347 (13)	371 (14)	267 (10)	395 (14)	350 (13)	2725 (100)
0	0 (0)	0 (0)	1 (50)	0 (0)	0 (0)	0 (0)	1 (50)	2 (100)
1	4 (19)	0 (0)	4 (19)	3 (14)	0 (0)	4 (19)	6 (29)	21 (100)

2	20 (22)	11 (12)	17 (19)	17 (19)	8 (9)	3 (3)	15 (16)	91 (100)
3	36 (15)	44 (19)	30 (13)	47 (20)	27 (12)	30 (13)	19 (8)	233 (100)
4	49 (13)	79 (21)	47 (13)	50 (14)	39 (11)	53 (14)	53 (14)	370 (100)
5	60 (16)	55 (15)	45 (12)	46 (13)	44 (12)	69 (19)	46 (13)	365 (100)
6	58 (20)	58 (20)	34 (12)	41 (14)	20 (7)	44 (15)	40 (14)	295 (100)
7	39 (18)	50 (23)	18 (8)	23 (11)	18 (8)	37 (17)	28 (13)	213 (100)
8	37 (19)	38 (20)	25 (13)	26 (13)	14 (7)	31 (16)	22 (11)	193 (100)
9	39 (22)	36 (20)	20 (11)	13 (7)	14 (8)	25 (14)	31 (17)	178 (100)
10	40 (21)	30 (15)	31 (16)	29 (15)	16 (8)	27 (14)	22 (11)	195 (100)
11	37 (18)	43 (21)	28 (14)	21 (10)	17 (8)	31 (15)	25 (12)	202 (100)
12	43 (23)	36 (19)	21 (11)	20 (11)	20 (11)	20 (11)	26 (14)	186 (100)
13	24 (13)	29 (16)	26 (14)	35 (19)	30 (17)	21 (12)	16 (9)	181 (100)
