PREDICTION OF THE PREVALENCE OF RESISTANCE OF *ACINETOBACTER BAUMANNII* TO COLISTIN IN THE CITY OF VALENCIA (SPAIN) WITH A NEW AGENT-BASED MODEL.

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Disclosure

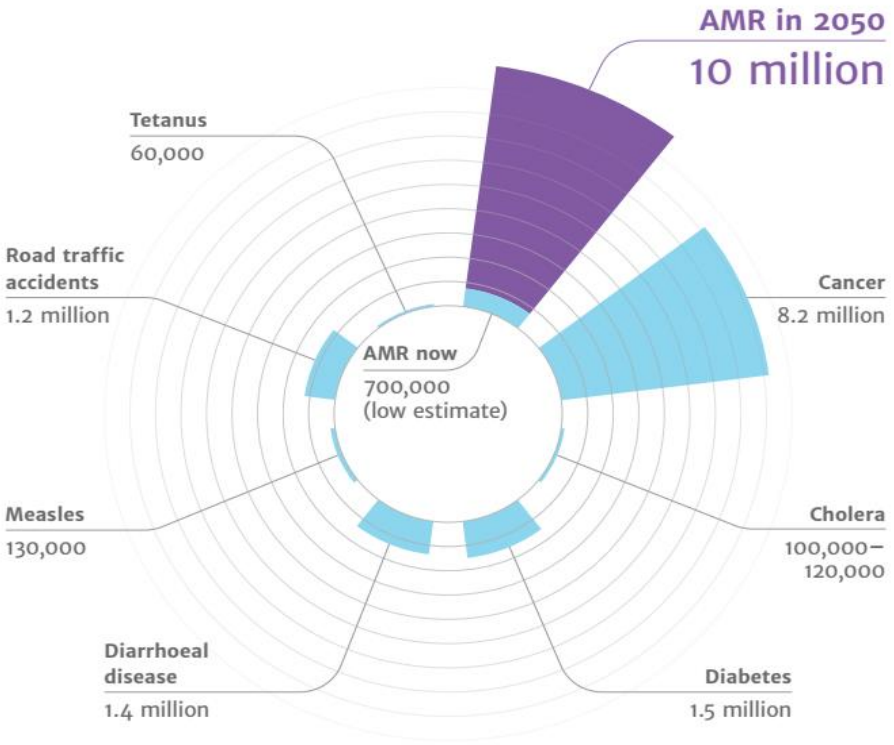
- JCO is an employee of MSD (IA) LLC, Guaynabo, Puerto Rico

Index

Background

Background

- There are around 700,000 deaths per year due to Antimicrobial Resistance (AMR).
- The economic impact will be more than $ 1 trillion US dollars by 2030.
- The *Acinetobacter baumannii* is a drug resistant pathogen considered an urgent threat.
- Colistin was first used in 1950, and in the 1990s its use increased.
- Various pathogens including *A. baumannii* are developing resistance against colistin.
- Mathematical models help us to predict antimicrobial resistance behavior.



