

# THE IMPACT OF NON-HUMAN TRANSMISSIONS ON THE FUTURE PREVALENCE OF ESBL-PRODUCING *KLEBSIELLA PNEUMONIAE*:

## A POPULATION BASED MATHEMATICAL MODELLING STUDY

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### BACKGROUND

- Prevalence of human colonization with extended-spectrum beta-lactamases (ESBL) producing *Klebsiella pneumoniae* continues to increase. Increasing colonization might be explained by different, interacting factors:
  - Migration of people between hospital and community settings (*local*)
  - Consumption of antimicrobial therapy (*local*)
  - Human-to-human transmission (*local*)
  - Travel to high prevalence countries (*external source of colonization*)
  - Consumption of contaminated food (*external source of colonization*)
- The roles of *local* and *external sources of colonization* in the dynamics of the spread of resistance has not been characterized. But such roles may determine the success of public health interventions
- the Swiss Centre for Antibiotic Resistance ([anresis.ch](http://anresis.ch)) has collected data on antimicrobial consumption and resistance testing since 2004

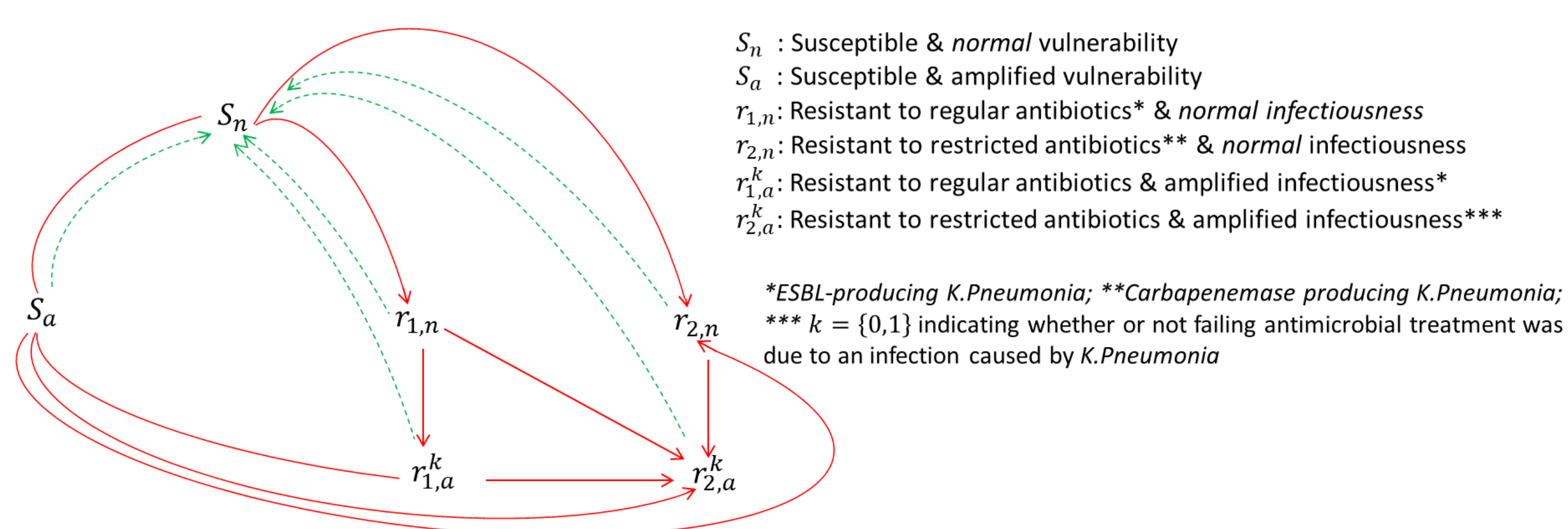
### OBJECTIVES

- To reconstruct the observed course of prevalence of resistance in hospital and community settings by means of a mathematical model
- To use this mathematical model to project future prevalence of *ESBL-producing K. pneumoniae* in scenarios that assume different contributions of *external sources of colonization*

### METHODS

- The model:**
- Mathematical model simulating the spread of colonization with resistant *K. pneumoniae* in two interconnected settings: hospitals and the community
  - Each setting was simulated with a core model (**Figure 1**).
  - Vulnerability to colonization and infectiousness can increase through antimicrobial treatment

Figure 1: Model states and transitions



**Parameterization:**  
The model was primarily informed with [anresis.ch](http://anresis.ch) data on antimicrobial consumption and hospitals occupancy in a Swiss canton with stable population structure. Published data informed the model parameters that reflect mechanisms representing biological processes

