Population-level antibiotic treatment policies in the setting of antibiotic resistance: A mathematical model of mass treatment of *Helicobacter pylori* in Mexico

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Background

***Helicobacter pylori* (*H. pylori*)**

- A bacterium found in the human **stomach**
- One of the **most prevalent** chronic bacterial infection in the world (50%)
- **Strongest** known biological risk factor for **gastric cancer**

Transmission & Persistence of *H. pylori*

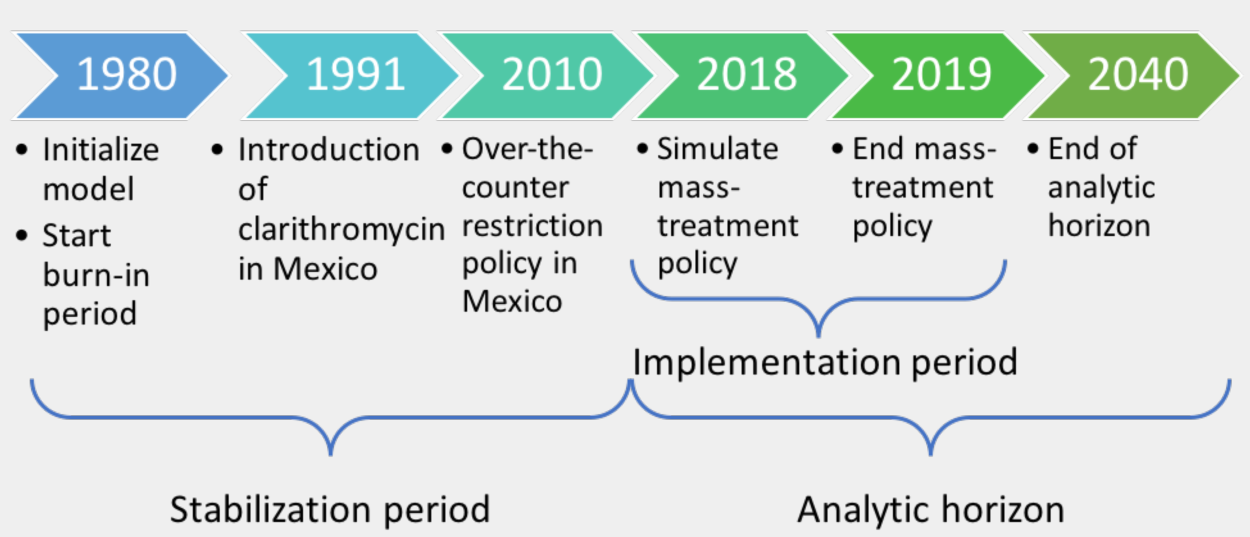
- Infection usually occurs early in **childhood** and risk seems to decrease with age
- Individuals who do not receive treatment generally have **life-long infections**

***H. pylori* treatment and resistance**

- Infection **can be cleared** with antibiotics but these can induce **antibiotic resistance** (ABR)
- ABR reduces the effectiveness of treatment and represents one of the **greatest emerging global health threats**

Objectives

- To develop an age-structured transmission model of *H. pylori* infection in Mexico that includes both **sensitive** and **resistant** strains
- To evaluate the impact of **population-based** antibiotic treatment policies on *H. pylori* infection and ABR in Mexico using a transmission model:
  - No mass treatment
  - Three clarithromycin-based antibiotic treatment policies assumed to be implemented in 2018:
    1. Treat children only (AB 2-6 year-olds)
    2. Treat older adults only (AB 40+ year-olds)
    3. Treat everyone regardless of age (AB all)



Mathematical model: System of ordinary differential equations (ODE)