Objectives

Objectives

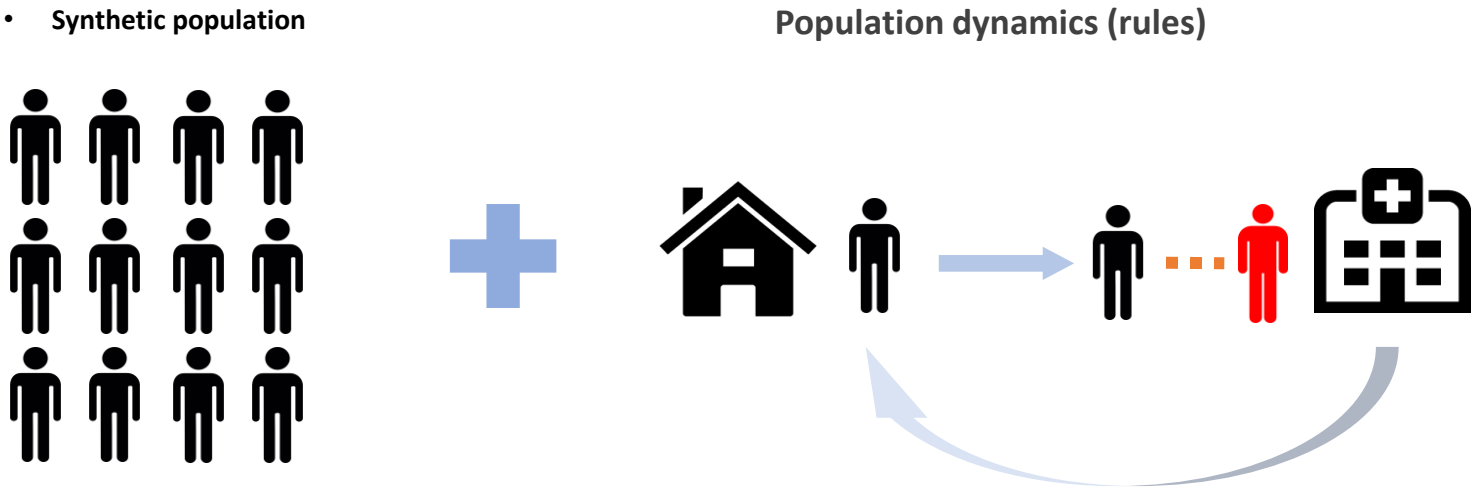
The objectives of the study were:

- to create an agent-based model;
- to calibrate the model;
- to predict the prevalence of resistance of *Acinetobacter baumannii* to colistin.

Methods

Methods

- Agent-based Model:
  - Synthetic population
  - Population dynamics
  - Calibration



Methods

- Aged-based Model:
  - Synthetic population (demographic information of the City of Valencia (2012-2020))

Table 1. Population by year.

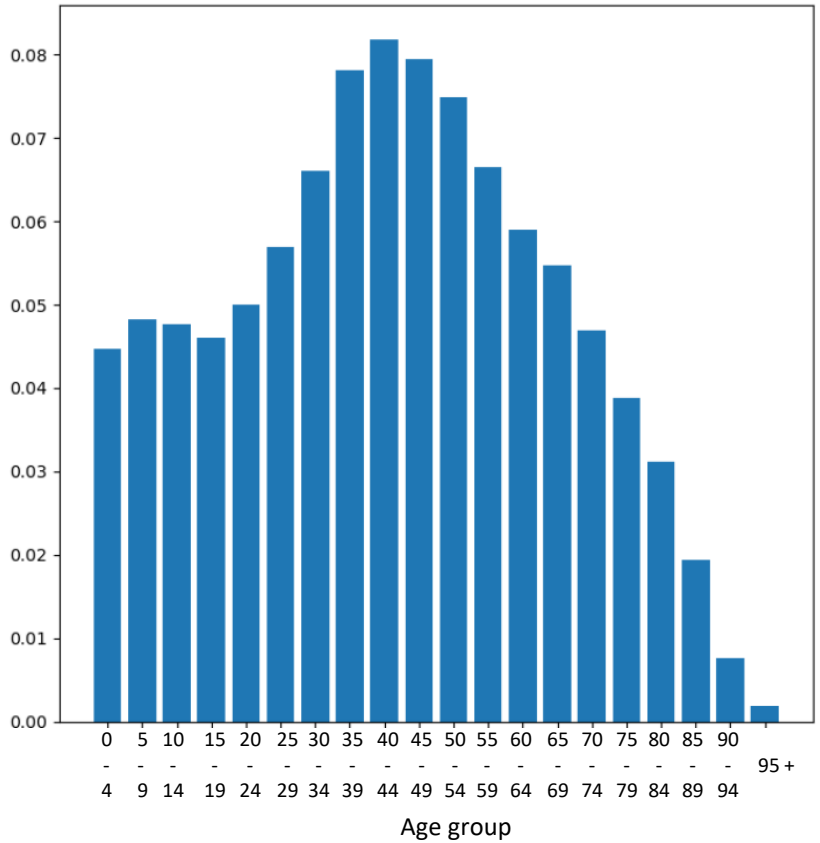
Year	Population
2012	790,584
2013	783,923
2014	776,382
2015	776,865
2016	779,008
2017	780,052
2018	785,985
2019	782,993
2020	788,965

