Infectious Disease Transmission and Vaccination Strategies in Mass Gatherings: What Lessons Have We Learned from Meningococcal Transmission in Hajj?

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Disclosure

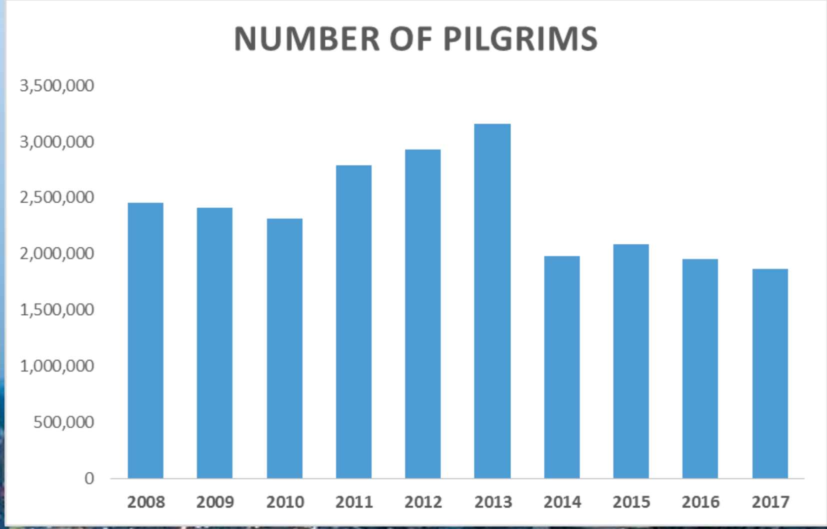
- This study is supported by the NSERC/Sanofi Industrial Research Chair Program in Vaccine Mathematics, Modelling and Manufacturing
- Amine Amiche, Alp Dogu, Ed Thommes, Laurent Coudeville, and Ombeline Jollivet are employees of Sanofi Pasteur
- The remaining authors report no conflict of interest

Introduction

Mass gatherings and infectious disease

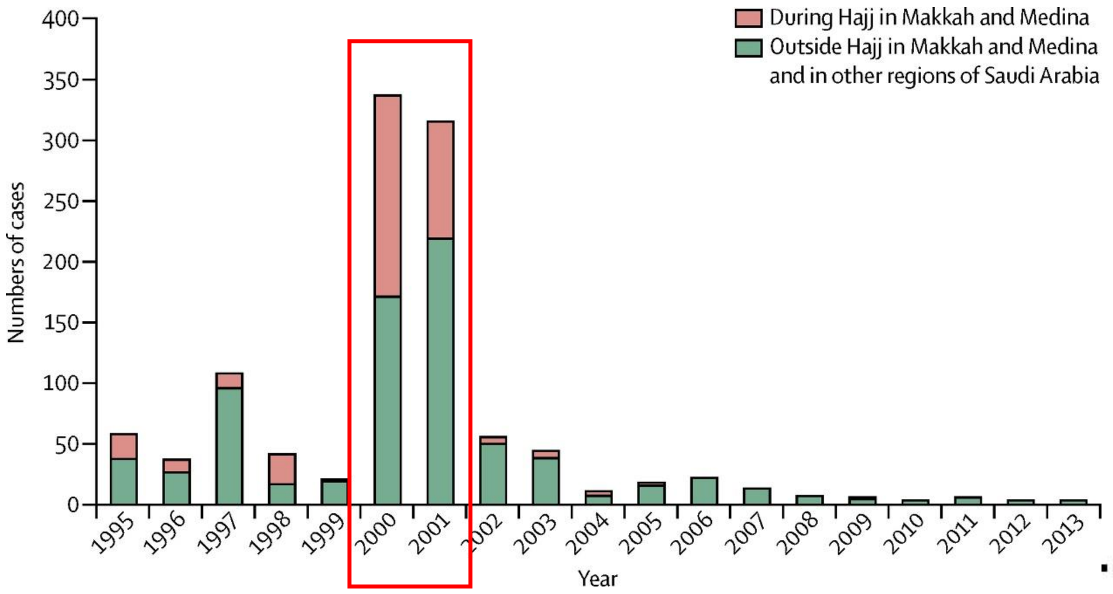
- Mass gatherings (MGs) are characterized by a high concentration of people at a specific time and location.
- May lead to increased:
  - risk of importation of infectious agents in the hosting country
  - risk of outbreak with an unexpectedly high mortality or morbidity
  - risk of international disease spread