<i>Grand Total</i>	78036 (15)	83085 (16)	76869 (15)	71539 (14)	70551 (14)	64846 (13)	61001 (12)	505927 (100)

Table S4. Antibiotic prescription rate by class of antibiotic stratified according to diagnosis. (Pedianet 2012-2018)

	Bronchitis/ bronchiolitis	Pharyngitis	Fever (unspecified)	Bacterial infection	SMMI	URTI	LRTI	UTI	Infection (unspecified)
Co-amoxiclav, (%)	15812 (24)	36383 (35)	823 (40)	291 (28)	8351 (44)	31298 (27)	879 (43)	2985 (35)	153 (39)
Amoxicillin, (%)	10186 (16)	33082 (32)	495 (24)	119 (12)	3574 (19)	22715 (20)	427 (21)	243 (3)	114 (29)
Macrolides, (%)	28760 (44)	9130 (9)	271 (13)	400 (39)	2784 (15)	35273 (31)	416 (20)	135 (2)	76 (19)
III-gen. cephalosporines, (%)	8973 (14)	18680 (18)	350 (17)	140 (14)	2506 (13)	16497 (14)	233 (11)	2293 (27)	25 (6)
II-gen. cephalosporines, (%)	1194 (2)	5298 (5)	64 (3)	36 (4)	1056 (6)	5583 (5)	74 (4)	348 (4)	13 (3)
J01xx, (%)	165 (0)	914 (1)	15 (1)	4 (0)	184 (1)	1713 (1)	3 (0)	2215 (26)	3 (1)
Thiamphenicol (%)	49 (0)	179 (0)	7 (0)	1 (0)	87 (0)	733 (1)	2 (0)	8 (0)	5 (1)