Distribution
Discrete uniform
(χ^2, *p-value* $\simeq 1$)
Mean Population
782,750

$$G \sim \hat{p}_G$$

$$E|G \sim \text{Unif}\left([e_i^G, e_s^G]\right)$$

Fig. 1 Age group distribution. Valencia City (2012-2020)

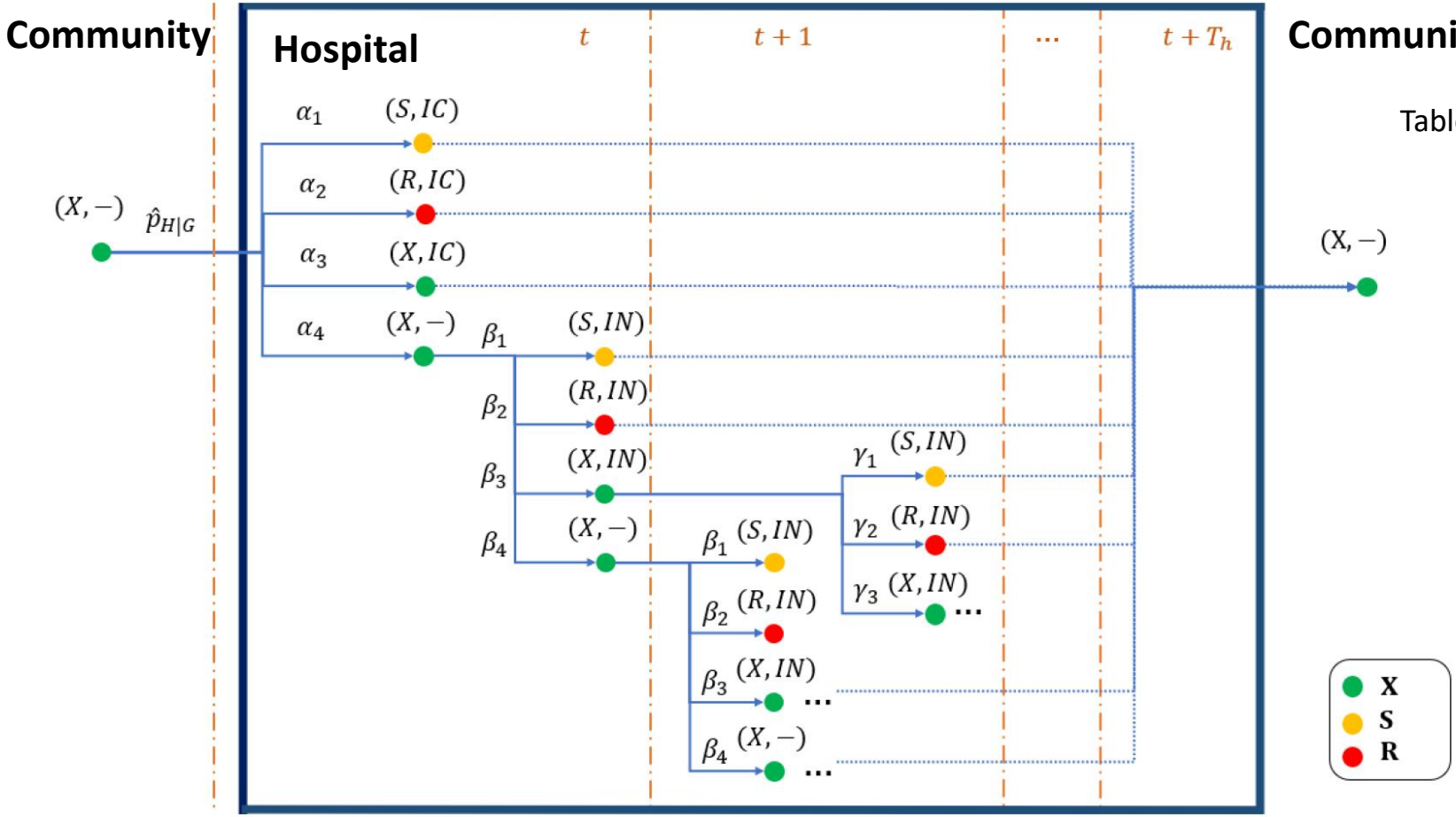


Data source: Valencian Government (GVA)

Methods

- Agent-based Model:
  - Population dynamics: hospital flow of patients (2016-2019), epidemiological information (2015-18)

Fig 2. Diagram of the dynamics of the agent-based model



Data source: Spanish Health Ministry

Table 2. Individual status.