- **Hajj is the holy pilgrimage for Muslims**
- **<u>~ 2-3 million </u>people gather in <u>0.65 km²</u> area located in Makkah**
- **Pilgrims arrive from ~ 180 countries**
- **Different age groups (majority >40 yo)**



Countries Groups	Ratio	1438
GCC countries	1.9%	35,017
Other Arab Countries	24.0%	443,372
Asian Countries Excluding Arab Countries	58.1%	1,075,485
African Countries Excluding Arab Countries	10.2%	188,624
European countries	4.6%	85,468
North and South America countries and Australia	1.2%	23,057
Total	30.8%	1,851,023

Meningococcal outbreaks shaped vaccination policy for Hajj



2000
- The 1[ST] Hajj-related serogroup W135 international meningococcal outbreak

2001
- The 2[ND] Hajj-related serogroup W135 international meningococcal outbreak
- Chemoprophylaxis for all local pilgrims at the end of Hajj before returning to their families

2002
- The quadrivalent A/C/W/Y meningococcal polysaccharide vaccine a requirement for all Hajj and Umrah pilgrims
- Introduction of a vaccination program for children and adults living in Mecca and Medina, healthcare workers in Saudi Arabia and government personnel serving pilgrims

2007
- The quadrivalent A/C/W/Y vaccine (polysaccharide or conjugate) required for all national and international pilgrims, residents of the holy cities, Hajj workers and those working at entry points to the Kingdom or are in direct contact with pilgrims
- Chemoprophylaxis for pilgrims arriving from the African meningitis belt, but no longer for pilgrims leaving the Hajj premises

2010
- The conjugated quadrivalent A/C/W/Y meningococcal vaccine used for the local target population aged from above 2 to 55 years

2013
- Introduction of the conjugate quadrivalent A/C/W/Y vaccine into the Saudi routine childhood vaccination program for children above 9 months old

Present

2015
- Vaccination with the quadrivalent A/C/W/Y vaccine required for all national and international pilgrims, residence of Mecca and Medina, Hajj workers and all workers at Saudi land, marine and air ports of entry
- Ciprofloxacin chemoprophylaxis at point of entry for pilgrims arriving from the African meningitis belt
- Awareness campaigns on meningococcal disease and preventative measures

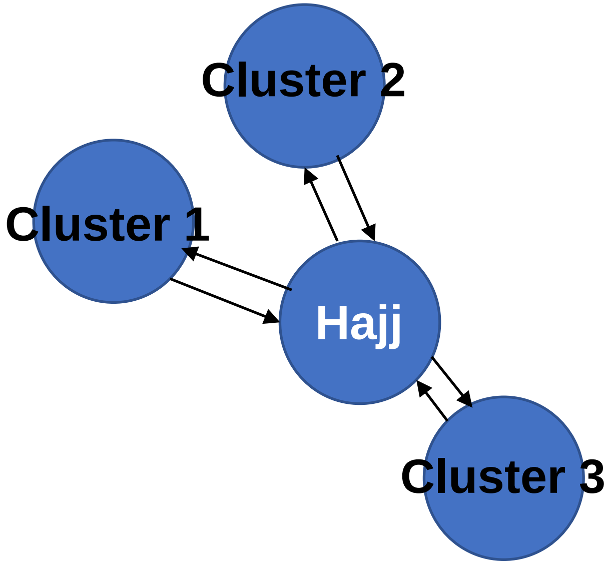
Questions

- What is the impact of the mass gathering event, Hajj, on the transmission of meningococcal disease ?
- What is the impact of different vaccination coverage and efficacies on the probabilities of outbreaks ?

