

# Modelling seasonal influenza in England: Approaches to capture immunity propagation



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# Propagation of seasonal influenza immunity is stronger if derived from natural infection.

## 1. Motivation & aims

Seasonal influenza-related respiratory illnesses cause an estimated annual death toll of 291,000-646,000 people [1]. Influenza vaccination can offer some protection against infection for the individual, while contributing to reduced risk of ongoing transmission via establishment of herd immunity [2]. Transmission models connected to data, when interfaced with health economic evaluations, are a key tool to inform national influenza vaccine policy [3]. However, prior modelling studies have typically treated each season and each strain circulating within that season independently.

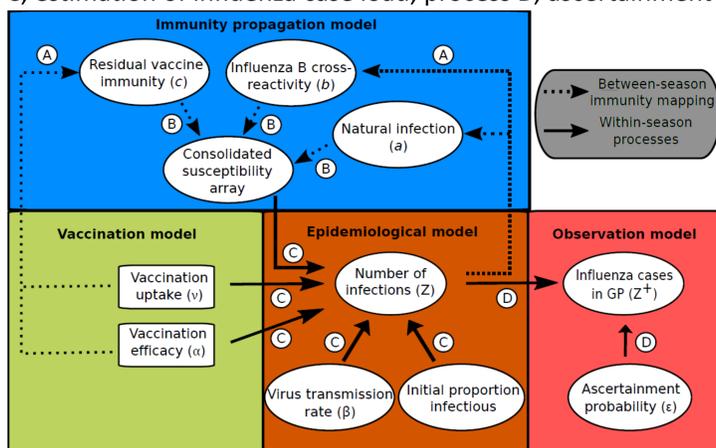
### Study objectives:

- Develop a mathematical model incorporating a mechanism to link prior season epidemiological outcomes to immunity at the beginning of the following season;
- Quantify contribution of differing sources of immunity propagation between years on seasonal influenza transmission dynamics in England, 2012/13 to 2017/18.

## 2. Model overview

- Non-age, multi-strain model, capturing the four strains targeted by the quadrivalent influenza vaccine: A(H1N1)pdm09, A(H3N2), B/Victoria, B/Yamagata.

Fig. 1: Model schematic. Process A (circled capitalised letters), propagation of immunity; process B, modulation of current influenza season virus susceptibility; process C, estimation of influenza case load; process D, ascertainment of cases.



## 3. Immunity propagation model component

Fig. 2: Interaction between prior season exposure and start of season susceptibility.

Mandated that  $0 < a, b, c_m < 1$ .

|                                       |                  | Strain susceptibility  |                        |                           |                           |
|---------------------------------------|------------------|------------------------|------------------------|---------------------------|---------------------------|
|                                       |                  | A(H1N1)pdm09           | A(H3N2)                | B/Victoria                | B/Yamagata                |
| Exposure history (h)                  | Naïve            | 1                      | 1                      | 1                         | 1                         |
|                                       | A(H1N1)pdm09     | a                      | 1                      | 1                         | 1                         |
|                                       | A(H3N2)          | 1                      | a                      | 1                         | 1                         |
|                                       | B/Yamagata       | 1                      | 1                      | a                         | b                         |
|                                       | B/Victoria       | 1                      | 1                      | b                         | a                         |
|                                       | Vaccinated (V)   | $c_{A(H1N1)}$          | $c_{A(H3N2)}$          | $c_{B/Victoria}$          | $c_{B/Yamagata}$          |
| Vaccinated (V) & Exposure history (h) | A(H1N1)pdm09 & V | $\min(a, c_{A(H1N1)})$ | $c_{A(H3N2)}$          | $c_{B/Victoria}$          | $c_{B/Yamagata}$          |
|                                       | A(H3N2) & V      | $c_{A(H1N1)}$          | $\min(a, c_{A(H3N2)})$ | $c_{B/Victoria}$          | $c_{B/Yamagata}$          |
|                                       | B/Victoria & V   | $c_{A(H1N1)}$          | $c_{A(H3N2)}$          | $\min(a, c_{B/Victoria})$ | $\min(b, c_{B/Yamagata})$ |
|                                       | B/Yamagata & V   | $c_{A(H1N1)}$          | $c_{A(H3N2)}$          | $\min(b, c_{B/Victoria})$ | $\min(a, c_{B/Yamagata})$ |

