Resistance Evolution in Respiratory Tract Pathogens During Hospitalization (P1052)

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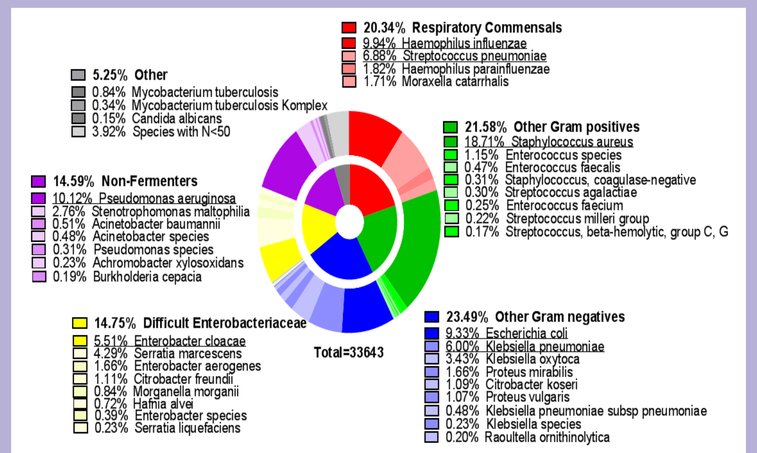
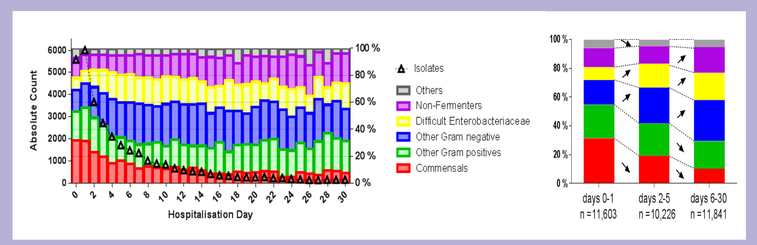
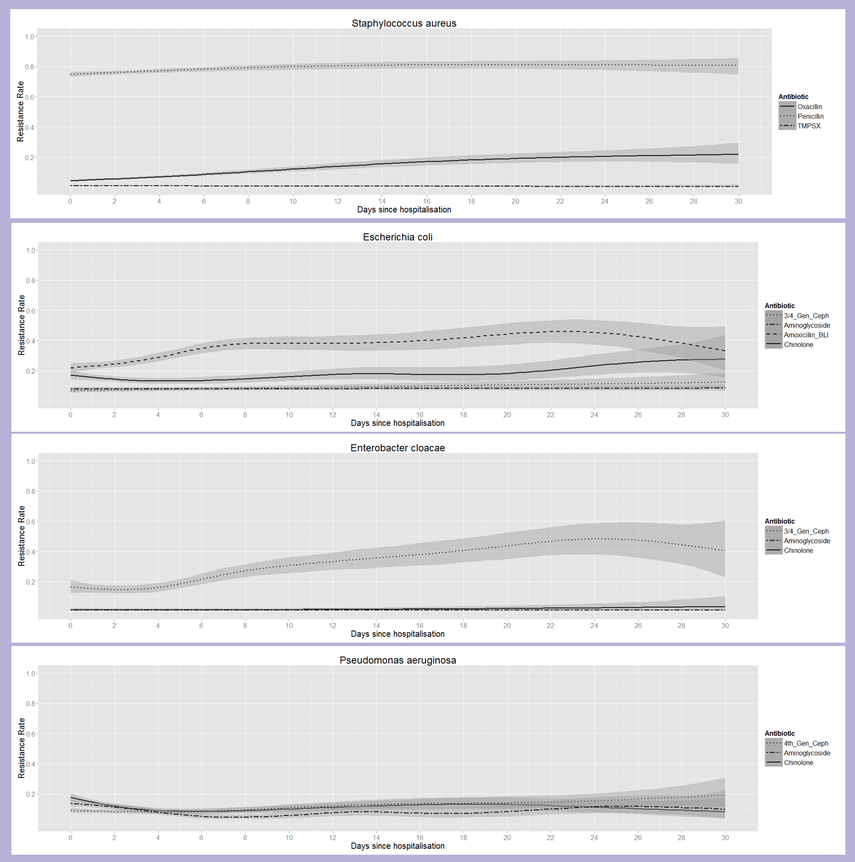
Recommendations for empirical antibiotic therapy of hospital-acquired pneumonia are currently based on local susceptibility patterns of commonly detected pathogens, patient characteristics and length of hospital stay. However, the influence of length of stay on antimicrobial resistance has not been systematically studied.

Using data from the Swiss Antibiotic Resistance Surveillance System (anresis.ch), antimicrobial resistance testing results from patients hospitalized between 2008-2014 were compiled and stratified for length of stay, sampling method, environmental (ward type, type of referral center, linguistic region) and host factors (age, sex). General additive and general linear models were applied to illustrate resistance odds.

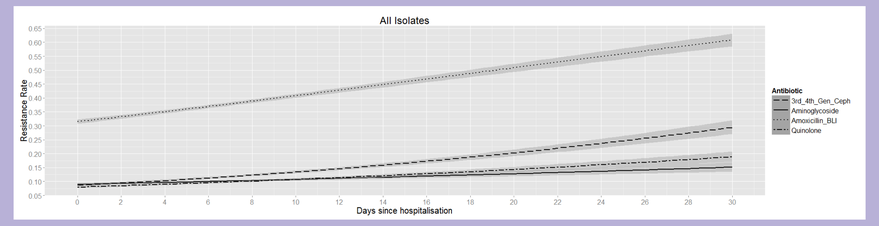




Allocation of primary isolates into species, bacterial group and recovery day
Top: Primary isolates were allocated into functional bacterial groups (bold, shown in the inner ring). Species with an overall incidence of > 5% are underlined. Bottom, Left: Bacterial groups are plotted according to their proportion of recovery on each hospitalization day. Superimposed is the absolute count of primary isolates recovered during a specific day of hospitalization (left). Grouping of days into community acquired (days 0-1), early nosocomial (2-5) and late nosocomial (6-30) was performed in order to study expansion/contraction of the bacterial groups (Bottom, Right).



