

# Quantifying the impact of antimicrobial usage on the acquisition of extended spectrum beta-lactamase producing *Enterobacteriaceae*

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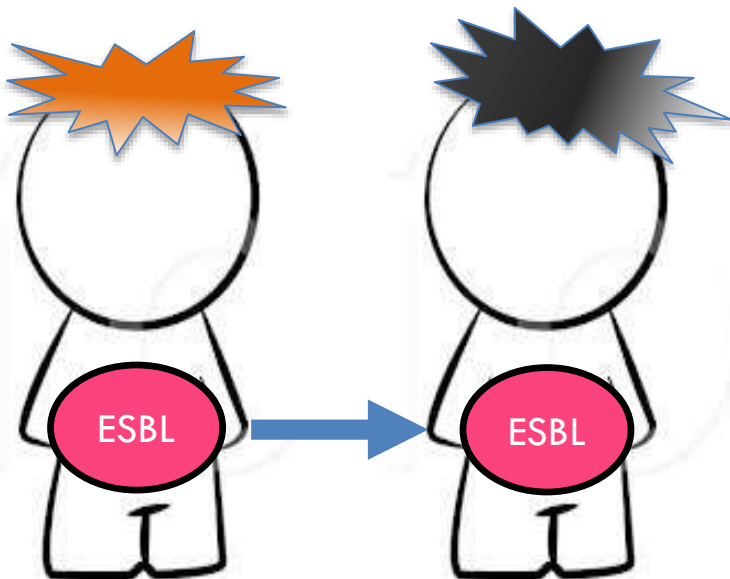
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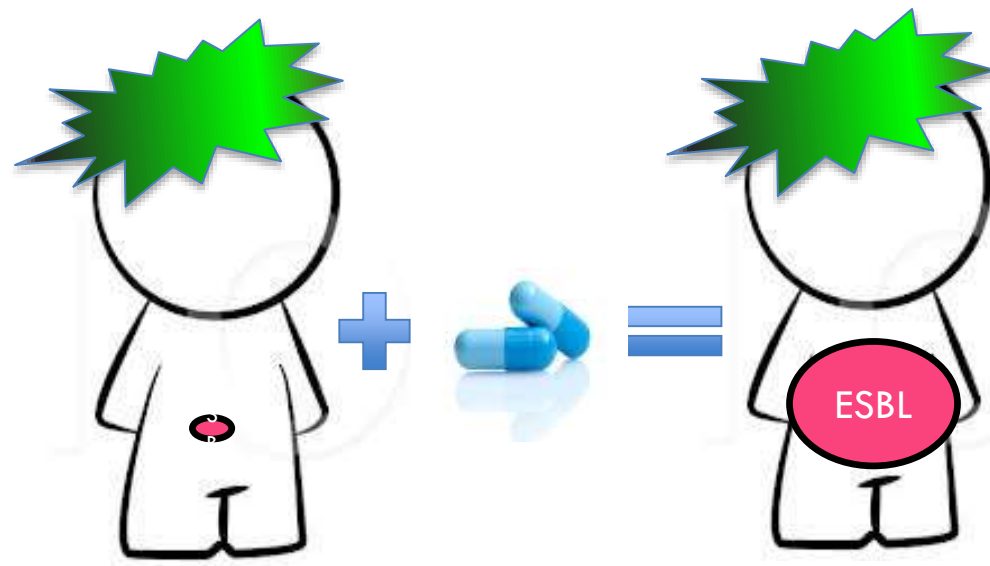
# Background

Global emergence of extended spectrum beta-lactamase producing (ESBL) Enterobacteriaceae