Age-specific susceptible-infected-susceptible (SIS) model with resistance

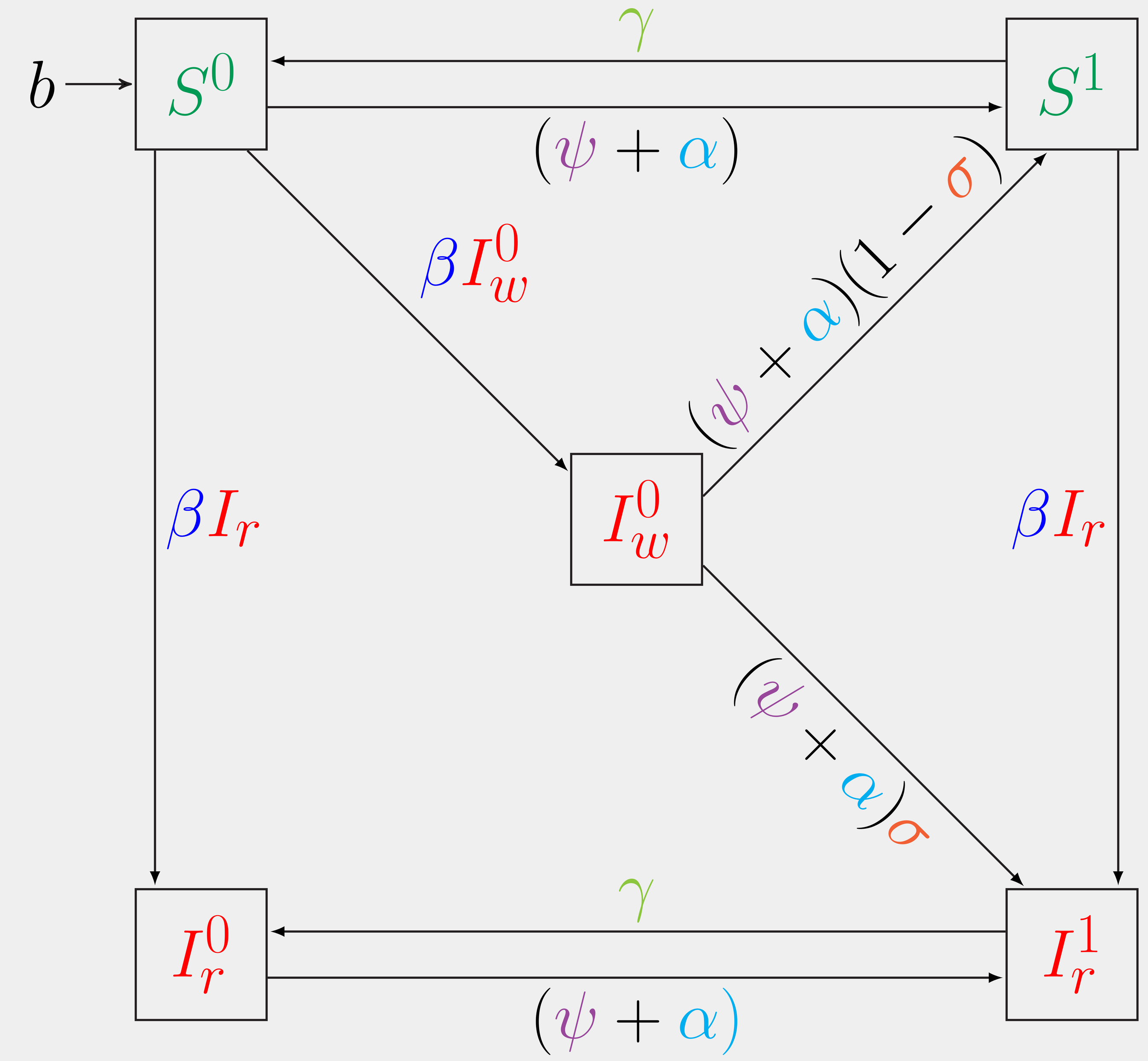


Table: Description of variables and parameters

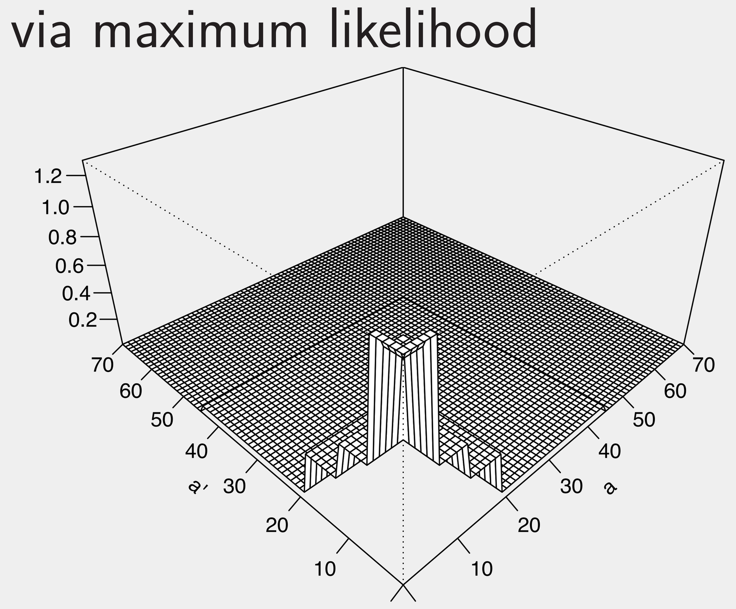
Symbol	Description
State variables	
S^0	Susceptible with NO treatment
S^1	Susceptible with treatment
I_w^0	Infected with sensitive strain and NO treatment
I_r^0	Infected with resistant strain and NO treatment
I_r^1	Infected with resistant strain and treatment
I_r	$= I_r^0 + I_r^1$
Parameters	
b	Birth rate
β	Mixing matrix
ψ	Antibiotic treatment policy
α	Background use of antibiotioc
$1/\gamma$	Average length of treatment (14 days)