Individual status
<u>Environment:</u> community (*C*) hospital (*H*)).
<u>Health Status:</u> susceptible (*X*), sensitive (*S*) resistant (*R*))
<u>Origin of infection:</u> no infection (-), community (*IC*) nosocomial (*IN*))
<u>Hospitalization time</u>: T_h

Table 3. Probability.

Probability	
α_1	$= \pi_{IC\|CH}\ \pi_{IAB\|IC}\ (1 - \hat{p}_{R\|IAB})$
α_2	$= \pi_{IC\|CH}\ \pi_{IAB\|IC}\ \hat{p}_{R\|IAB}$
α_3	$= \pi_{IC\|CH}\ (1 - \pi_{IAB\|IC})$
α_4	$= 1 - \pi_{IC\|H}$
β_1	$= \pi_{IN\|H}\ \pi_{IAB\|IN}\ (1 - \hat{p}_{R\|IAB})$
β_2	$= \pi_{IN\|H}\ \pi_{IAB\|IN}\ \hat{p}_{R\|IAB}$
β_3	$= \pi_{IN\|H}\ (1 - \pi_{IAB\|IN})$
β_4	$= 1 - \pi_{IN\|H}$
γ_1	$= \beta_1$
γ_2	$= \beta_2$
γ_3	$= 1 - \beta_1 - \beta_2$

Methods

- Agent-based Model:
  - Parameters: Probability of admission by age group, mean LOS, resistance probability, probability of hospital infection ($\pi = \{\pi_{IC|CH}, \pi_{IN|H}, \pi_{IAB|IC}, \pi_{IAB|IN}\}$).

Fig 3. Probability of admission by age group. Valencia 2016-2019.

$$\hat{p}_{H|G} \simeq \mathbb{P}(H|G)$$

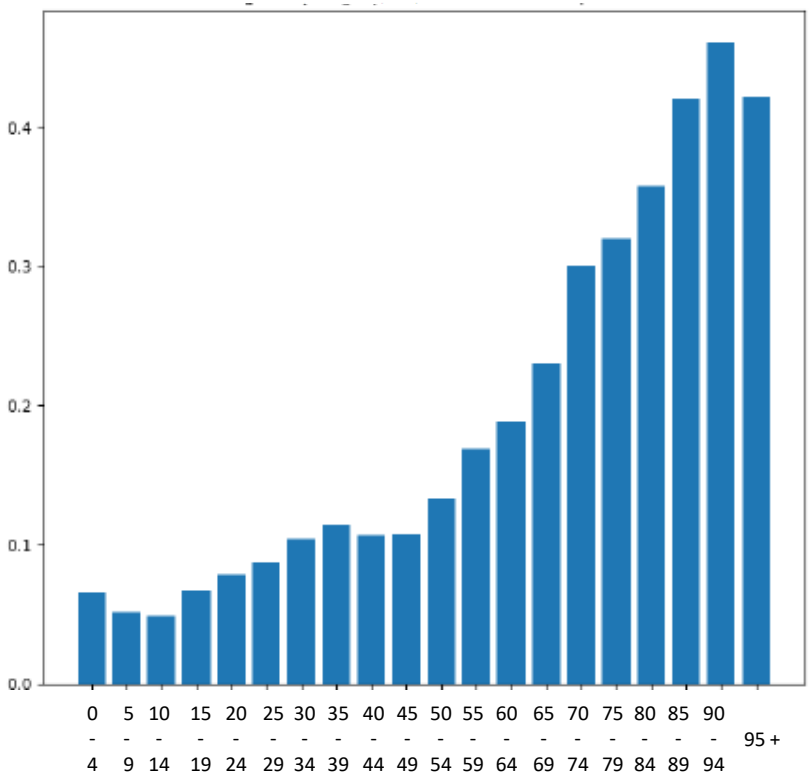


Fig 4. Mean length of hospital stay by age group. Valencia 2016-2019.

$$T_h|G = \bar{T}_h|G + \delta\bar{T}_h|G = (1+\delta)\bar{T}_h|G$$

δ = increment of LOS (δS= 0.0645, δR=0.3889, δX=0)