Lincosamides, (%)	5 (0)	19 (0)	1 (0)	0 (0)	8 (0)	61 (0)	0 (0)	1 (0)	0 (0)
Other aminoglycosides, (%)	17 (0)	26 (0)	0 (0)	2 (0)	17 (0)	295 (0)	1 (0)	13 (0)	0 (0)
Fluoroquinolones, (%)	31 (0)	32 (0)	1 (0)	3 (0)	44 (0)	59 (0)	0 (0)	87 (1)	1 (0)
Other antibiotics, (%)	87 (0)	318 (0)	12 (1)	27 (3)	310 (2)	1089 (1)	5 (0)	288 (3)	6 (2)

	STI	AI	BI	NA	AOM	Pneumonia	Prophylaxis	Sinusitis	Viral infection
Co-amoxiclav, (%)	1947 (51)	60 (39)	35 (49)	33584 (39)	22933 (36)	1944 (28)	620 (40)	3016 (31)	4209 (35)
Amoxicillin, (%)	526 (14)	17 (11)	9 (13)	13362 (16)	19448 (30)	856 (13)	202 (13)	2113 (22)	3004 (25)
Macrolides, (%)	667 (17)	4 (3)	13 (18)	17065 (20)	2583 (4)	2939 (43)	161 (11)	1138 (12)	2371 (20)
III-gen. cephalosporines, (%)	454 (12)	28 (18)	2 (3)	13223 (15)	13462 (21)	956 (14)	293 (19)	1801 (18)	1310 (11)
II-gen. cephalosporines, (%)	145 (4)	6 (4)	1 (1)	4394 (5)	4853 (8)	119 (2)	66 (4)	313 (3)	559 (5)
J01xx, (%)	25 (1)	0 (0)	0 (0)	1584 (2)	258 (0)	3 (0)	16 (1)	26 (0)	88 (1)