σ	Probability that treatment induces mutation on sensitive strains and therefore does not clear colonization

Mixing matrix

- Who-acquires-infection-from-whom (WAIFW) matrix: Divided the population into $N = 6$ discrete age classes: $[0,2)$, $[2,6)$, $[6,12)$, $[12,19)$, $[19,45)$, $[45,70)$

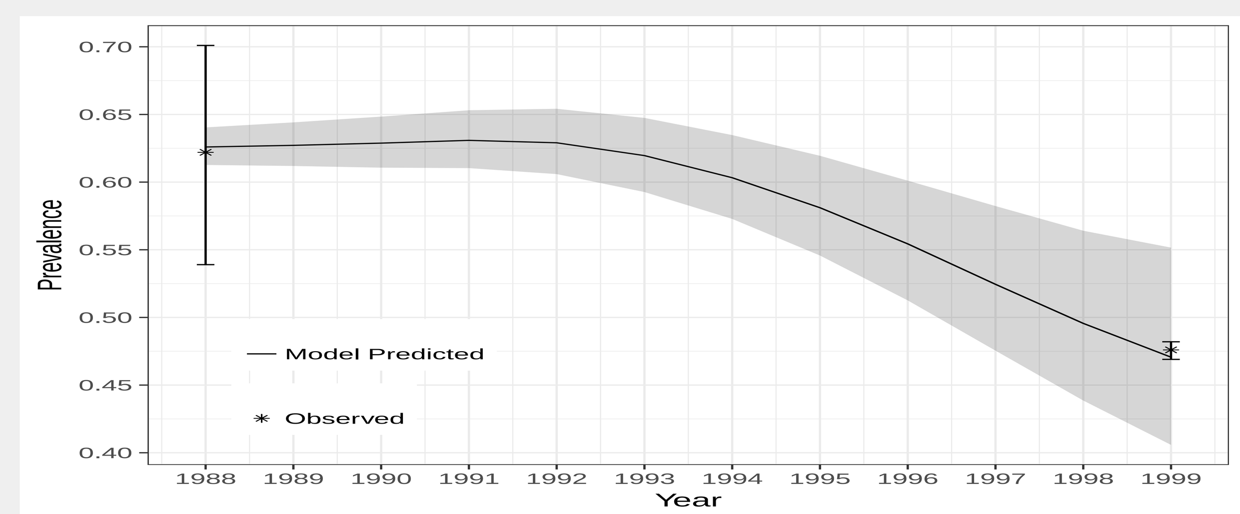
$$\beta = \begin{pmatrix} \beta_1 & \beta_1 & \beta_1 & \beta_4 & \beta_5 & \beta_6 \\ \beta_1 & \beta_2 & \beta_3 & \beta_4 & \beta_5 & \beta_6 \\ \beta_1 & \beta_3 & \beta_3 & \beta_4 & \beta_5 & \beta_6 \\ \beta_4 & \beta_4 & \beta_4 & \beta_4 & \beta_5 & \beta_6 \\ \beta_5 & \beta_5 & \beta_5 & \beta_5 & \beta_5 & \beta_6 \\ \beta_6 & \beta_6 & \beta_6 & \beta_6 & \beta_6 & \beta_6 \end{pmatrix}$$

