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:

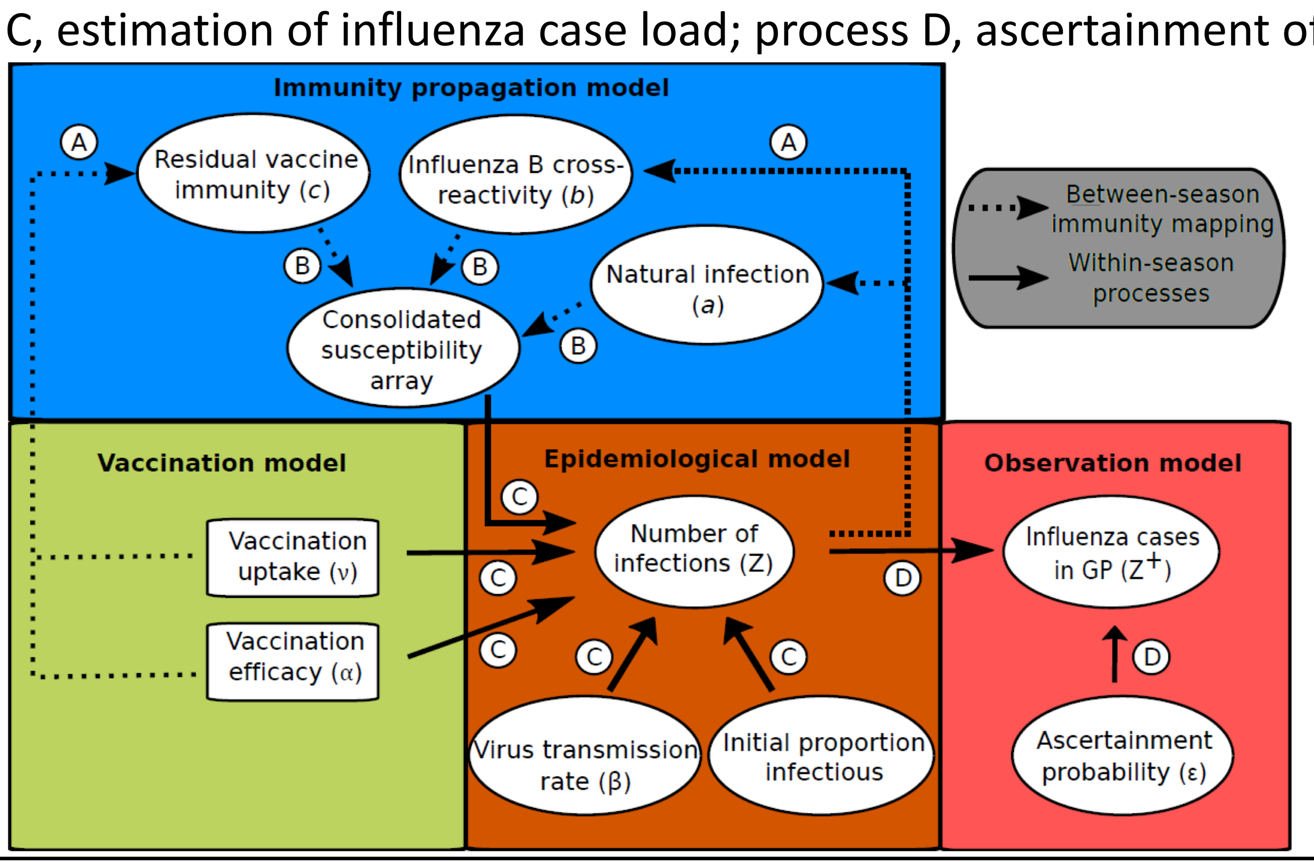
i. Develop a **mathematical model** incorporating a mechanism to **link prior season** epidemiological outcomes to immunity at the beginning of the following season;

ii. 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 $0 < a, b, c_m < 1$.