Thiamphenicol (%)	23 (1)	0 (0)	0 (0)	595 (1)	273 (0)	5 (0)	8 (1)	623 (6)	100 (1)
Lincosamides, (%)	0 (0)	0 (0)	1 (1)	105 (0)	11 (0)	1 (0)	25 (2)	18 (0)	11 (0)
Other aminoglycosides, (%)	6 (0)	0 (0)	0 (0)	335 (0)	81 (0)	2 (0)	9 (1)	42 (0)	46 (0)
Fluoroquinolones, (%)	3 (0)	3 (2)	1 (1)	239 (0)	39 (0)	10 (0)	56 (4)	61 (1)	7 (0)
Other antibiotics, (%)	48 (1)	34 (22)	10 (14)	1544 (2)	324 (1)	11 (0)	77 (5)	646 (7)	335 (3)

Table S5. Heatmap of the number of treatment changes (switch or prolongation) switch and prolongation with the relative prevalence on total treatment switch and prolongation. Pedianet, 2012-2018

ANTIBIOTIC 1	ANTIBIOTIC 2									
	Amoxicillin	Co-amoxiclav	Fluoroquinolones	II-gen. cephalosporins	III-gen. cephalosporins	J01XX	Macrolides	Other	Other aminoglycosides	Grand Total
TREATMENT SWITCH AND PROLONGATION										
Amoxicillin, N(%)	3107 (8.2)	1052 (2.8)	5 (0)	300 (0.8)	841 (2.2)	35 (0.1)	1321 (3.5)	13 (0)	8 (0)	6682 (17.7)