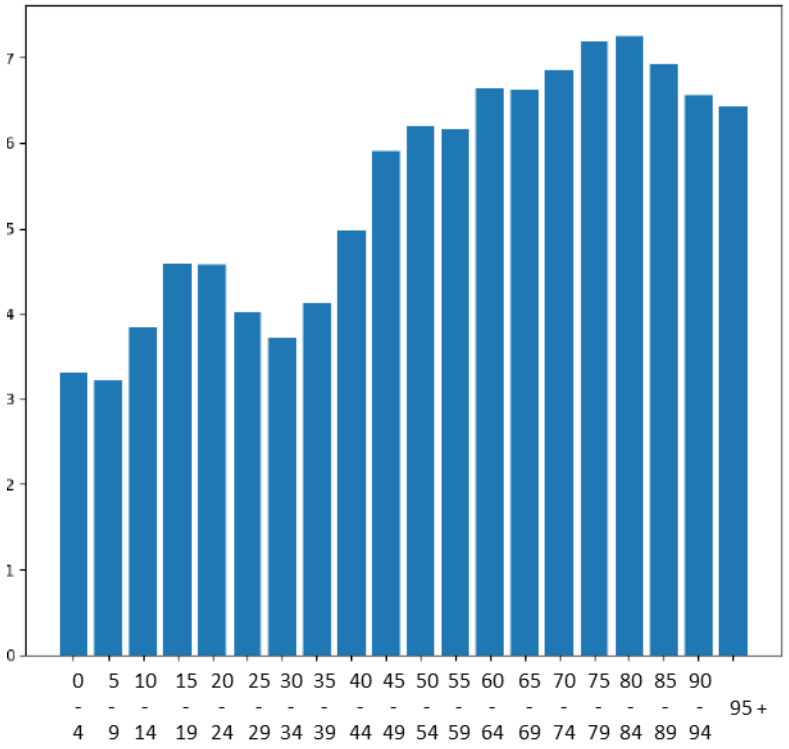
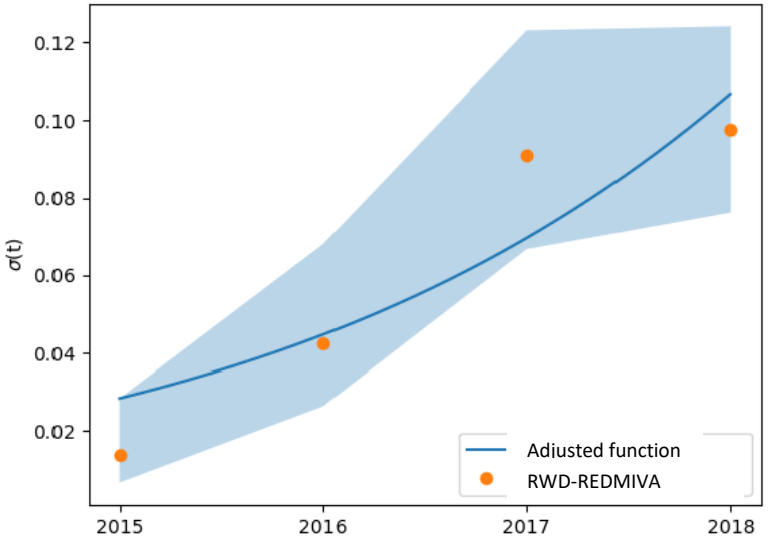


Fig 5. Resistance probability of *A. baumannii* to colistin. Valencia 2015-2018.