- Calibration:**
- Model fitted to data on *ceftriaxone* and *carbapenem* susceptibility
  - We estimated human-to-human transmission rates of resistant *K. pneumoniae* in each setting (community versus hospitals)
  - The model assessed the role of the *external force of colonization* by assuming can explain different fractions of the observed prevalence (**\*external force of colonization equivalent**)

### RESULTS

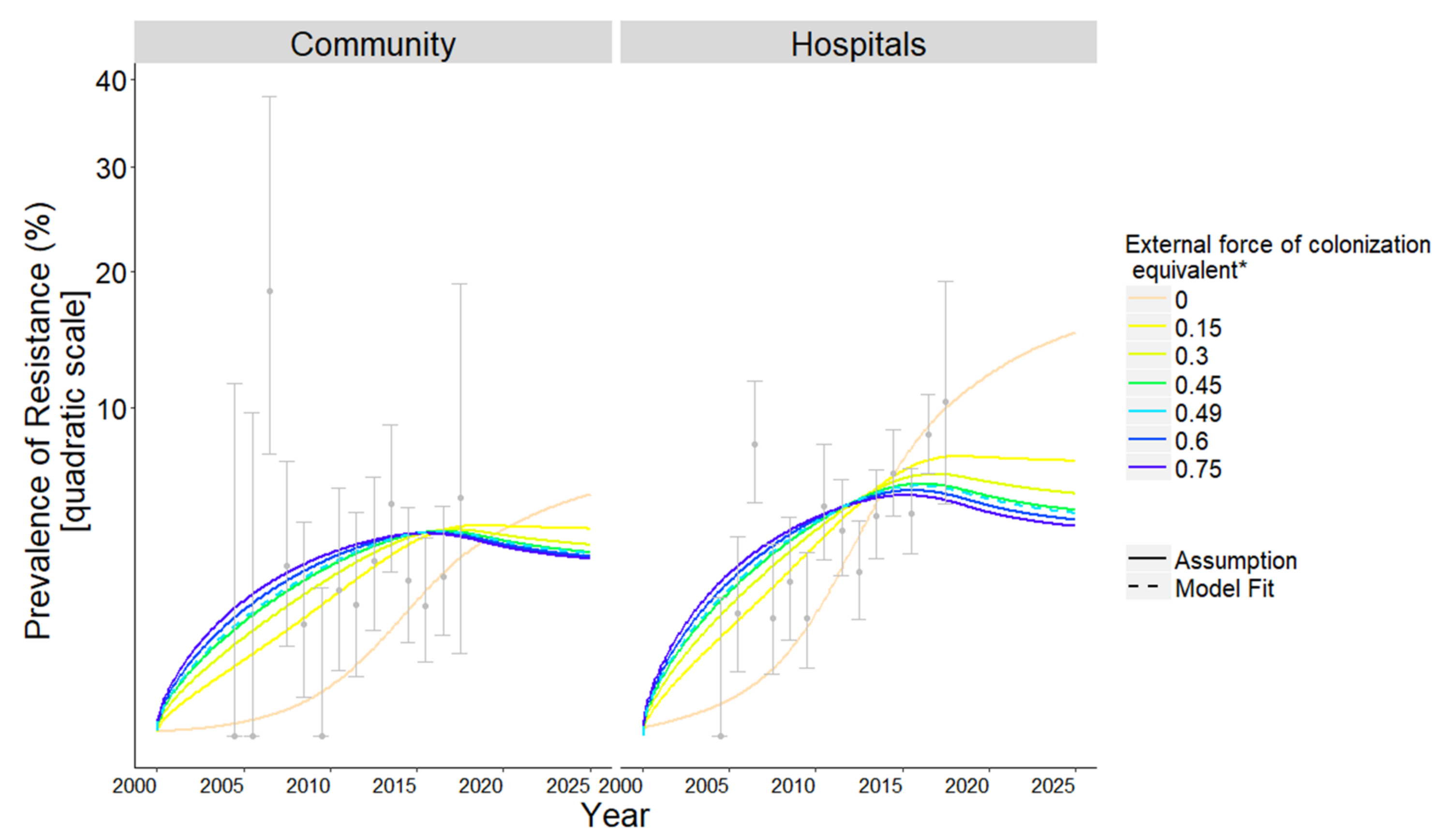
**Model fit**  
The model reconstructed the observed trends in prevalence of ESBL-producing *K. pneumoniae* between 2004 and 2017 (**Figure 2**)

- External force of colonization:**
- We investigated **hypothetical values** for external forces of colonization implying that external sources accounted for **0% to 75%** of all colonizations observed by the surveillance (**external force of colonization equivalent**; **Figures 2 and 3**)