Co-amoxiclav, N(%)	522 (1.4)	8132 (21.5)	25 (0.1)	442 (1.2)	1796 (4.8)	116 (0.3)	2406 (6.4)	45 (0.1)	17 (0)	13501 (35.7)
Fluoroquinolones, N(%)	1 (0)	15 (0)	59 (0.2)	1 (0)	9 (0)	1 (0)	4 (0)	(0)	(0)	90 (0.2)
II-gen. cephalosporins, N(%)	99 (0.3)	366 (1)	2 (0)	986 (2.6)	269 (0.7)	16 (0)	338 (0.9)	9 (0)	2 (0)	2087 (5.5)
III-gen. cephalosporins, N(%)	245 (0.6)	1080 (2.9)	11 (0)	229 (0.6)	3890 (10.3)	42 (0.1)	1271 (3.4)	28 (0.1)	9 (0)	6805 (18)
J01XX, N(%)	92 (0.2)	286 (0.8)	4 (0)	40 (0.1)	124 (0.3)	81 (0.2)	149 (0.4)	14 (0)	(0)	790 (2.1)
Macrolides, N(%)	420 (1.1)	1679 (4.4)	9 (0)	262 (0.7)	1253 (3.3)	46 (0.1)	3900 (10.3)	22 (0.1)	6 (0)	7597 (20.1)
Other, N(%)	14 (0)	43 (0.1)	2 (0)	7 (0)	29 (0.1)	5 (0)	27 (0.1)	55 (0.1)	(0)	182 (0.5)
Other aminoglycosides, N(%)	9 (0)	10 (0)	1 (0)	2 (0)	5 (0)	(0)	1 (0)	(0)	20 (0.1)	48 (0.1)
Grand Total, N(%)	4509 (11.9)	12663 (33.5)	118 (0.3)	2269 (6)	8216 (21.7)	342 (0.9)	9417 (24.9)	186 (0.5)	62 (0.2)	37782 (100)
ONLY TREATMENT SWITCH										
