VIMP Methods

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1 Methods

1.1 Agent-Based Model Overview

We used an agent-based model (ABM) built with the `FRED` (Framework for Reconstructing Epidemic Dynamics) programming language [5] to simulate the transmission dynamics representing $H3N2$ influenza within a synthetic population. The model is largely the same as that used in previous research investigating the effect of altering vaccine efficacy and uptake [6], but we re-describe it here for convenience. The simulation represented the population of Allegheny County, Pennsylvania (N = 1,218,695), based on a 2010 U.S. Census-derived synthetic population dataset [10]. The simulation period spanned from August 15, 2023, to August 9, 2024. The model integrated modules for disease progression, transmission, seasonality, pre-existing immunity, vaccination, behavioral responses (staying home when sick), scheduled school closures, and detailed tracking of outcomes by demographic groups.

1.2 Population and Setting

The model utilized a synthetic population that represents individuals and their daily interaction patterns within households, block groups, schools, classrooms, workplaces, and offices that make up a 2010 US Census-derived synthetic population dataset for Allegheny County, PA [10].

1.3 Disease Transmission and Progression

Influenza transmission was modeled based on proximity within shared locations. Seasonality of transmission was implemented using a sinusoidal function modifying the daily transmissibility of individual agents. This function causes transmissibility to peak around the winter solstice (day 355 of the year) and reach a minimum value, corresponding to a 50% reduction from the peak (`seasonal_reduction`), around the summer solstice. The daily seasonal transmissibility for an agent, $T(d)$, is calculated as:

$$T(d) = I_0 \times \left(1.0 - R_{\max} \times \left(1 - 0.5 \times \left(1 + \cos\left(\frac{2\pi d_{\text{peak}}}{365}\right)\right)\right)\right)$$

where:

- $T(d)$ is the final seasonal transmissibility on a given day d.
- I_0 is the agent's base transmissibility (corresponding to the `infectious` parameter value, potentially modified by other factors like disease state).
- $R_{\max}$ is the maximum fractional seasonal reduction in transmissibility (corresponding to `seasonal_reduction`, set to 0.5).
- d_{peak} is the absolute distance in days from the peak transmissibility day (day 355 of the year, approximately the Winter Solstice).

The natural history of infection followed an SEIR-like (Susceptible-Exposed-Infectious-Recovered) structure with additional states:

- `Susceptible (S)`: Individuals susceptible to infection. Susceptibility could be modified by vaccination or pre-existing immunity (see Vaccination and Pre-existing Immunity). Susceptibility ranges from 0-1, with 1 being high susceptibility and 0 being no susceptibility.
- `Exposed (E)`: Latent period following infection. Duration followed a log-normal distribution with parameters ($meanlog = 1.9$, $sdlog = 1.23$) days. For all individuals younger than 65 years old, there is a 25% chance of progressing to an asymptomatic infection, and a 75% chance of progressing to a symptomatic infection. All individuals 65 years or older progress to symptomatic infections.
- `Pre-symptomatic Infectious (Ps)`: A 1-day period where individuals are 50% as infectious as they they will be once transitioning to the Symptomatic Infectious state.
- `Symptomatic Infectious (Is)`: Individuals exhibit symptoms and are fully infectious. Duration followed a lognormal distribution ($meanlog = 5.0$, $sdlog = 1.5$) days.
- `Asymptomatic Infectious (Ia)`: Individuals are 50% as infectious as those with symptomatic infections but show no symptoms. Duration followed a lognormal distribution ($meanlog = 5.0$, $sdlog = 1.5$) days.
- `Hospitalized (H)`: A non-infectious state entered from `Is` based on age- and vaccination-status-specific probabilities (see Hospitalization and Mortality Rates).
- `Recovered (R)`: Individuals recovered from infection. Immunity wanes monthly in this state by 0.03 per month, capped at 0.85, which represents 15% protection compared to baseline susceptibility.

- `Died`: Individuals removed from the simulation due to infection, entered from the `H` state based on age- and vaccination-status-specific probabilities (see Hospitalization and Mortality Rates).

The simulation was seeded by importing 50 exposed individuals on October 15th.

1.4 Hospitalization and Mortality Rates

Probabilities of hospitalization (from `Is`) and death (from `H`) were stratified by age group and vaccination status (see Table 1 and Table 2, respectively). Probabilities of hospitalization for adults were obtained from [7], while probabilities of hospitalization for children were obtained from [3]

Table 1: Probability of Hospitalization (Given Symptomatic Infection) by Age and Vaccination Status

Age Group	**Vaccination Status**	**Probability (Infection → Hospitalized)**
0-4 yrs	Unvaccinated	0.00955
0-4 yrs	Vaccinated	0.00446
5-17 yrs	Unvaccinated	0.00420
5-17 yrs	Vaccinated	0.00175
18-49 yrs	Unvaccinated	0.00724
18-49 yrs	Vaccinated	0.00247
50-64 yrs	Unvaccinated	0.01548
50-64 yrs	Vaccinated	0.00467
65+ yrs	Unvaccinated	0.09636
65+ yrs	Vaccinated	0.08455