Patient-to-patient/  
Exogenous acquisition

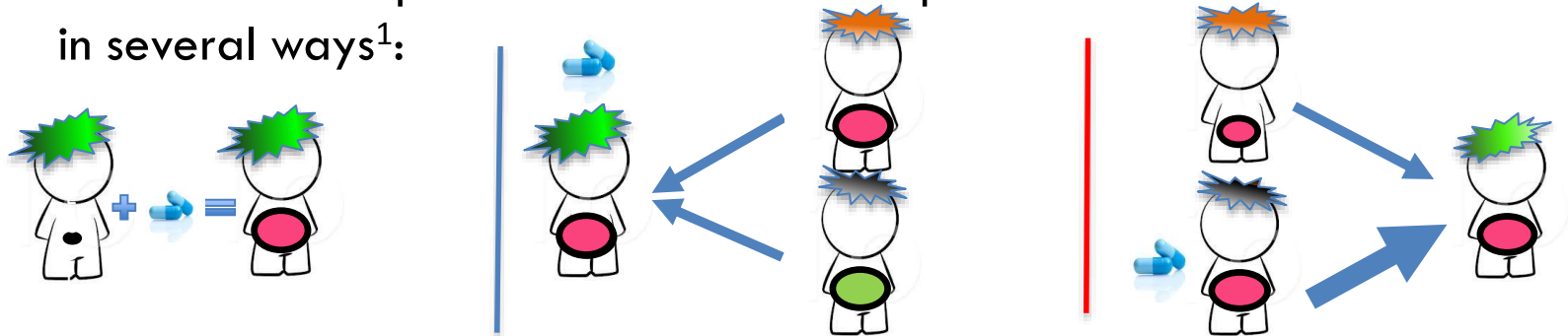


Selection/  
Endogenous acquisition



# Background

- Antimicrobial exposure can affect the acquisition risk of resistant bacteria in several ways<sup>1</sup>:



- Previous exposure to antimicrobials associated with ESBL carriage/infection<sup>e.g. 2, 3,4</sup>
- Statistical methods and data used have limitations.
- As a result, do not inform to what extent the likelihood of acquisition of resistant bacteria is changed during or after treatment.
- Can be investigated by fitting mechanistic models to detailed carriage data.

<sup>1</sup> Lipsitch & Samore. EID 2000 8(4): 347 – 352; <sup>2</sup> Ascioğlu et al 2013. Micr Drug Resist 20 (6): 583-590;

<sup>3</sup> Tumbarello et al. AAC 2006 50(2): 498-504; <sup>4</sup> Pena et al. CMI 2006 12: 279-284

# Aim

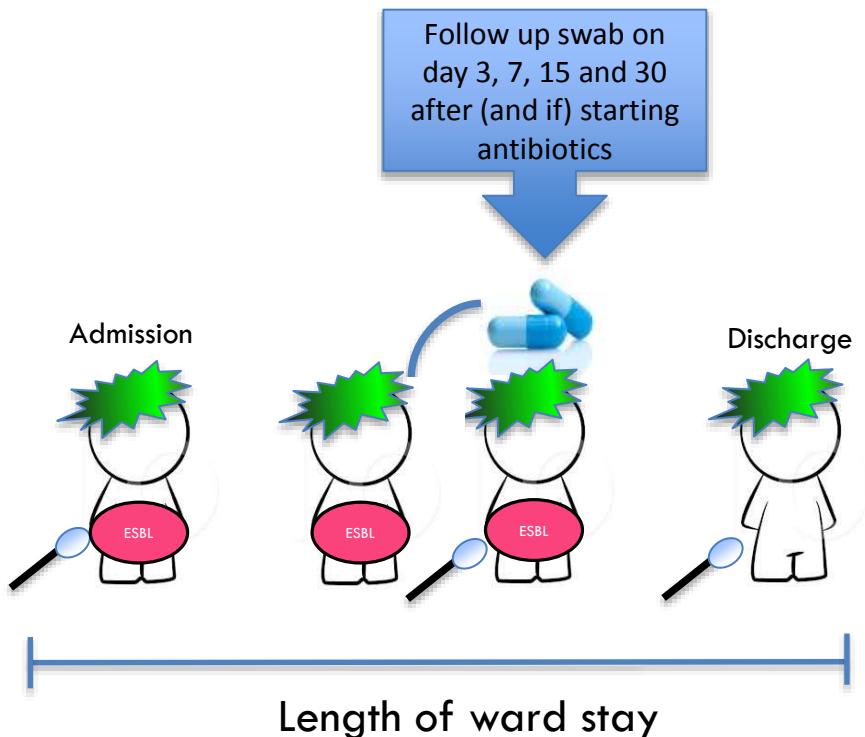
Using mathematical modelling we aim to:

1. Determine the relative importance of endogenous (selection) and exogenous (nosocomial transmission) acquisition of ESBL-producing *E. coli* in hospitals
2. Quantify the individual-level impact of antimicrobial therapy on a patient's rate of acquiring ESBL-producing *E. coli* in hospital

# Methods

## Data

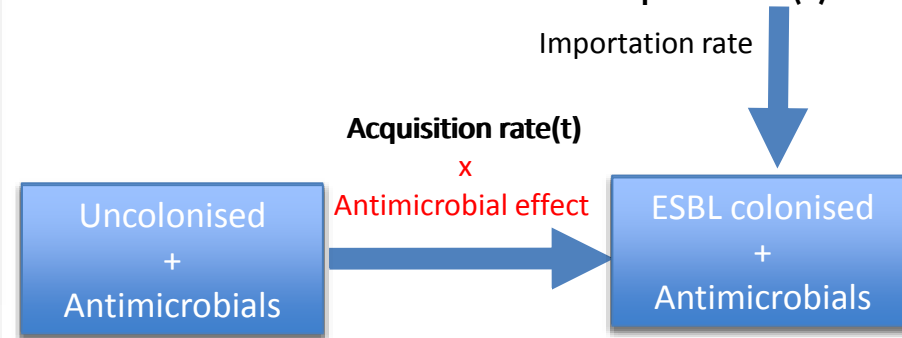
Two-year prospective European cohort study (**medical** and **surgical** wards in **Romania** and **Serbia**): phenotypic ESBL colonization data



## Model

Markov chain Monte Carlo data augmentation algorithm<sup>1</sup>

Acquisition rate(t) = selection rate + transmission rate x colonised patients(t)