Amoxicillin, N(%)	(0)	1049 (5.99)	5 (0.03)	300 (1.71)	840 (4.79)	35 (0.2)	1320 (7.53)	13 (0.07)	8 (0.05)	3570 (20.37)
Co-amoxiclav, N(%)	520 (2.97)	(0)	25 (0.14)	440 (2.51)	1792 (10.23)	115 (0.66)	2402 (13.71)	45 (0.26)	17 (0.1)	5356 (30.57)
Fluoroquinolones, N(%)	1 (0.01)	15 (0.09)	(0)	1 (0.01)	9 (0.05)	1 (0.01)	4 (0.02)	(0)	(0)	31 (0.18)
II-gen. cephalosporins, N(%)	98 (0.56)	366 (2.09)	2 (0.01)	(0)	269 (1.54)	16 (0.09)	338 (1.93)	9 (0.05)	2 (0.01)	1100 (6.28)
III-gen. cephalosporins, N(%)	244 (1.39)	1078 (6.15)	11 (0.06)	228 (1.3)	(0)	42 (0.24)	1270 (7.25)	28 (0.16)	9 (0.05)	2910 (16.61)
J01XX, N(%)	92 (0.53)	285 (1.63)	4 (0.02)	40 (0.23)	124 (0.71)	(0)	149 (0.85)	14 (0.08)	(0)	708 (4.04)
Macrolides, N(%)	420 (2.4)	1676 (9.57)	9 (0.05)	261 (1.49)	1252 (7.15)	46 (0.26)	(0)	22 (0.13)	6 (0.03)	3692 (21.07)
Other, N(%)	14 (0.08)	42 (0.24)	2 (0.01)	7 (0.04)	29 (0.17)	5 (0.03)	27 (0.15)	(0)	(0)	126 (0.72)
Other aminoglycosides, N(%)	9 (0.05)	10 (0.06)	1 (0.01)	2 (0.01)	5 (0.03)	(0)	1 (0.01)	(0)	0 (0)	28 (0.17)