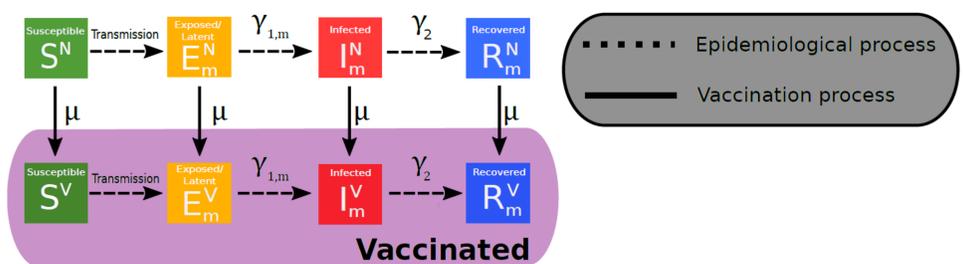
- Propagated vaccine immunity related linearly to prior season vaccine efficacy:  $c_m^y = 1 - \xi \alpha_m^{y-1}$ ;  $\xi \in (0, 1)$

## 4. Transmission & observation model components

- Vaccination model:** 'Leaky' vaccine
- Epidemiological model:** SEIR-type deterministic, ODEs (Fig. 3).
  - Track incidence rate (per 100,000) of new strain m influenza infections in season y:

$$Z_m(y) = \left( \int_{y-1}^y \gamma_{1,m} (E_m^N + E_m^V) dt \right) \times 100,000.$$

Fig. 3: Transmission model schematic (for a single strain).

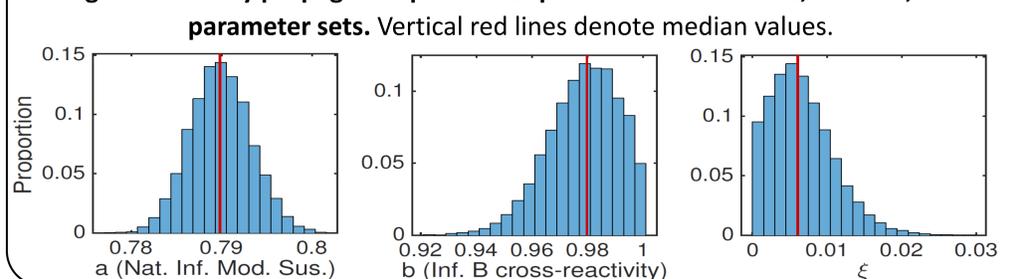


- Observation model:** Estimate ascertainable influenza cases:  $Z_m^+(y) = \epsilon_y Z_m(y)$ .

## 5. Results: Parameter inference

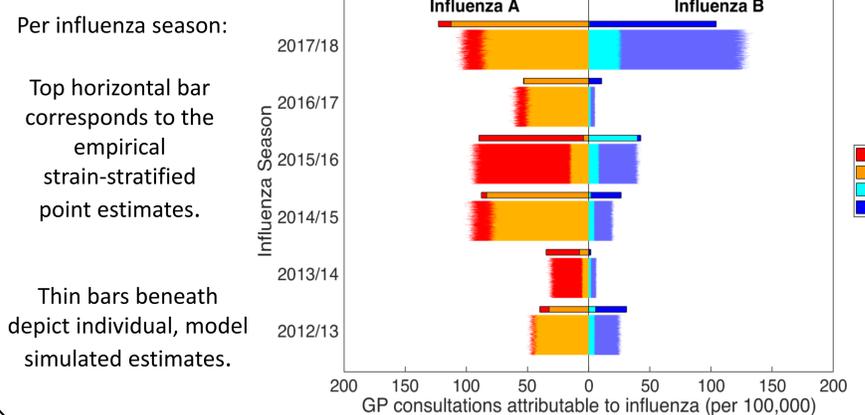
- Invoked an adaptive-population Monte Carlo ABC algorithm [4]. Prior season influenza B cross-reactivity and carry over vaccine efficacy had little impact on immunity.

Fig. 4: Immunity propagation parameter posterior distributions, from 10,000 parameter sets. Vertical red lines denote median values.



## 6. Results: Goodness-of-fit

Fig. 5: Posterior predictive distributions for influenza positive GP consultations.



## 7. Outlook

- Augment model with age structure.
- Couple transmission model with economic evaluation frameworks.
- Appraise cost-effectiveness of prospective seasonal influenza vaccine programmes.

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