Table 2: Probability of Mortality (Given Hospitalization) by Age and Vaccination Status

Age Group	**Vaccination Status**	**Probability (Hospitalized → Death)**
0-4 yrs	Unvaccinated	0.00919
0-4 yrs	Vaccinated	0.00559
5-17 yrs	Unvaccinated	0.00951
5-17 yrs	Vaccinated	0.00559
18-49 yrs	Unvaccinated	0.03258
18-49 yrs	Vaccinated	0.02172
50-64 yrs	Unvaccinated	0.06211
50-64 yrs	Vaccinated	0.04026
65+ yrs	Unvaccinated	0.10974
65+ yrs	Vaccinated	0.05410

1.5 Pre-existing Immunity

A proportion of the population started with pre-existing immunity to H_3N_2, based on age-stratified estimates: $0-4$ yrs (25.08%), $5-17$ yrs (18.48%), $18-49$ yrs (13.32%), $50-64$ yrs (16.08%), 65+ yrs (4.32%). These age-stratified estimates are 45% of 3x the CDC's estimated 2019-2020 disease burden [2]. Individuals with pre-existing immunity had their initial susceptibility set based on a normal distribution ($\mu = 0.5, \sigma = 0.1$). This immunity waned over time if the agent was not subsequently infected or vaccinated, with susceptibility increasing by 0.03 per month towards a maximum susceptibility of 0.85.

1.6 Vaccination

Vaccination became available from September 16th. Individuals became eligible based on age-specific coverage rates for 2023-2024 Flu season, obtained from the CDC [1]: 6mo-17 yrs (55.4%), $18-49$ yrs (32.8%), $50-64$ yrs (46.2%), 65+ yrs (69.7%) from the CDC. Eligible individuals received the vaccine after a random delay (uniform distribution between 1 and 45 days). Vaccine-induced immunity took effect 14 days post-vaccination.

The model assumed a vaccine effectiveness (VE) of 42% base on the CDC's VE estimates for the 2023-2024 season [4].

- For individuals without prior immunity, susceptibility was set to $(1 - \text{VE}) = 0.58$ upon immunization.
- For individuals with prior immunity, vaccination boosted existing immunity, reducing their current susceptibility by a factor of VE (new susceptibility = old susceptibility $\times (1 - \text{VE})$).

Vaccine-induced immunity waned monthly. For those without prior immunity, susceptibility increased by 0.07 (`VEwane`) per month. For those with prior immunity, susceptibility increased by 0.07 per month until it reached their pre-vaccination immunity level, after which it increased by 0.03 per month (as per natural immunity waning).

1.7 Behavioral Response

Individuals in the symptomatic infectious state (`Is`) had a 40% probability of staying home, where they stopped attending school / work / other locations, but remained present in their home.

1.8 School Closures

Schools were closed based on predefined dates corresponding to Winter Break (Dec 20 - Jan 02), Spring Break (Mar 10 - Mar 15), and Summer Break (Jun 15 - Aug 25). School administrators (`ADMIN` condition) controlled closures.

1.9 Simulation Scenarios

Our main contribution is that we used the ABM to quantify the effect of specific interventions on vaccination and vaccine intent in terms of disease burden. These scenarios altered the age-stratified vaccination rates described in the section Vaccination. Each scenario was simulated 100 times to account for model stochasticity.

Vaccination Decrease Scenarios

To explore the potential impact of factors reducing vaccine uptake, we simulated three scenarios based on estimates reported in [8]. This study provided lower bound, central, and upper bound estimates for potential decreases in vaccination intent for the COVID-19 vaccine following experimental exposure to COVID-19 vaccine misinformation. In these scenarios, the baseline vaccination rate for *all age groups* was reduced by the same absolute percentage points:

1. **Lower Bound Decrease:** Baseline rates reduced by 3.9 percentage points.
2. **Central Estimate Decrease:** Baseline rates reduced by 6.2 percentage points.
3. **Upper Bound Decrease:** Baseline rates reduced by 8.5 percentage points.

TODO: This decrease scenario should either be justified by assuming the drop in intent in the Loomba et al. study = a drop in vaccination rate. OR, modeling must be done of NIS data to get an estimate for how intent translates into vaccination over time, which can then be used to translate the drop in intent to drop in vaccination. Working on the latter.

Vaccination Increase Scenarios

To investigate the potential benefits of interventions aimed at increasing vaccine uptake, we simulated three scenarios based on estimates from [9]. This study provided lower bound, central, and upper bound estimates for potential *relative* increases in vaccination coverage (e.g., achievable through interventions like text message reminders). In these scenarios, the baseline vaccination rate for *all age groups* was multiplied by factors corresponding to these relative increases:

1. **Lower Bound Increase:** Baseline rates multiplied by 1.025 (representing a 2.5% relative increase over baseline).
2. **Central Estimate Increase:** Baseline rates multiplied by 1.045 (representing a 4.5% relative increase over baseline).
3. **Upper Bound Increase:** Baseline rates multiplied by 1.07 (representing a 7.0% relative increase over baseline).

TODO: Do they have data available to get age-specific changes in vaccination.

References

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