Methodology

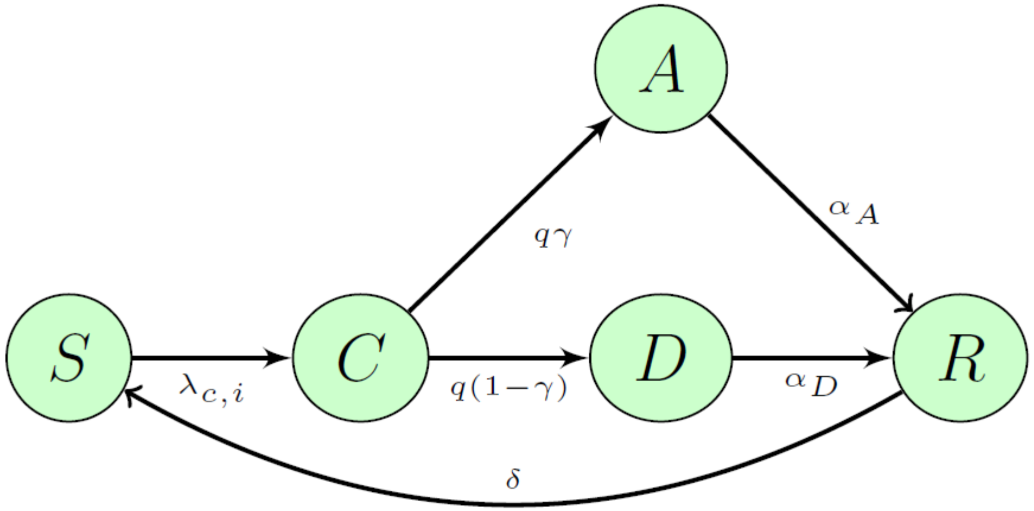
The Model

- A compartmental, meta-population, and age structured
  - to simulate meningococcal transmission among pilgrims in Mecca, whole KSA, and other pilgrims' origin.

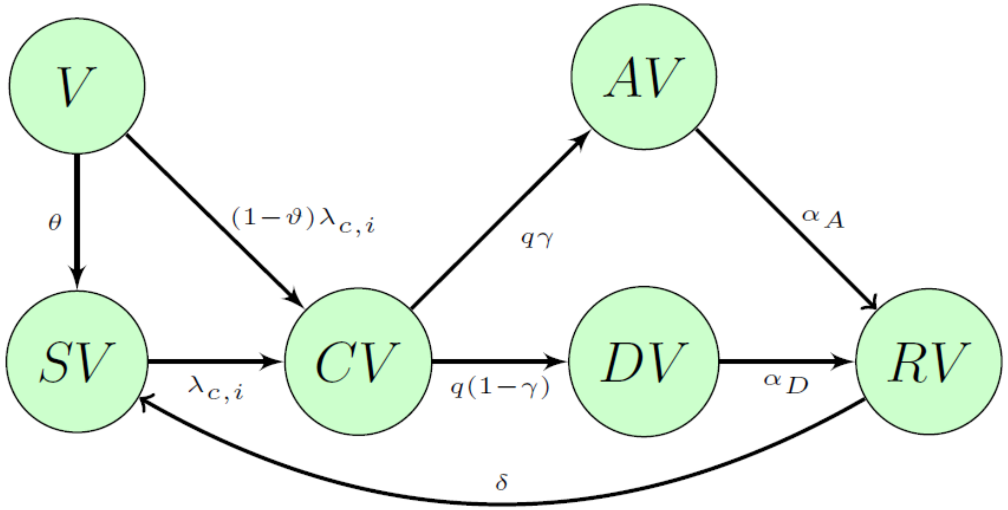


- Each cluster shares the same representation of the infection and demographic processes.
- The processes are simulated following a set of ordinary differential equations