Antimicrobial effect > 1 = increased rate of acquisition

Treatment with cephalosporins

<sup>1</sup> Worby et al. AJE 2013 177(11): 1306 - 1313

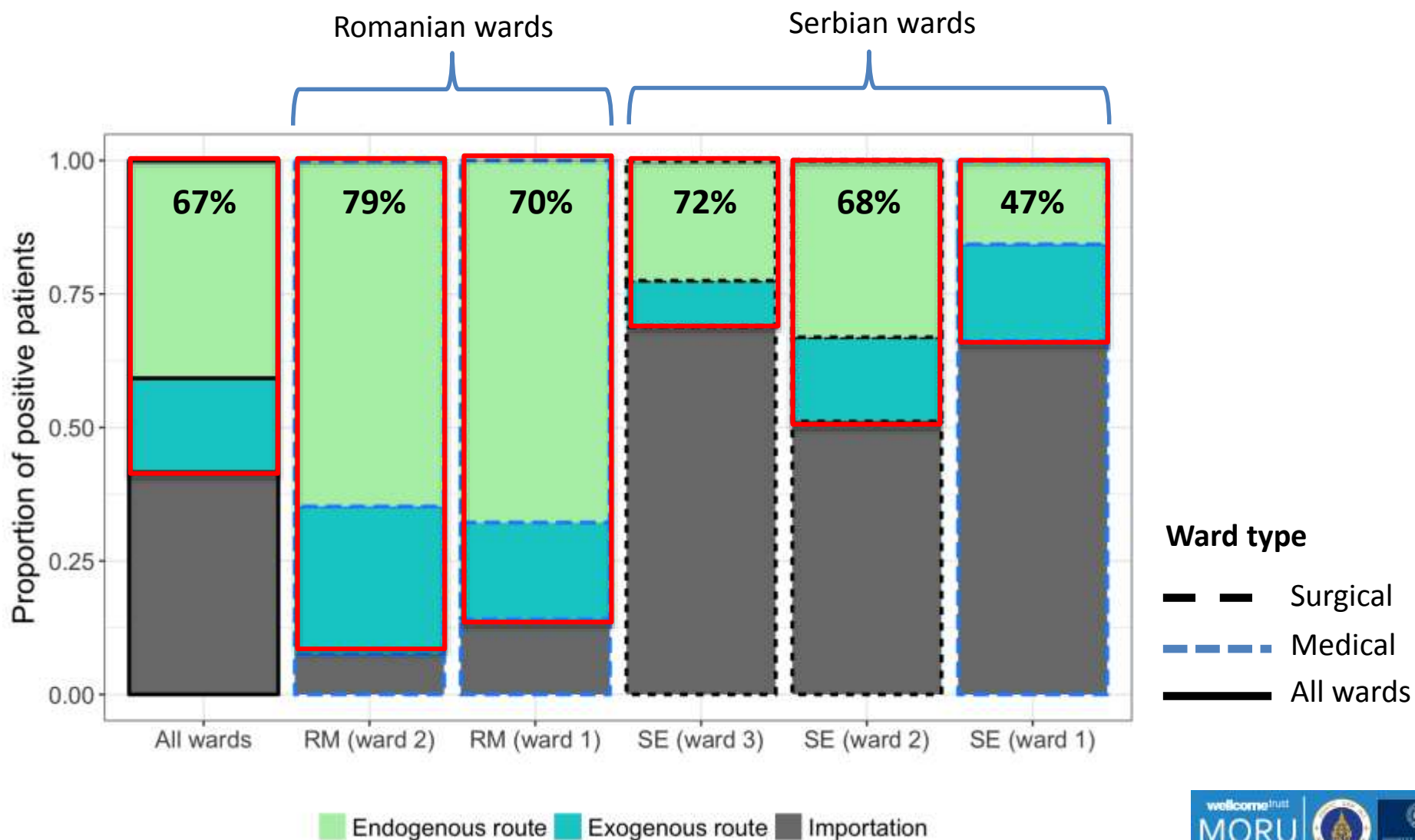
# Summary statistics observed data

| Ward        | Ward type               | n            | Swabs per patient | Importations (%) | Acquisitions (%) | Cephalosporin (%) |
|-------------|-------------------------|--------------|-------------------|------------------|------------------|-------------------|
| SE (ward 1) | Surgical (orthopedic)   | 185          | 4.0               | 9.2              | 11.9             | 57.8              |
| SE (ward 2) | Medical (neurological)  | 675          | 2.1               | 3.6              | 5.0              | 19.0              |
| SE (ward 3) | Medical (endocrinology) | 480          | 2.4               | 5.4              | 3.3              | 12.3              |
| RM (ward 1) | Surgical (orthopaedic)  | 776          | 2.2               | 7.1              | 28.7             | 37.9              |
| RM (ward 2) | Surgical (orthopaedic)  | 701          | 2.3               | 7.9              | 28.7             | 42.9              |
| <b>All</b>  |                         | <b>2,817</b> | <b>2.4</b>        | <b>7.1</b>       | <b>17.6</b>      | <b>31.6</b>       |