### RESULTS

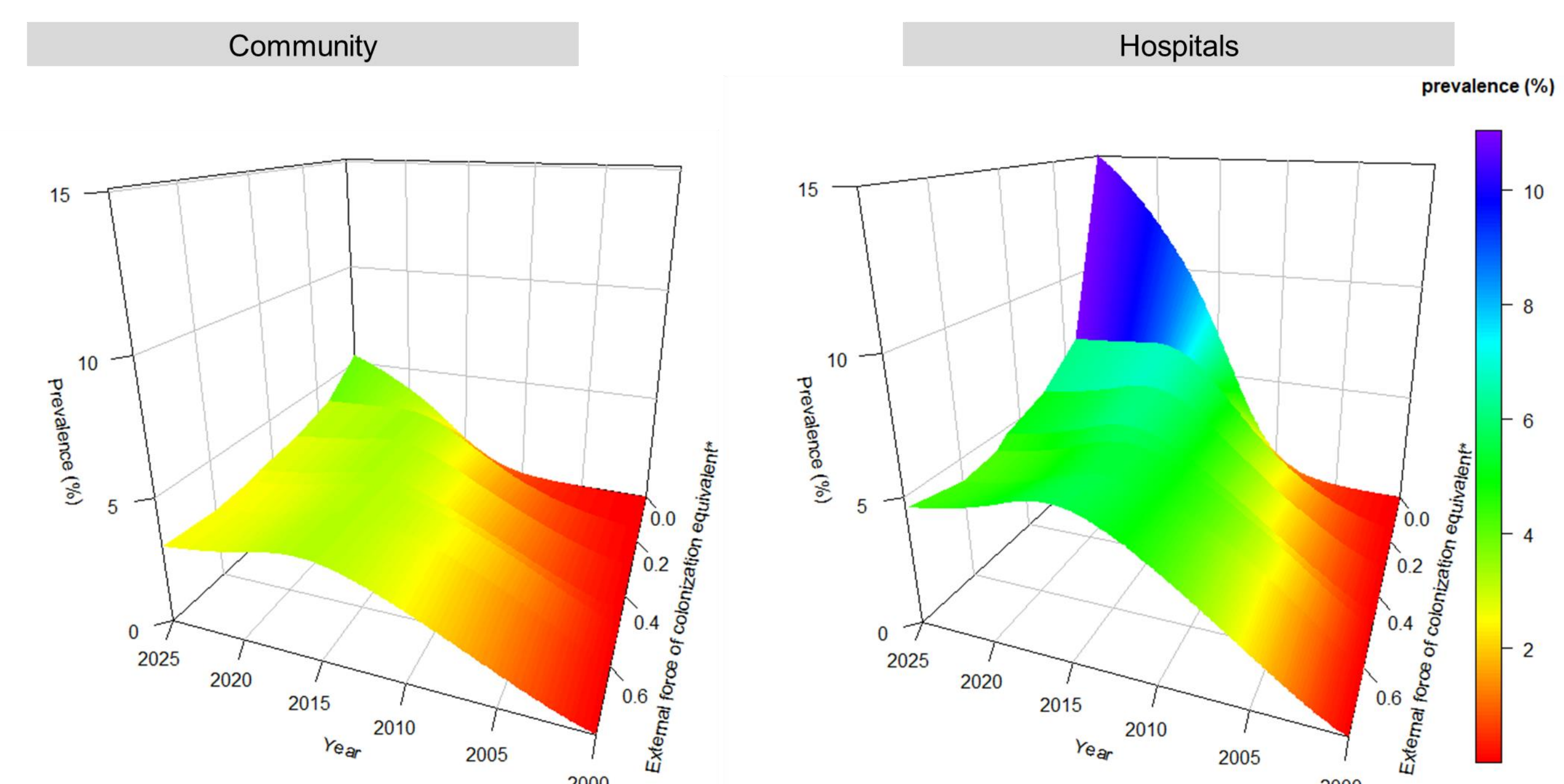
- The best model fit implies an external force of colonization equivalent of **49%** (**Figure 2**).
- Assuming Increasing values for the external force of colonization resulted in lower, stabilizing future prevalence (**Figure 2**).

Figure 2: Prevalence versus time and external force of colonization: Detailed projections including data points (grey dots and error bars with 95% confidence intervals).



- As expected, prevalence of resistance in the community was systematically lower than that in hospitals (maximum values: < 6% versus < 16% ; **Figure 3**).

Figure 3: Prevalence versus time and external force of colonization



### DISCUSSION

- The model suggests that the prevalence of ESBL-producing *K. pneumoniae* could stabilize in the near future.
- This effect depends on the magnitude of the *external force of colonization*.
- Quantifying this factor may be critical for planning interventions to reduce prevalence.

### ACKNOWLEDGEMENTS

Patients, health-care workers who contributed to data collection and [www.anresis.ch](http://www.anresis.ch); this project is funded by **@RAMI: INSEL GRANT DETAILS**