- Estimated via maximum likelihood

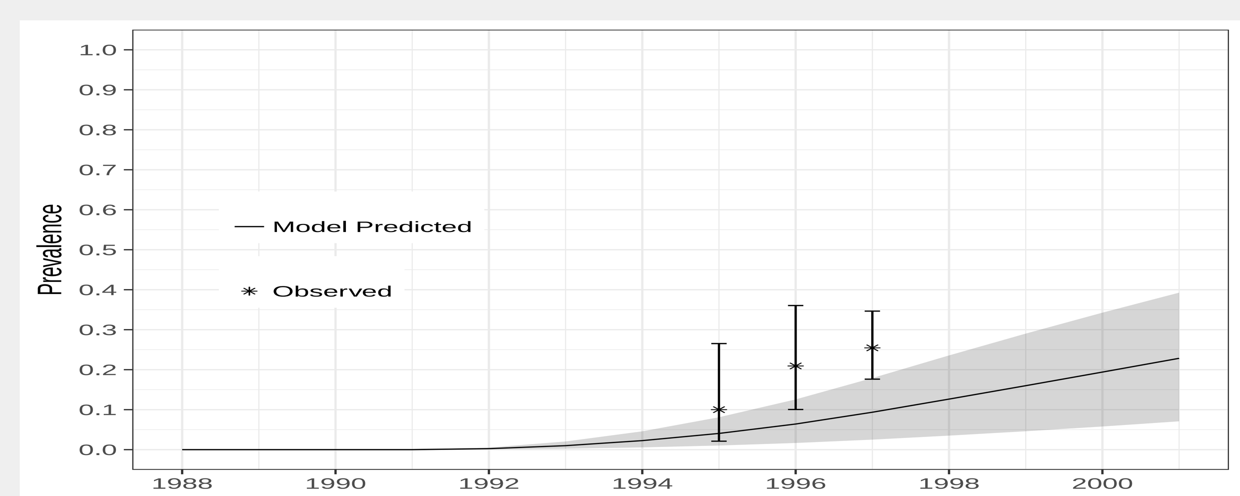


Validation

- Prevalence of infection

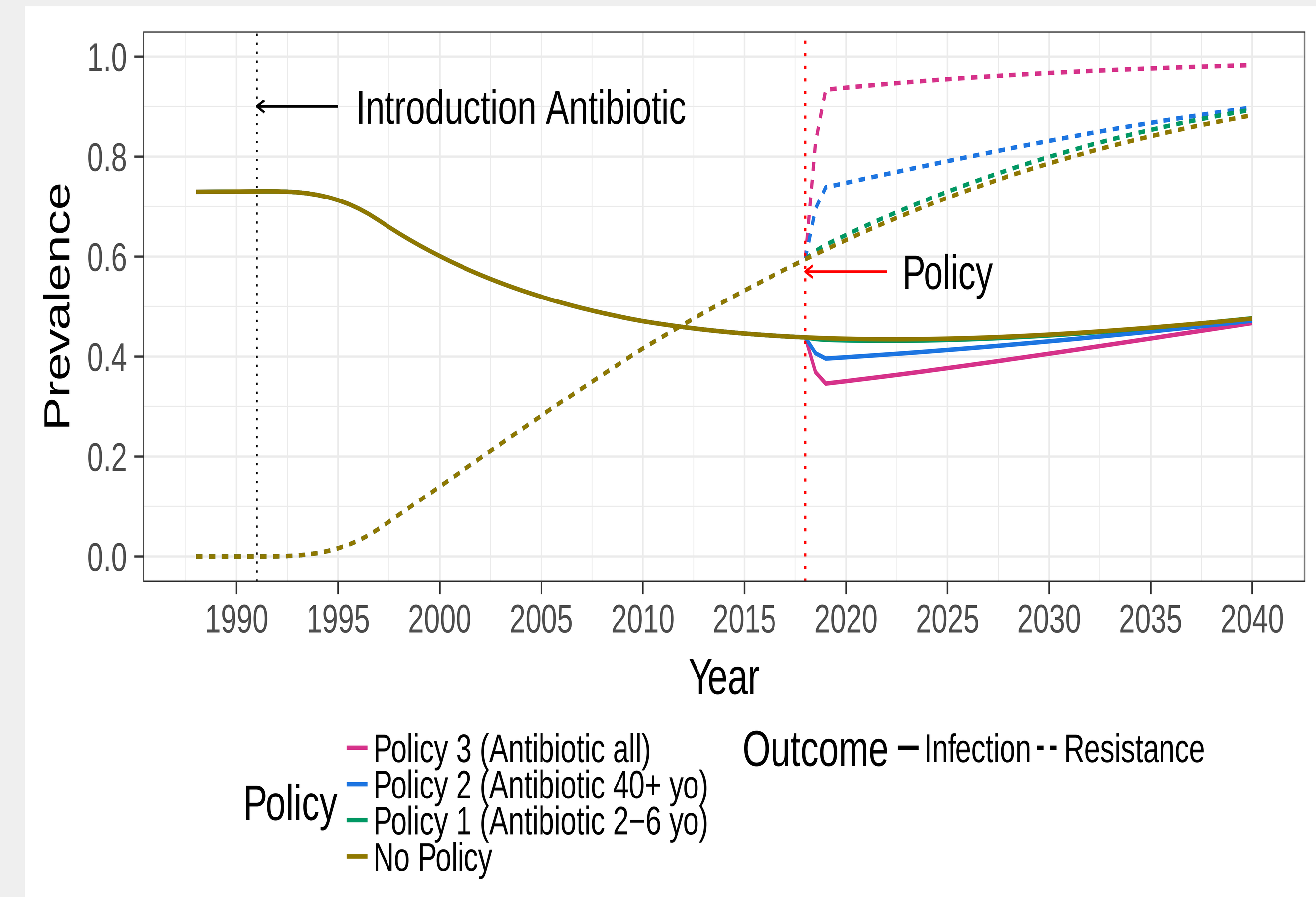


- Prevalence of resistance



Results

Impact of different antibiotic mass-treatment policies on prevalence of *H. pylori* infection and resistance



- In the absence of a mass-treatment policy, our model predicts infection begins to rise in 2022
- After the first year of implementation, policy 3 (AB all) decreases infection by 21% but increases ABR by 57%
- The decrease in infection relative to the increase in ABR for policy 3 (AB all) is 37%, it's highest for policy 2 (AB 40+ year-olds), 39%, and lowest for policy 1 (AB 2-6 year-olds), 23%
- These results agree across all scenarios considered in sensitivity analysis for different WAIFW matrices and antibiotic treatment background use

Conclusions

- In general, any mass-treatment policy will have a greater effect on increasing resistance than on reducing infection
- As the proportion of resistant strains increases and becomes more prevalent than sensitive strains, infection starts rising again
- Policy decisions will need to balance the costs of increased future resistance against short-term reductions in prevalence

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