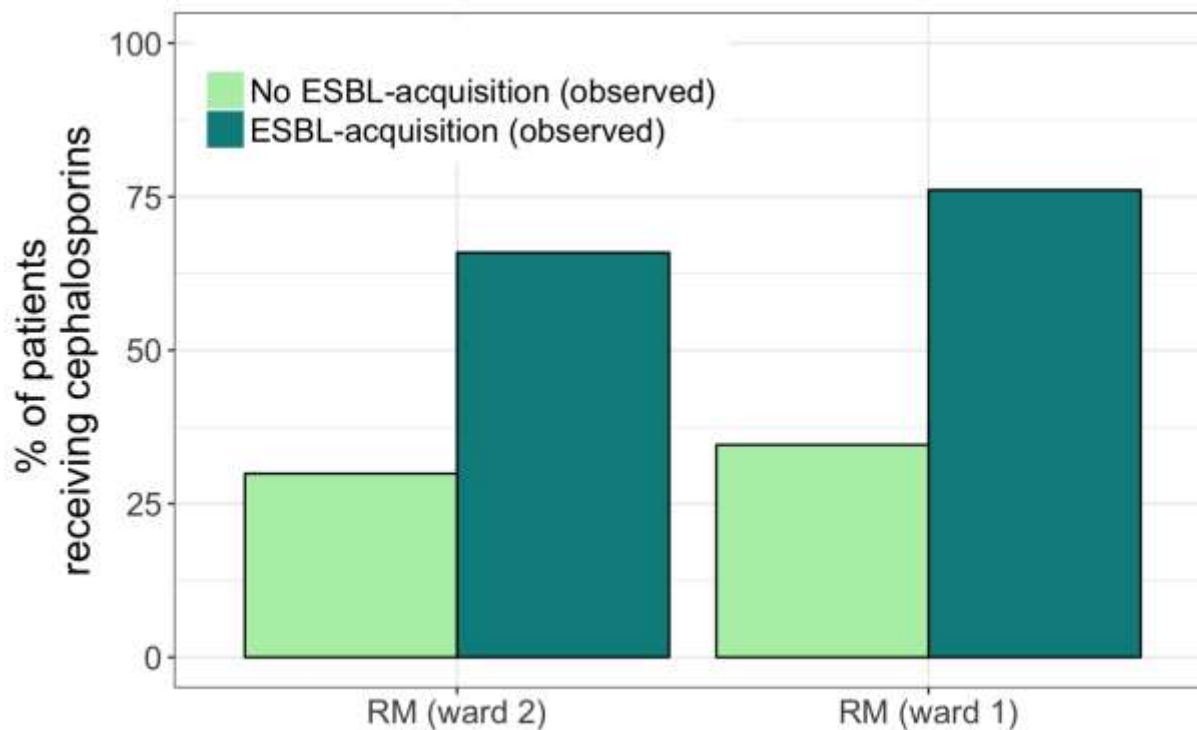
SE = Serbia

RM = Romania

## Relative importance of acquisition routes of ESBL-producing *E. coli*



## The effect of cephalosporin exposure on the acquisition rate of ESBL-producing *E. coli*



**Estimated ESBL-acquisition Rate Ratio (RR) of cephalosporin treated vs not treated patients**

**RM (surgical ward 1)** 0.86 (95%CI: 0.60 – 1.19)

**RM (surgical ward 2)** 1.16 (95%CI: 0.75 – 1.74)



# Conclusions

- **A minority (~30% [Range: 20 – 50]) of hospital-based ESBL-producing *E. coli* acquisitions originated from nosocomial patient-to-patient transmission**
  - Largest fraction of ESBL colonisations imported (Serbia)
  - Largest fraction of ESBL colonisations with an endogenous source (Romania)
- **No strong evidence for cephalosporin treatment resulting in an increased risk of ESBL-producing *E. coli* acquisition in hospital**
  - Clinically important effects of antibiotics cannot be ruled out
  - Work in progress; fitting to a larger dataset
  - Model does not include potential confounders (e.g. other antimicrobials)
  - Investigate the effect of exposure to combination of antimicrobials
  - Need to evaluate how robust these results are to model assumptions
- **Data-augmentation algorithm provides a useful framework to estimate the effect of antimicrobial exposure, without having to make strong assumptions on how and when people acquire a resistant bacteria.**

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**R-GNOSIS**