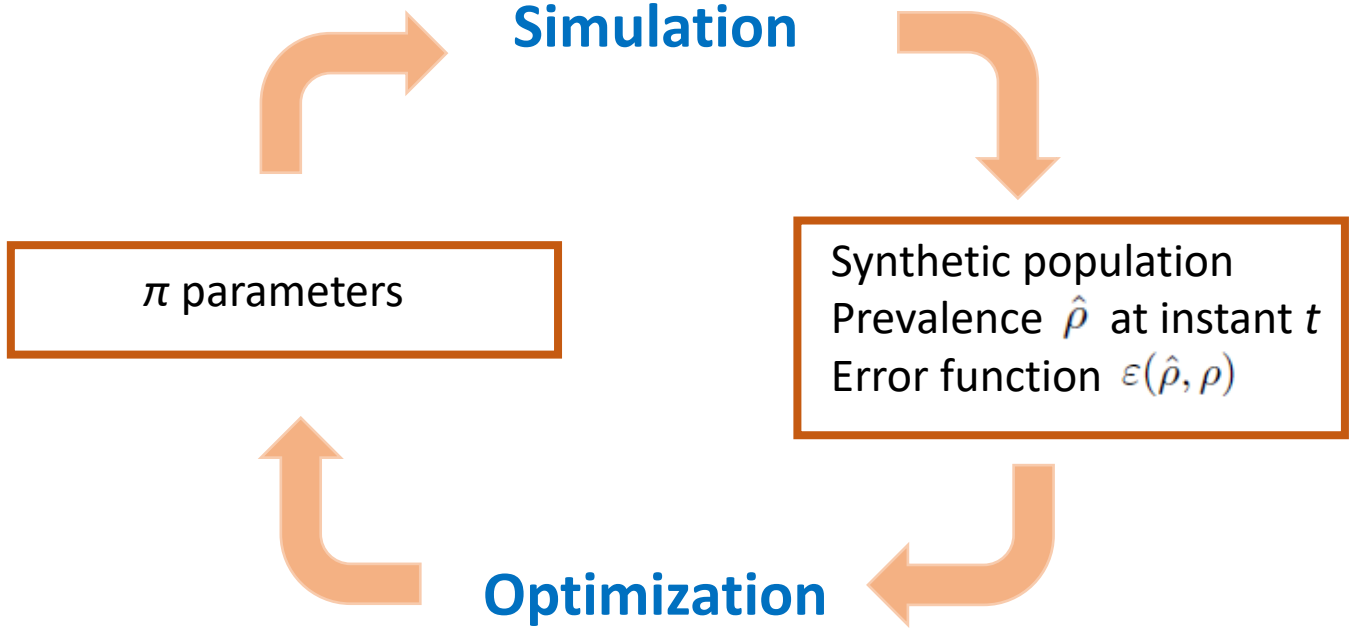


Data source: Valencian micro-surveillance network (REDMIVA)

Methods

- Agent-based Model:
  - Calibration:

Fig 6. Model calibration.



Particle Swarm Optimization (PSO) algorithm

Data source: Nosocomial infection prevalence surveys in Spain (EPINE)