Resistance rate for selected species in respiratory tract isolates
Generalized additive model of important antibiotics or antibiotic groups: Resistance rates (lines) per hospitalization day for the most representative species of the bacterial groups are shown. Top to Bottom: *Staphylococcus aureus*, *Escherichia coli*, *Enterobacter cloacae* and *Pseudomonas aeruginosa*. The corresponding 95% confidence intervals are grey-shaded.



Overall Resistance rate for respiratory tract isolates
Overall Resistance rates per hospitalization day for important antibiotics or antibiotic groups of primary isolates with testing available (lines) were calculated and displayed by using a generalized linear model. The corresponding 95% confidence intervals are grey-shaded.

	Amoxicillin_BLI	Aminoglycoside	3/4 Gen Ceph	Chinolone
Samples (n)	24,765	24,759	23,641	28,325
Background				
Resistance rate	0.467*** (0.433, 0.503)	0.066*** (0.058, 0.075)	0.113*** (0.102, 0.126)	0.0745*** (0.066, 0.083)
Increase in resistance odds / day	1.065*** (1.056, 1.075)	1.038*** (1.025, 1.051)	1.063*** (1.054, 1.072)	1.031*** (1.020, 1.042)
Recovery method = BAL				
Odds of increase in resistance compared to background	0.760** (0.644, 0.894)	1.125 (0.877, 1.430)	1.047 (0.821, 1.323)	0.922 (0.729, 1.156)
Increase in resistance odds / day compared to background	1.025** (1.006, 1.045)	1.033** (1.010, 1.056)	1.022 (0.999, 1.046)	1.037*** (1.015, 1.058)
Age > 60				
Odds of increase in resistance compared to background	1.497*** (1.391, 1.611)	0.721*** (0.641, 0.811)	Not in final model	0.881* (0.787, 0.985)
Increase in resistance odds / day compared to background	0.991* (0.983, 0.999	1.014* (1.003, 1.026)	Not in final model	1.021*** (1.010, 1.032)
Unit Type = ICU				
Odds of increase in resistance compared to background	1.058 (0.984, 1.139)	1.966***(1.743, 2.221)	1.100 (0.980, 1.235)	1.652*** (1.472, 1.854)
Increase in resistance odds / day compared to background	0.978*** (0.970, 0.986)	0.969***(0.958, 0.980)	0.982** (0.972, 0.993)	0.968***(0.958, 0.978)
Sex = Female				
Odds of increase in resistance compared to background	Not in final model	1.196*** (1.094, 1.306)	1.089 (0.998, 1.187)	1.189*** (1.093, 1.294)
Increase in resistance odds / day compared to background	Not in final model	Not in final model	Not in final model	Not in final model
Tertiary Referral Center = yes				
Odds of increase in resistance compared to background	0.749*** (0.694, 0.809)	1.131* (1.002, 1.276)	0.715*** (0.659, 0.776)	0.644*** (0.593, 0.700)
Increase in resistance odds / day compared to background	0.987** (0.979, 0.996)	0.975*** (0.964, 0.986)	Not in final model	Not in final model
Linguistic Region = Latin Languages				
Odds of increase in resistance compared to background	Not in final model	1.139* (1.010, 1.283)	0.785*** (0.695, 0.885)	1.336*** (1.195, 1.494)
Increase in resistance odds / day compared to background	Not in final model	1.010 (0.0998, 1.022)	0.991 (0.980, 1.002)	1.011* (1.000, 1.021)

Adjusted generalized linear model with time interaction for overall resistance
"Background" reports the rate of resistance and the odds ratio of an increase in resistance / day for samples with levels *recovery method* = sputum or tracheobronchial secretion, *age* ≤ 60, *unit type* = general ward, *sex* = male, *tertiary referral center* = no and *linguistic region* = German language. Each factor was independently included in the equation and with a time-interacting (days since hospitalization). Only factors that were not excluded by a backwards stepwise path approach are shown in this final model. Thus, odds ratio for resistance and increase / day compared to the background values are reported for the alternative levels (e.g. *recovery method* = bronchoalveloar lavage). Significant results are indicated with *p<0.05; **p<0.01; ***p<0.001. The 95% confidence intervals are in brackets.

The current concept of early versus late hospital-acquired pneumonia implies that antimicrobial resistance develops in a biphasic manner and assumes length of stay is a crucial predictor. Our findings suggest a more complicated picture: Overall resistance development is i) the result of a shift towards more resistant species, ii) an overlap of distinct resistance evolution patterns for individual species (*monophasic or biphasic),* and iii) dependent on sampling methods, environmental and host factors. As increasing resistance was not observed for all antibiotics, length of stay appears not to be the primary contributor. These findings question the current clinical classification as a guide for choosing empirical antibiotics for hospital-acquired pneumonia.

Abbreviation: TMPSX, Trimethoprim / Sulfamethoxazol; BLI, Beta Lactamase Inhibitor; Gen Ceph, Generation Cephalosporine

Disclosures: none