P0175 Dynamics of serotype/serogroup specific antibiotic resistance of *Streptococcus pneumoniae* in Switzerland (2004-2013)

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Introduction and Purpose

- Nasopharyngeal colonization by *Streptococcus pneumoniae* is a prerequisite for invasive pneumococcal disease (IPD) and for acquisition and exchange of antibiotic resistance.
- 7-valent pneumococcal conjugate vaccine (PCV7) was added to the infant vaccine schedule in Switzerland in late 2006 and was replaced by PCV13 in 2011.
- There was a significant decline in PCV7 serotypes among adults with IPD in Switzerland (Meichtry *et al.).*
- PCVs may have influenced not only incidence of pneumococcal disease but also antibiotic resistance.
- A surveillance of the dynamics of antibiotic resistance within both invasive and colonizing *S. pneumoniae* is important.
- **Objective of the study:** To simultaneously describe the dynamics of antibiotic resistance in *S. pneumoniae* in non-invasive and invasive pneumococcal isolates from Switzerland from 2004-2013.

Methods

- Swabs were collected by sentinel general practitioners and paediatricians for culturing non-invasive *S. pneumoniae* at the NZPn (National Reference Laboratory for Pneumococcal Disease)
- All clinical microbiology laboratories were obliged to send invasive *S. pneumoniae* isolates to the NZPn.
- Invasive and non-invasive *S. pneumoniae* isolates were cultured and serotyped using standardised methods (Quellung reaction). Antibiograms were received for penicillin, Co-trimoxazole, ceftriaxone and erythromycin.
- 2x2 χ^2-tests and Cochran-Armitage test of trend, to examine time trends of resistance rates within distinct demographic groups were used for analyses. $P<0.05$ is considered significant.
- Serotype/serogroup specific antibiotic resistance of invasive and colonizing *S. pneumoniae* isolates was calculated by multivariate logistic regression analysis. Odds ratios (OR) with 95% confidence intervals (95%CI) were adjusted adjusted for age group, geographical origin and serotype/serogroup.

Results

1. Characteristics of isolates included in this study

- In total, 2,067 non-invasive and 10,152 invasive pneumococcal isolates were analysed from January 2004 to December 2013.
- The patient population for the non-invasive *S. pneumoniae* differed from the invasive populations by a significant higher proportion of children below the age of 5 years and by consisting of outpatients exclusively (Table 1).
- Roughly a fourth of all isolates were retrieved from the west as compared to the rest of Switzerland.
- Overall, 26 serotypes/serogroups were identified with an prevalence of >0.7% of which 20 serotypes/serogroups were either significantly more often found in non-invasive or invasive isolates, respectively.

Table 1: Characteristics of invasive and non-invasive pneumococcal isolates from Switzerland (2004-2013)

	Non-Invasive		Invasive		
	N	%	N	%	*P*
Total isolates	2067		10152		
Age (years)					
<5	1317	63.7	624	6.1	.000
5-64	684	33.1	3889	38.3	
>64	65	3.1	5017	49.4	
NA	1	0.0	622	6.1	
Region					
West	841	40.7	2593	25.5	.000
Other	1224	59.2	7559	74.5	
NA	2	0.1	0		
Serotype/Serogroup					
1 (PCV13)	21	1.0	472	4.6	.000
3 (PCV13)	305	15.0	1373	13.5	.09
4 (PCV13)	34	1.7	604	5.9	.000
6a (PCV13)	126	6.2	334	3.3	.000
6b (PCV13)	99	4.9	264	2.6	.000
6c	21	1.0	112	1.1	.8
7f (PCV13)	52	2.6	955	9.4	.000
8	14	0.7	515	5.1	.000
9	22	1.1	306	3.0	.000
9v (PCV13)	52	2.6	468	4.6	.000
10	43	2.1	137	1.3	.01
11	103	5.1	203	2.0	.000
12	2	0.1	88	0.9	.000
14 (PCV13)	90	4.4	967	9.5	.000
15	109	5.3	188	1.9	.000
18c (PCV13)	56	2.7	235	2.3	.2
19a (PCV13)	142	7.0	681	6.7	.7
19f (PCV13)	269	13.2	368	3.6	.000
20	6	0.3	80	0.8	.02
22f	53	2.6	459	4.5	.000
23	60	2.9	172	1.7	.000
23f (PCV13)	147	7.2	475	4.7	.000
24	12	0.6	76	0.7	.4
33	17	0.8	112	1.1	.3
35	63	3.1	127	1.3	.000
38	22	1.1	76	0.7	.1
Other	99	4.9	305	3.0	.000
NA	28	1.4	0	0.0	ND

* *P*-value calculated with 2x2 χ2-test.