Baseline transmission



Transmission with vaccination



Susceptible(S), Short-term carrier(C), Asymptomatic carrier(A), Diseased(D), and Recovered(R)

Populations were clustered in 5 groups

Table 1: **Cluster information.**

Clusters	Country or territories	Carriage rate (%)	Source
Cluster 1: Mecca	Mecca (Hajj city)	4.2 [2.0; 17.8]	Calibrated
Cluster 2: KSA outside Mecca	Kingdom of Saudi Arabia (Hajj country) except Mecca	1.2 [0.5-3.2]	Calibrated
Cluster 3: High endemic	African meningitis belt countries (Benin, Burkina Faso, Cameroon, Central African, Republic,Chad, Ivory Coast, Congo, Democratic Republic of Congo, Ethiopia, Gambia, Guinea, Ghana, Mali, Mauritania, Niger, Nigeria, Senegal, South Sudan, Sudan, Togo)	6.3	[29]
Cluster 4: Medium endemic	South Africa, Asia (except Turkey, Malaysia, the Philippines, Indonesia, Russia, China), Arabic Non-GCC	4.0	[29]
Cluster 5: Low endemic	Gulf Cooperation Coucil countries (except KSA), Europe, Americas, Australia, Turkey, Malaysia, The Philippines, Indonesia, Russia, China	2.0	[29]

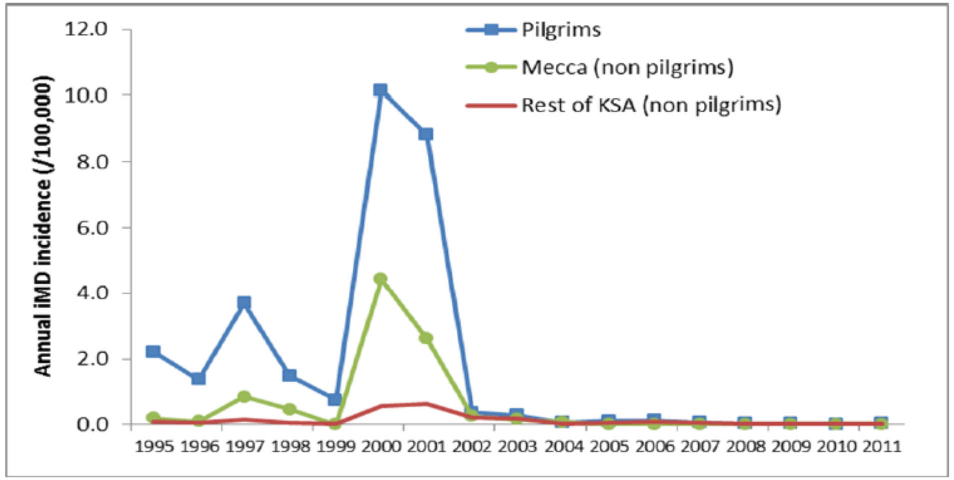
Key model parameters (base case)

Table 2: **Disease and vaccine parameters**

Parameters	Definitions	Values	Reference
q	Rate of moving out from short-term carriage status ($year^{-1}$)	52	[11]
γ	Proportion of short-term carriers remaining asymptomatic (%)	99.98	[9]
α_A	Recovery rate from asymptomatic carrier status ($year^{-1}$)	1	[12], [9]
α_D	Recovery rate from disease status ($year^{-1}$)	52	[11]
ϵ	Relative infectiousness IMD modification parameter	0.5	Assumed
δ	Waning rate of recover-induced immunity ($year^{-1}$)	0.0839	[21]
ϑ	Vaccine efficacy (%)	93	[41]
θ	Waning of vaccine induced immunity ($year^{-1}$)	0.1	[21], [10]
	Age for routine vaccination schedule in KSA (year)	1	[43]
	Routine vaccination coverage rate (%)	96	[25], [42]