Exposure history (h)	Strain susceptibility: A(H1N1)pdm09	A(H3N2)	B/Victoria	B/Yamagata
Naïve	1	1	1	1
A(H1N1)pdm09	a	1	1	1
A(H3N2)	1	a	1	1
B/Victoria	1	1	a	b
B/Yamagata	1	1	b	a
Vaccinated (V)	$c_{A(H1N1)}$	$c_{A(H3N2)}$	$c_{B/Victoria}$	$c_{B/Yamagata}$
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:

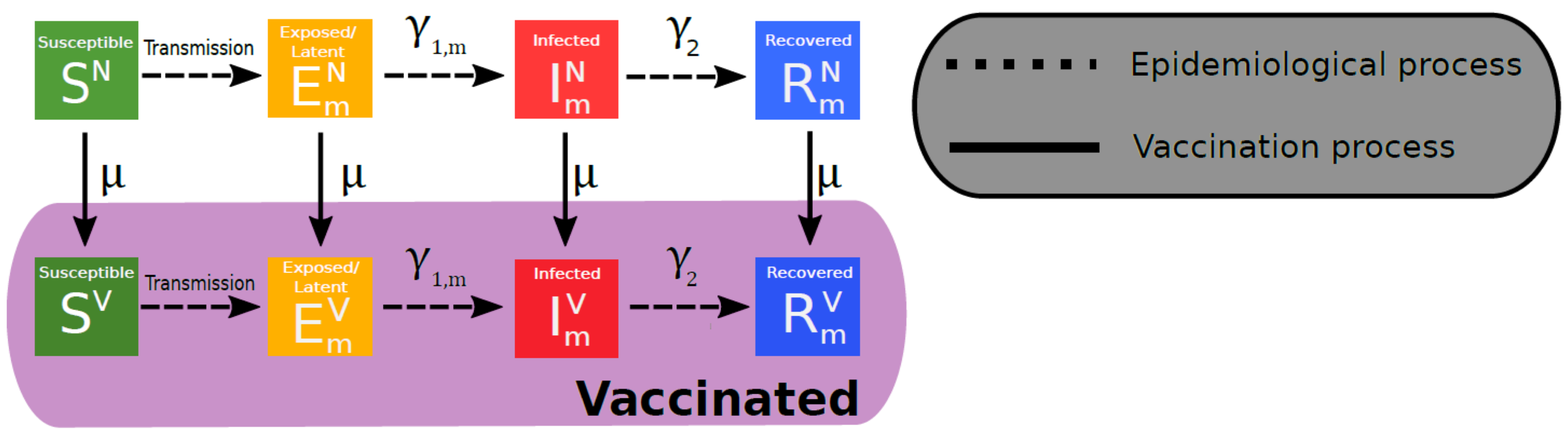
$$c_m^y = 1 - \xi \alpha_m^{y-1}; \quad \xi \in (0,1)$$

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:

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

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

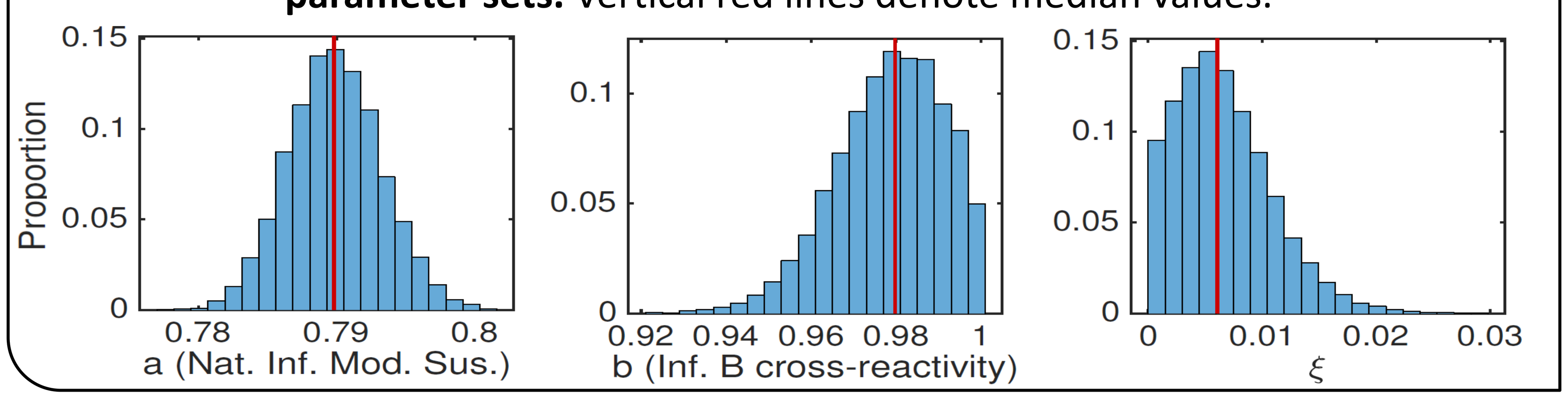


- **Observation model** - Estimate ascertainable influenza cases: $Z_m^+(y) = \epsilon_y Z_m(y)$.