2. Influence of PCV on antibiotic resistance in *S. pneumoniae*

- For invasive pneumococcal isolates, trend tests showed significantly decreasing antibiotic resistance rates for distinct age groups for penicillin, erythromycin and Co-trimoxazole (Table 2).
- For children aged less than 5 years with non-invasive pneumococcal isolates, decreasing antibiotic resistance rates were also shown for penicillin, erythromycin and Co-trimoxazole.
- Overall, the resistance rates for all tested antibiotics were significantly higher in very young study subjects.

3. Serotype/serogroup specific antibiotic resistance of *S. pneumoniae*

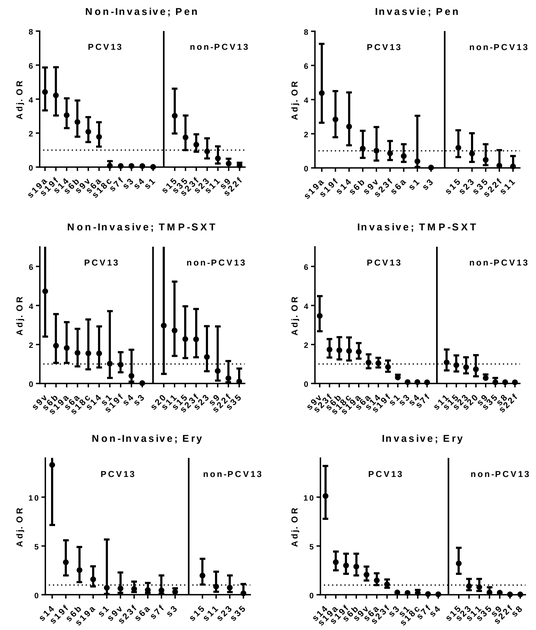
- Multivariate logistic regression analysis revealed 10 serotypes with significantly higher antibiotic resistance rates of which eight were covered by PCV13 (Figure).
- The serotypes most resistant for penicillin (19A), Co-trimoxazole (9V) and erythromycin (14) were simultaneously identified within non-invasive and invasive isolates.
- A future focus should be given to the potentially rising, non-PCV13 serogroups 15 and 35 as they are also associated with increased antibiotic resistance.

Table 2: Time trends of antibiotic resistance rates in % (n), Switzerland 2004-2013

Age group	Antibiotic	2004	2013	*P*[b]
<5 years invasive	penicillin	15.1 (11)	3.4 (1)	.77
	ceftriaxone	2.4 (2)	0 (0)	.41
	erythromycin	26.5 (18)	11.1 (3)	**.02**
	TMP-SMX[a]	31.3 (20)	11.1(3)	.08
5-64 years invasive	penicillin	14.4 (43)	6.9 (25)	**.03**
	ceftriaxone	1.5 (5)	1.9 (7)	.26
	erythromycin	15.6 (46)	8.1 (29)	**.01**
	TMP-SMX[a]	31.7 (82)	15.6 (52)	**<.0001**
>64 years invasive	Penicillin	7.2 (29)	7.1 (34)	.12
	ceftriaxone	0.7 (3)	1.0 (5)	.21
	erythromycin	11.4 (44)	11.1 (51)	.24
	TMP-SMX[a]	22.6 (80)	4.8 (23)	**<.0001**
<5 years non-invasive	penicillin	21.6 (40)	9.7 (3)	**.03**
	ceftriaxone	1.4 (3)	(0)	.14
	erythromycin	20.3 (38)	9.7 (3)	**.015**
	TMP-SMX[a]	30.6 (52)	25.9 (7)	**.0008**

[a] TMP-SMX; Co-trimoxazole
[b] Exact *P* values for Cochran-Armitage trend tests. Statistical tests include all numbers from 2004-2013 but only 2004 and 2013 are shown.

Figure: Multivariate logistic regression analysis of serotype/serogroup specific antibiotic resistance*.



* The 'other' serotypes (below 1%) served as the reference group.
TMP-SXT; Co-trimoxazole. Ery; erythromycin. Pen; penicillin. Adj. OR; Adjusted Odds ratio (see Methods)

Reference (further reading):

Serotype epidemiology of invasive pneumococcal disease in Swiss adults: a nationwide population-based study.
Meichtry J, Born R, Küffer M, Zwahlen M, Albrich WC, Brugger SD, Mühlemann K, Hilty M. Vaccine. 2014 Sep 8;32(40):5185-91

Conclusions

- **As for 2013 antibiotic resistance rates are on an all-time low for distinct age groups/ and antibiotics both for colonizing and invasive pneumococcal isolates.**
- **Decreasing resistance rates were attributable to the reduction of more resistant serotypes due to the introduction of PCV7 and PCV13.**
- **Certain non-PCV13 serotypes prone to carry resistance have to be carefully monitored in the future.**

Acknowledgements

The NZPn is funded by the Swiss Federal Office of Public Health. Markus Hilty received an educational grant from Pfizer AG. However, Pfizer AG has no influence on any aspects of this surveillance or decision to publish. All other authors have no conflicts. We thank all the general practitioners and paediatricians of the Sentinel study for providing samples for the characterisation of colonizing *S. pneumoniae.*