Model calibration

- Using the historical epidemiological data from meningococcal surveillance, the model was calibrated to identify the best fit of the surveillance data from 1995-2001, and was validated from 2002-2011



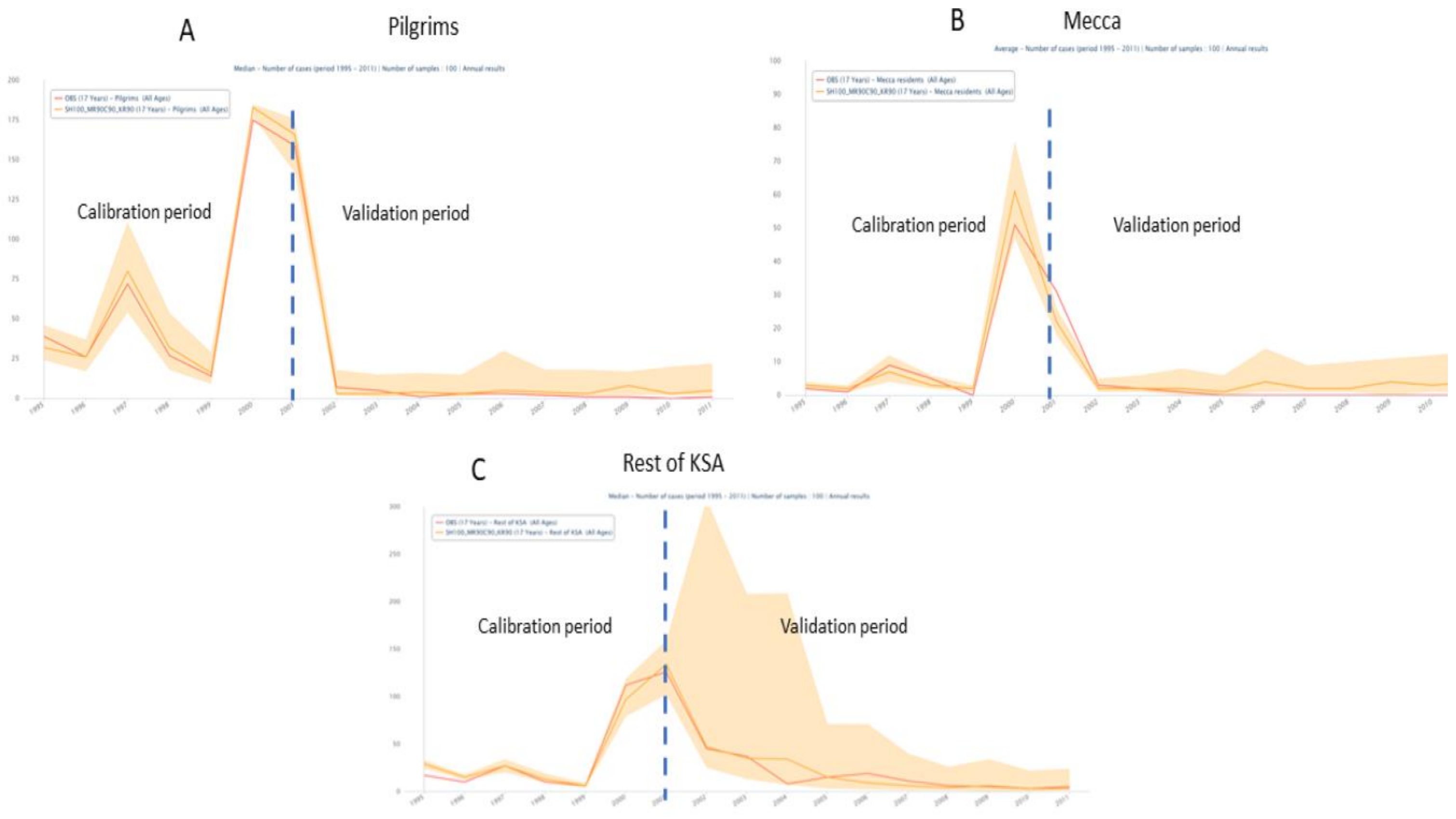
- Cluster-specific transmission parameters: Beta_c
- Hajj-specific transmission parameters: Beta_H
- year-to-year variation in IMD transmission