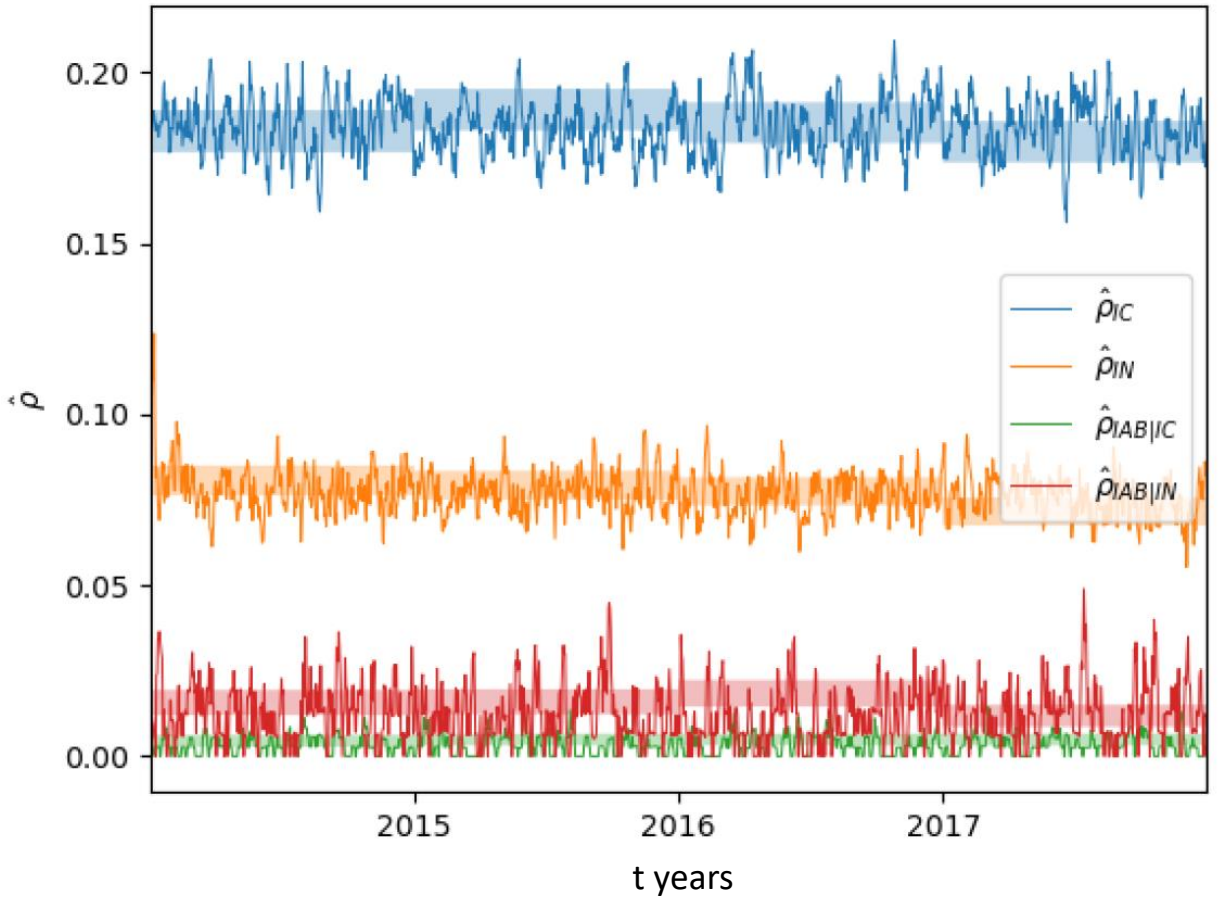
Results

Results

Table 5 . Optimal parameters π^* of the agent-based model

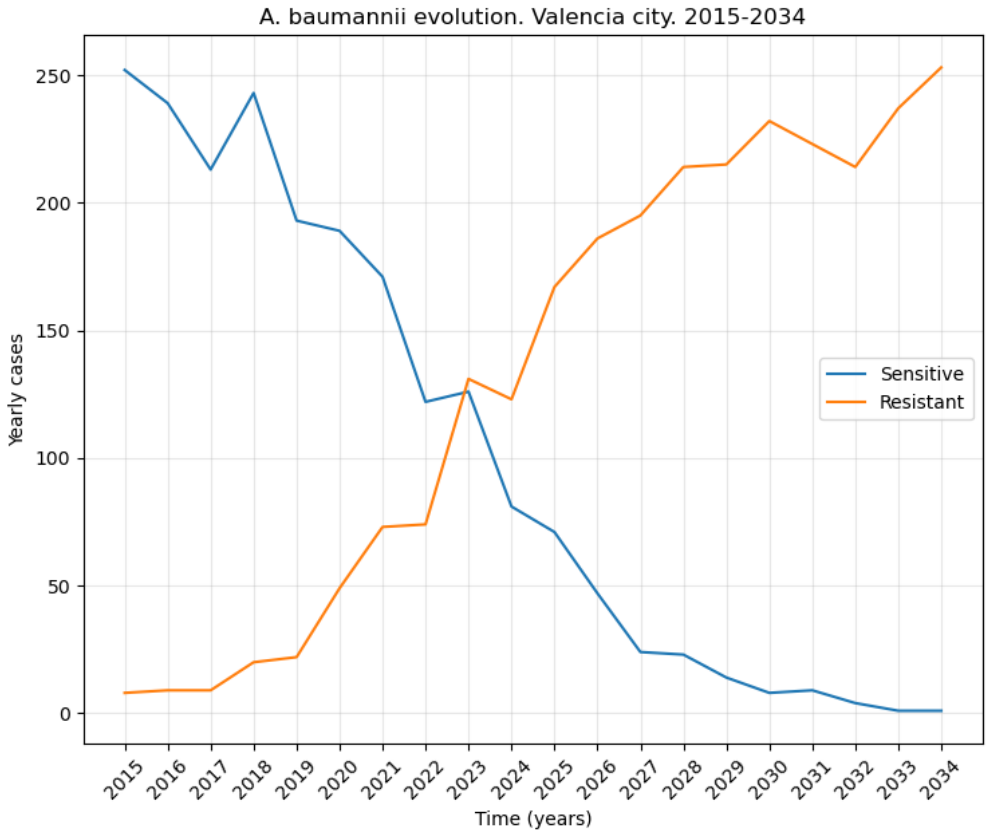
Parameter	Value
$\pi_{IC\|CH}$	0.183745
$\pi_{IN\|H}$	0.025784
$\pi_{AB\|IC}$	0.003065
$\pi_{AB\|IN}$	0.009559
Error $\varepsilon(\hat{\rho}, \rho)$	0.010502