Grand Total, N(%)	1398 (7.98)	4521 (25.8)	59 (0.34)	1279 (7.3)	4320 (24.65)	260 (1.48)	5511 (31.45)	131 (0.75)	43 (0.25)	17522 (100)

Figure S1. Antibiotic index in different years stratified by patient years of age. Pedianet, 2012-2018

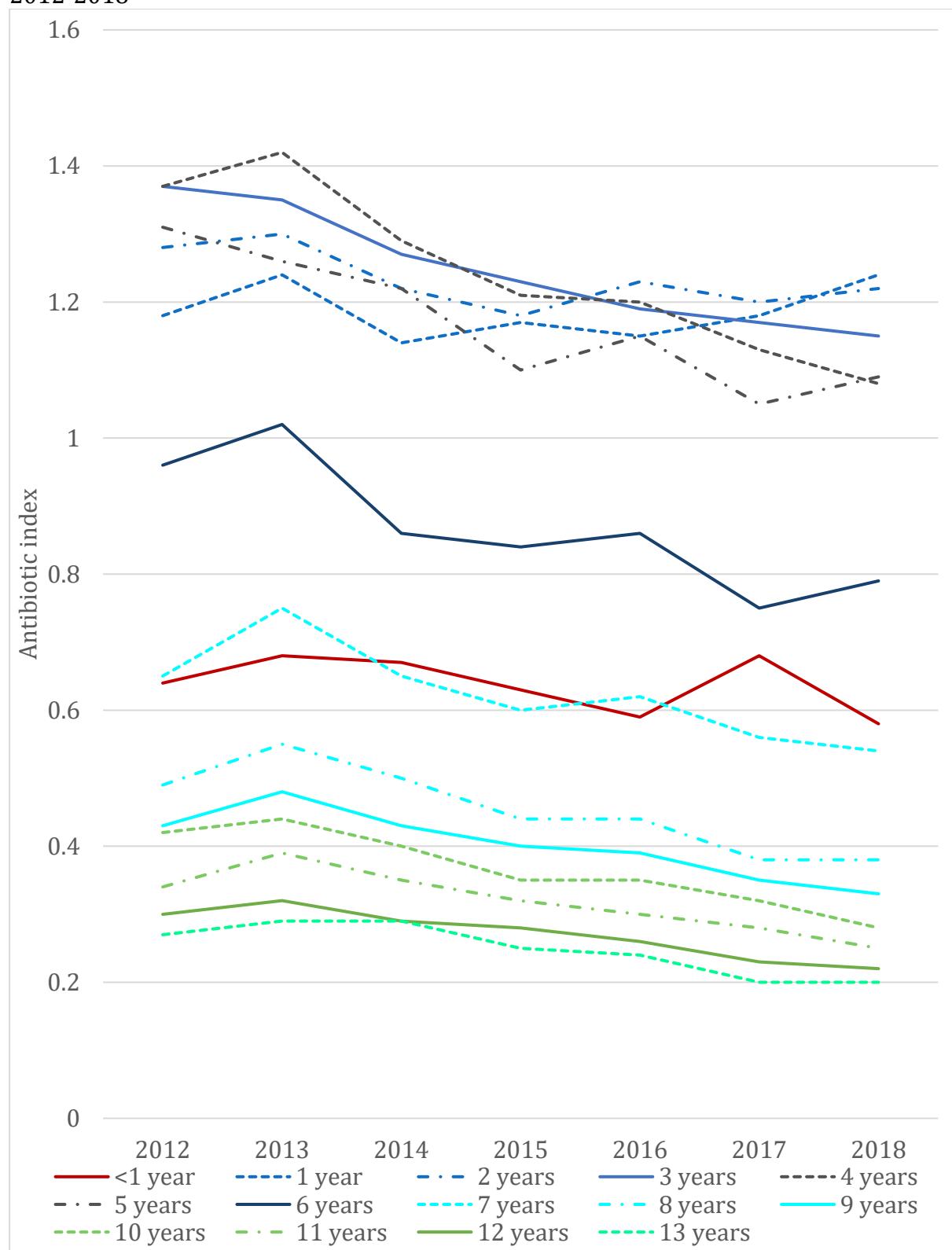
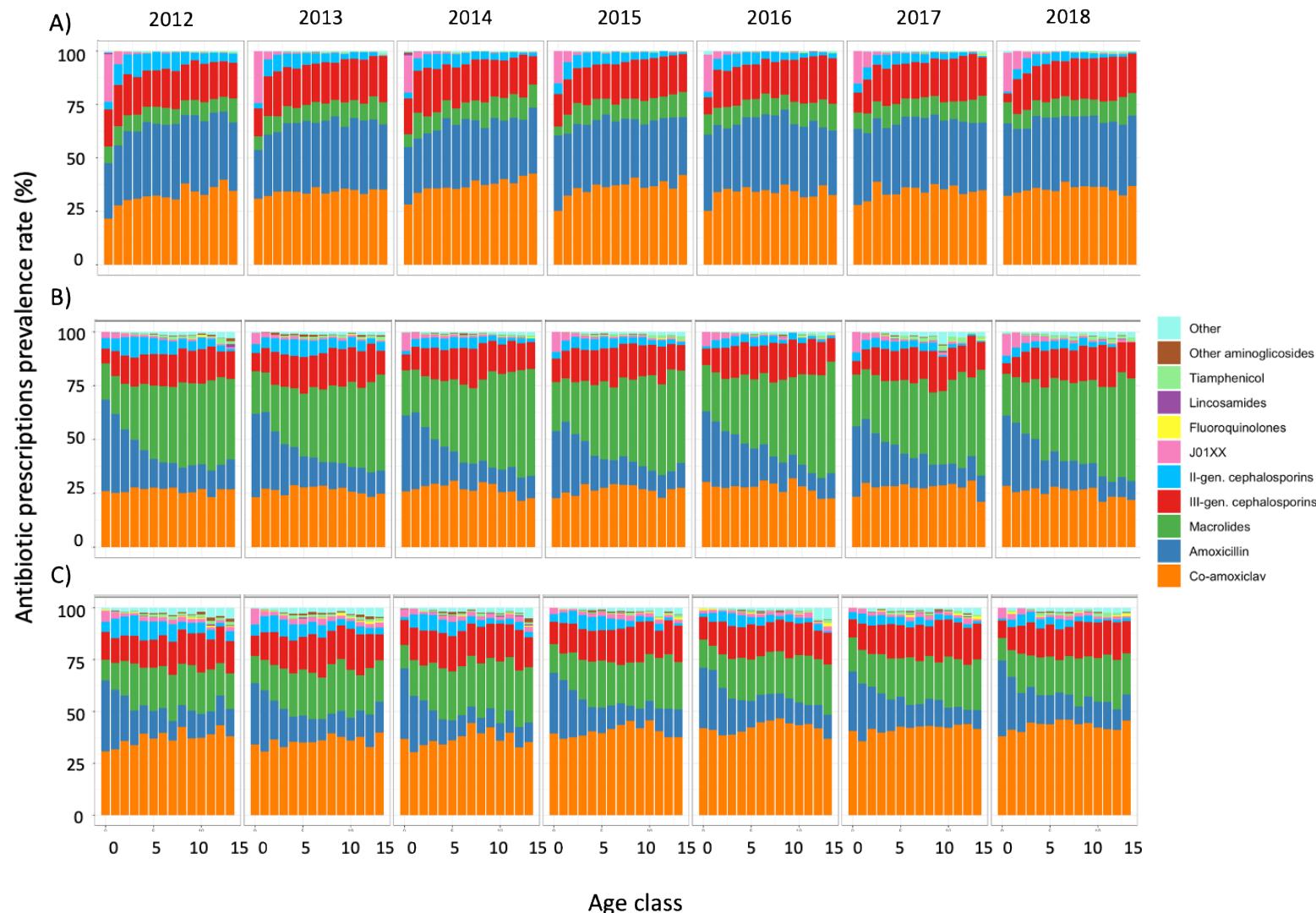
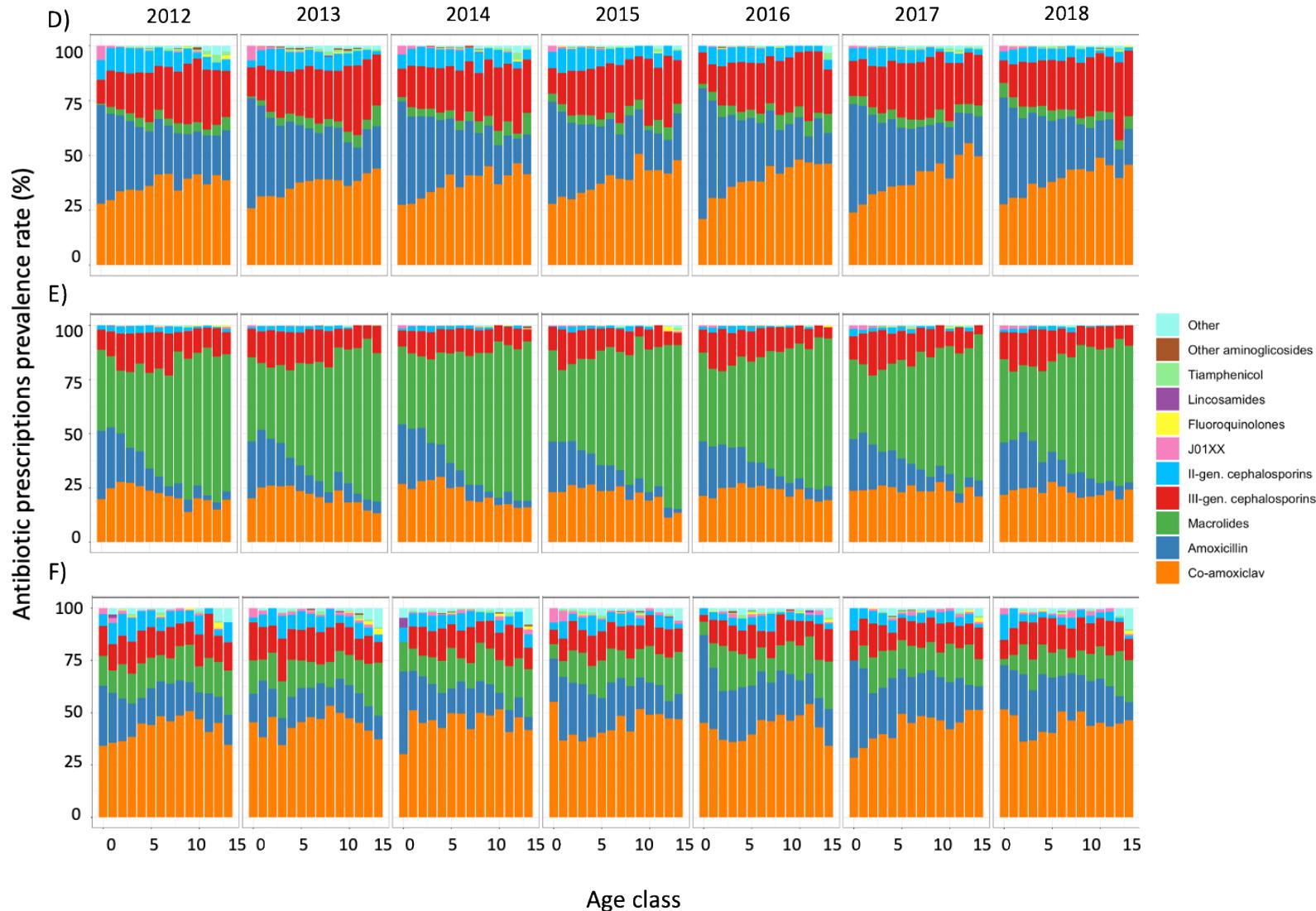
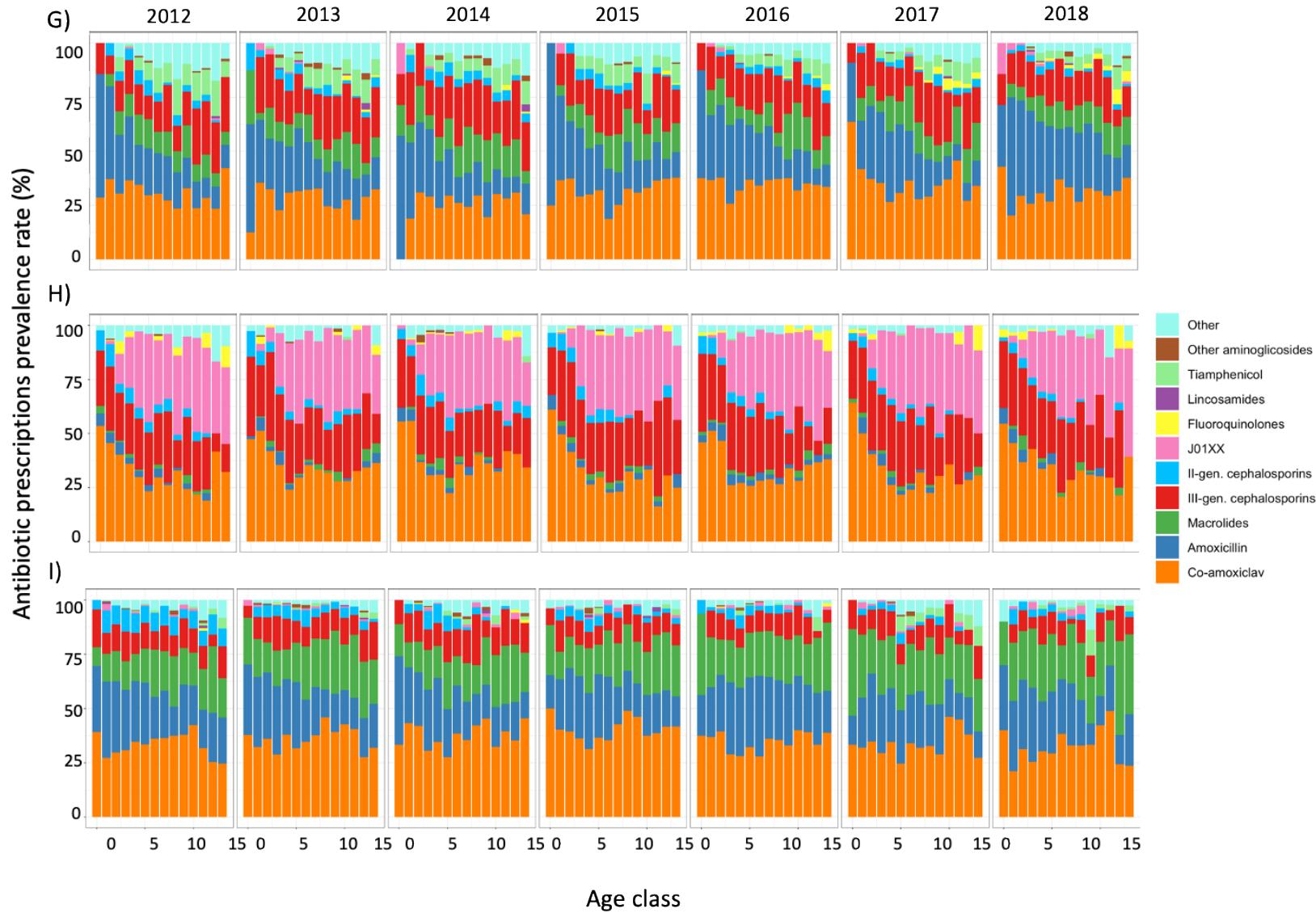


Figure S2. Figure 2s.a Prescription index prevalence rate of antibiotic classes for Pharyngitis (panel A), URTI (panel B), No diagnosis (panel C), AOM (panel D), bronchitis/bronchiolitis (panel E), SMMI (panel F), sinusitis (panel G), UTI (panel H), viral infections (panel I), STI (panel L), pneumonia (panel M) stratified by year and age class. Only diagnosis with prescription for all the strata are reported. Pedianet, 2012-2018







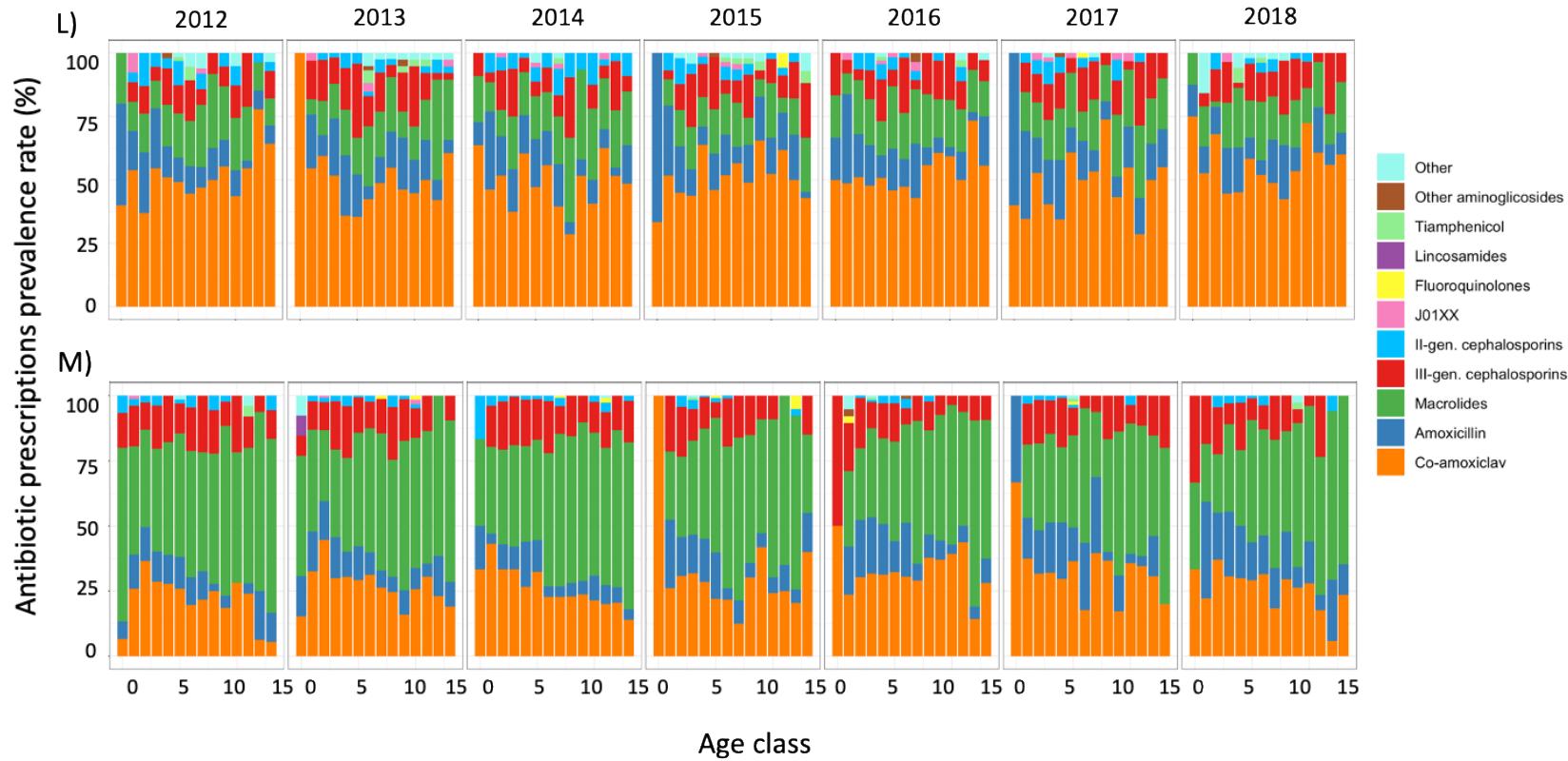


Figure S3. Treatment episodes with at least one switch stratified by diagnosis.