$$\lambda_p = \frac{\sum_{c=1}^{N}\sum_{j=1}^{n_c} \beta_H \beta_y \beta_c (C_{c,j}^p + A_{c,j}^p + CV_{c,j}^p + AV_{c,j}^p + \epsilon D_{c,j}^p + \epsilon DV_{c,j}^p)}{\sum_{c=1}^{N}\sum_{j=1}^{n_c} P_{c,j}^p}$$

β_H corresponds here to the specific Hajj density effect

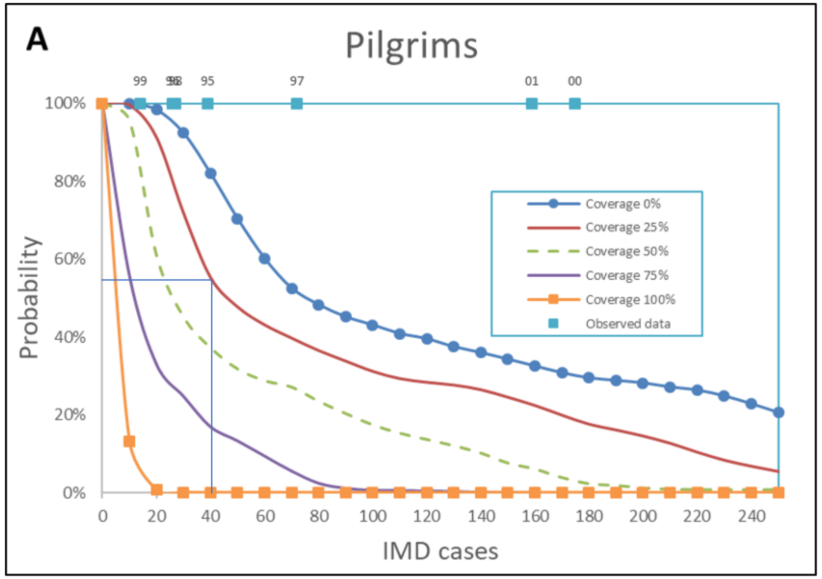
Results

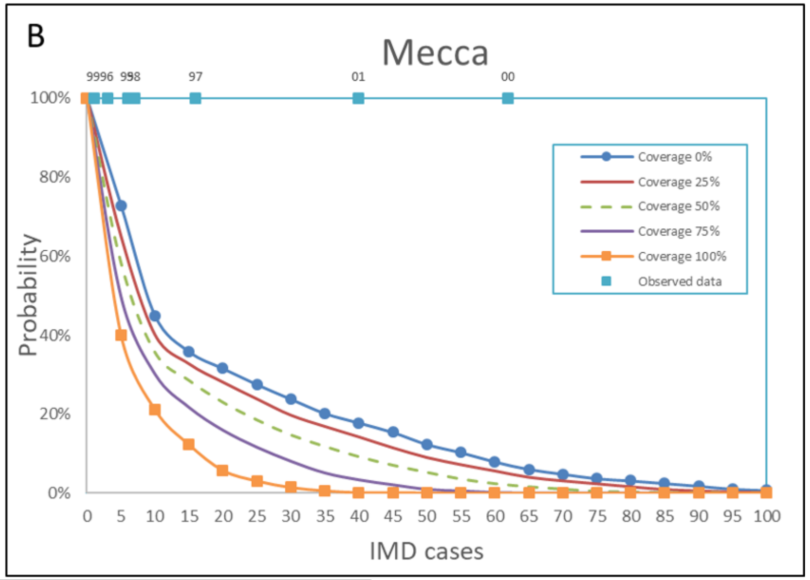
Calibration results and density effect