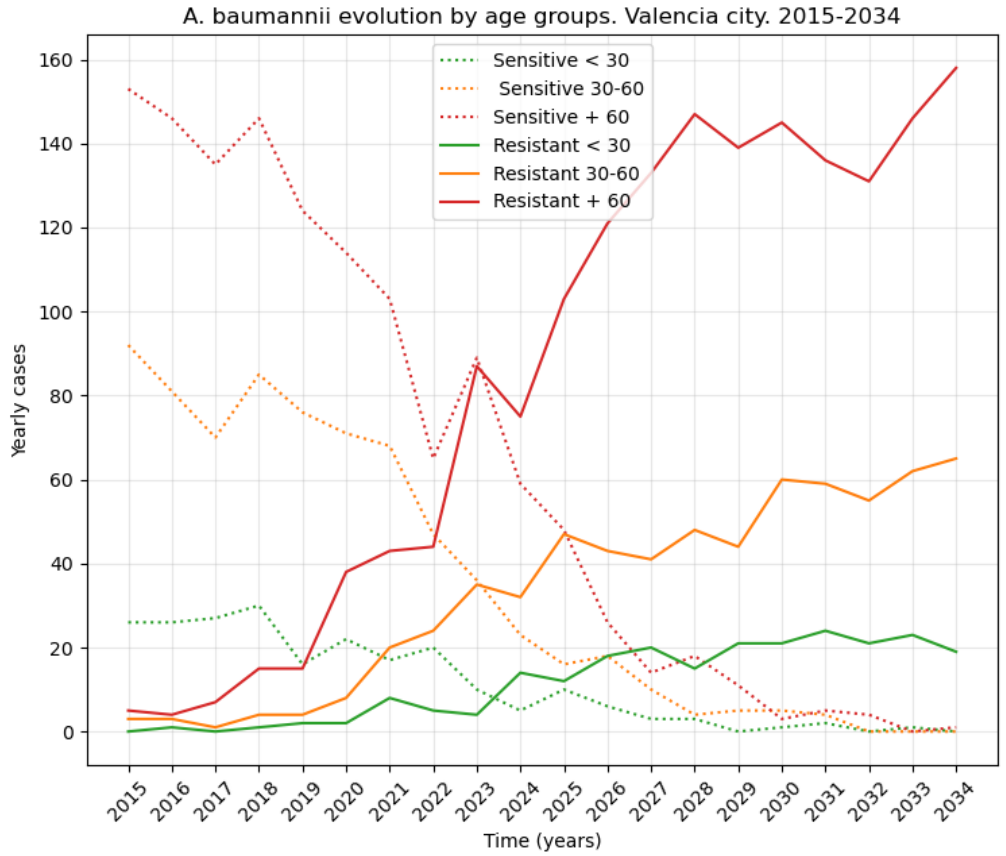
Fig 6. Estimated daily prevalence $\hat{\rho}_x \in \hat{\rho}$ versus confidence intervals $\left[\rho_x^i, \rho_x^s\right]$



Results

- Time horizon of 20 years





Conclusions

Conclusions

- The prevalences estimated by the model after the calibration process fit correctly the confidence intervals of the real world prevalences.
- It is possible to predict and temporalize the evolution of colistin-resistant *A. baumannii* in the City of Valencia.
- The model returns data in number of individuals, for which all characteristics are known.
- The prediction informs us of the importance of implementing AMR prevention and control programs.
- Modifications to the dynamics can be proposed to simulate future action measures to delay the evolution of resistance.

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