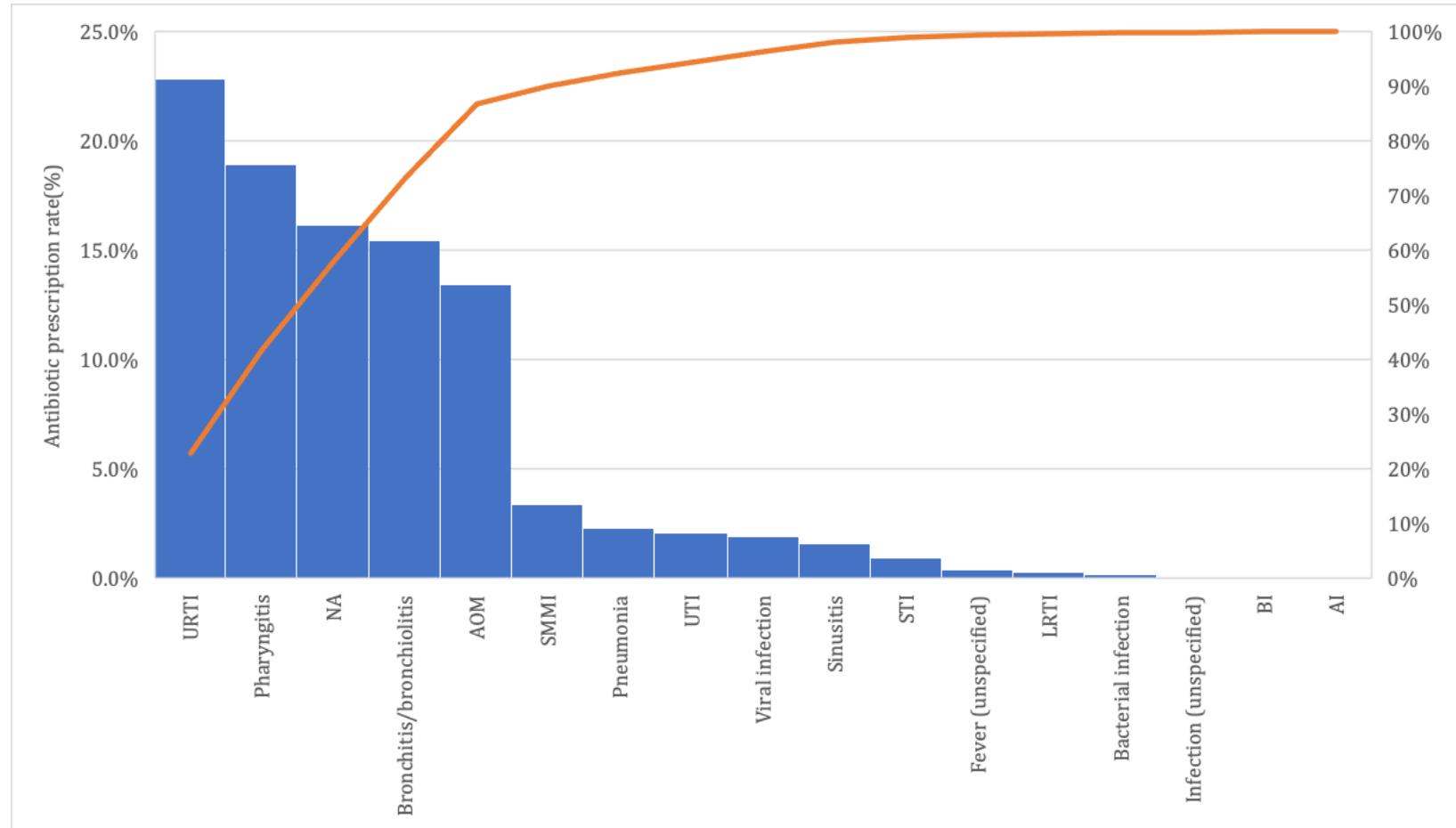


Figure S4. Annual number of patients followed by the 140 FPs participating in Pedianet from 2012 to 2018.