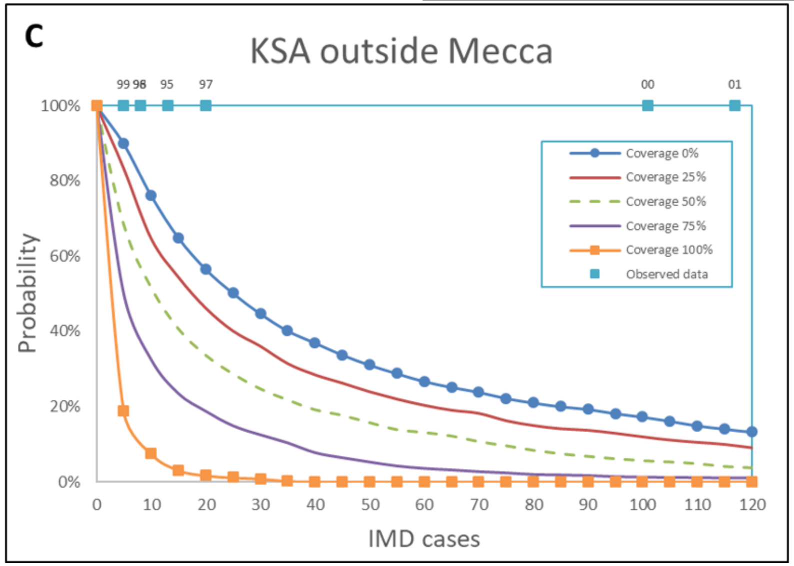
Parameter	Description	Central estimate	Range
β_H	density effect in Hajj	78.5	$[68.5, 89.6]$
β_L	baseline transmission	12.5%	$[6.0, 25.5]$
β_y	year-to-year transmission variability	80.8%	$[26.2, 209.2]$

Impact of lack of vaccination compliance among pilgrims





Decrease of vaccination coverage among pilgrims could lead to outbreaks among pilgrims, yet also among other populations in Mecca and KSA