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.



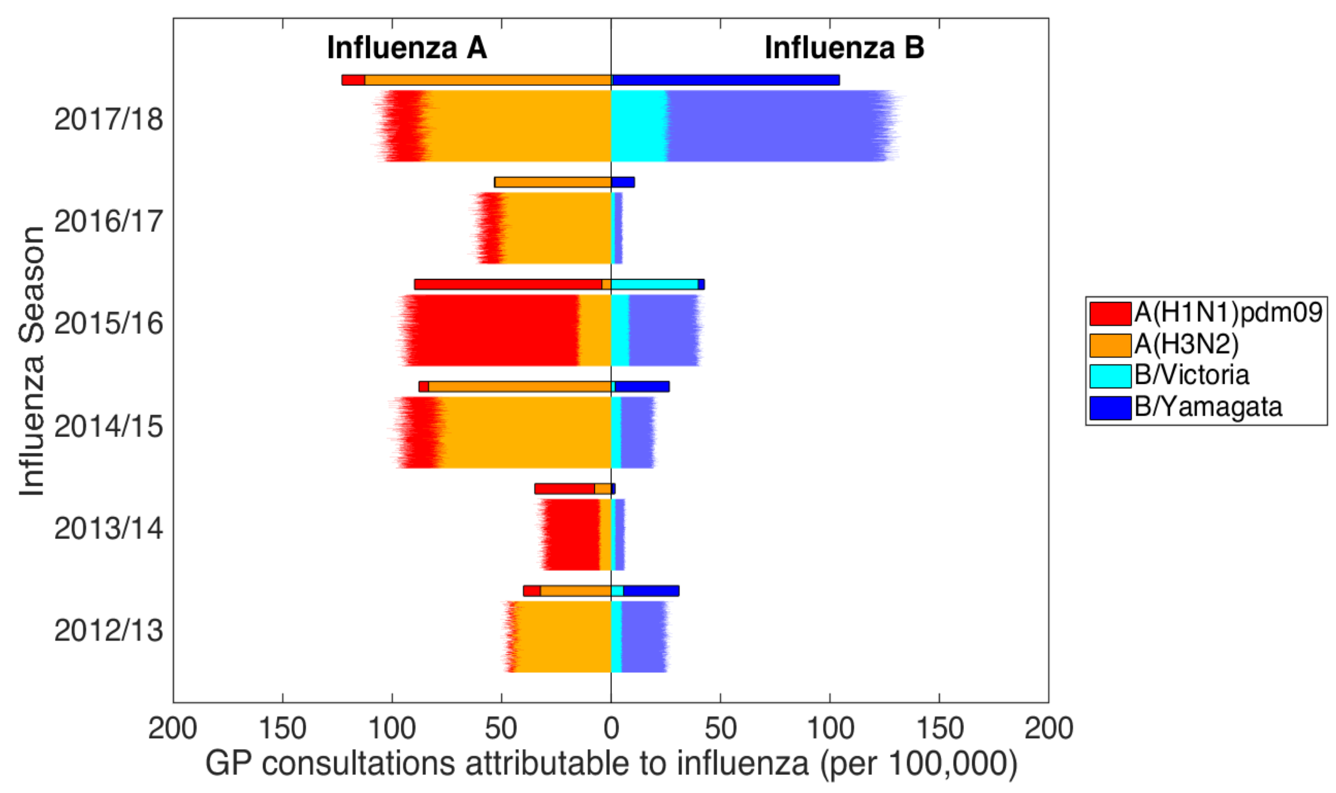
6. Results: Goodness-of-fit

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

Per influenza season:

Top horizontal bar corresponds to the empirical strain-stratified point estimates.

Thin bars beneath depict individual, model simulated estimates.



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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