Impact of routine vaccination on Hajj-associated IMD

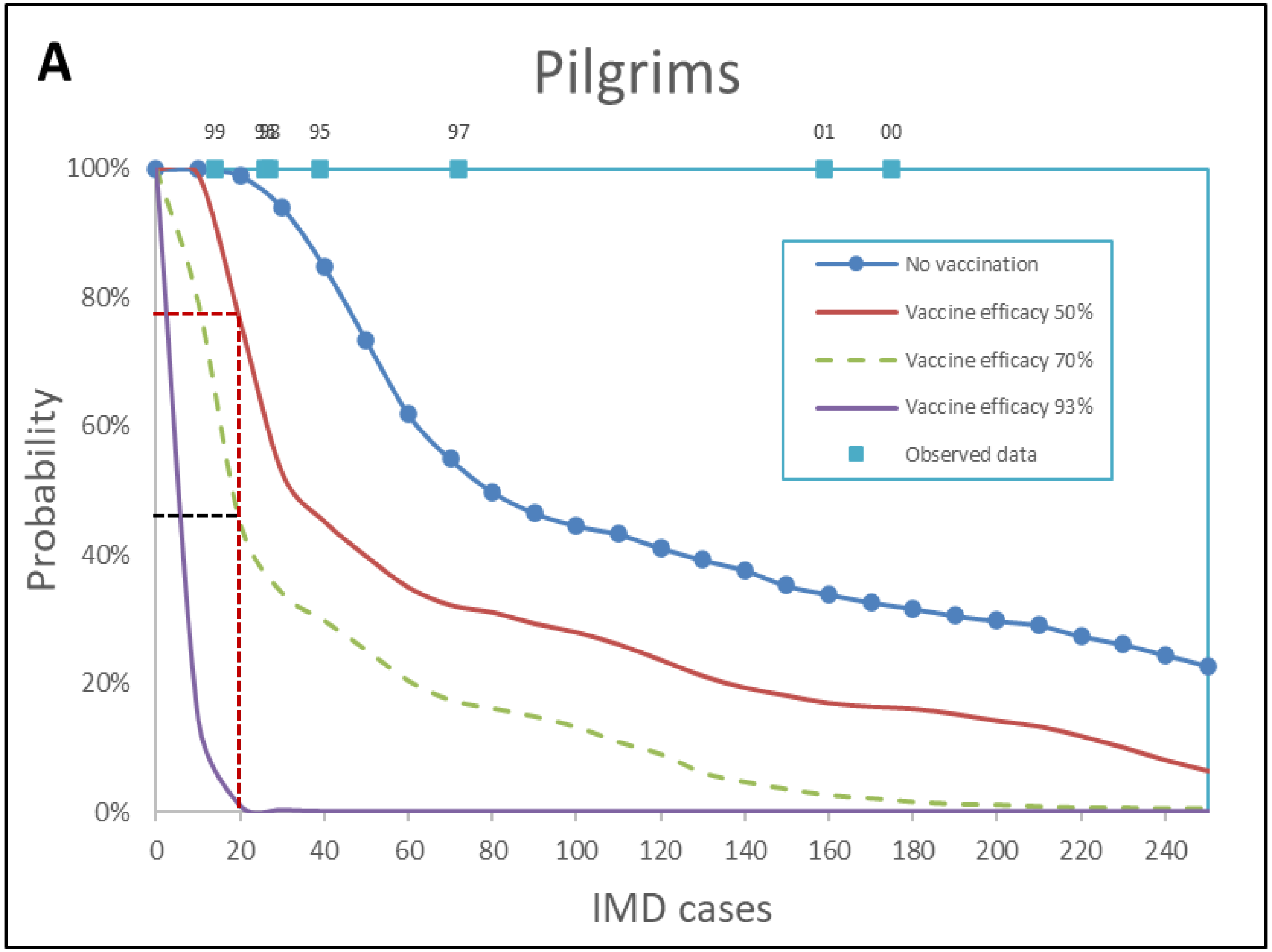
Routine vaccination across KSA reduces the number of IMD cases due to Hajj.
Routine vaccination in Mecca only have small impact on Hajj-related IMD across the country

Table 4: Impact of routine vaccination on the number of IMD cases per decade in the whole KSA.

	Current routine vaccination in KSA (1y.o.)	Routine vaccination only in Mecca	No routine vaccination in KSA
2012-2021	99 [40,220]	114 [41,301]	138 [49,341]
2022-2031	154 [62,397]	233 [77,1113]	284 [95,1218]
2052-2061 (+40y)	399 [140,811]	729 [147,2331]	853 [195,2522]

The impact of vaccine efficacy on IMD outbreaks

- Reduced vaccine efficacy would significantly increase the risk of outbreaks during Hajj



Interpretations and Conclusions

- Hajj is a catalyst for IMD transmission not only among pilgrims, but also among the populations from which the pilgrim are originating
- Higher density significantly increases the transmission of IMD
- Maintaining a high vaccination rate among pilgrims is important to prevent outbreaks during Hajj and outside
- Maintaining a routine vaccination in KSA is important to reduce Hajj-associated outbreaks
- Efficacy of the vaccine plays an important role in reducing the impact of Hajj

Limitations

- Simplified IMD transmission in Hajj:
  - only 5 clusters were considered in our model whereas pilgrims originate from more than 100 countries
  - No serogroup-specific modeling
- Data for calibration lack granularity to better express the epidemiological changes overtime and impact of vaccination
- Other preventive and non-pharmaceutical interventions were not considered

Thank you

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