ASKEM Final Evaluation (February 2025): Epidemiology Decision-maker Scenario

Viral Interactions and Coinfection During Respiratory Virus Season

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Scenario Background

The typical respiratory virus season in the United States spans fall and winter and often includes surges in common respiratory viruses like COVID-19, influenza, and RSV. These drive increased emergency department visits, hospitalizations, and deaths. For many of these respiratory viruses, the age groups at highest risk of severe illness include infants, young children, and older adults[1].

This scenario is set in September 2025, at the start of the new back-to-school period, and just ahead of the typical fall/winter surges for many of the mentioned respiratory illnesses. You are a modeler working in a public health department in the United States serving a municipality of 1 million residents. You are supporting public health decision makers who are concerned about what the upcoming respiratory infection season will look like, specifically for COVID-19, influenza, and RSV – all of which will be co-circulating in the general population. You should assume that the demographics of the area you serve reflect those of the United States at a national level.

[1] https://www.cdc.gov/respiratory-viruses/data/most-impacted.html

Decision-maker Priorities

Within this context, decision makers would like you to leverage modeling to help them explore potential future outcomes related to the following:

1. **Understanding the role of coinfection and nature of viral interaction**: Coinfections occur when a person is simultaneously infected with more than one virus. The relationship between viral coinfections and clinical outcomes is based on the specific mechanisms of viral interactions, which depend on various factors like the timing of infections, the order of infections, the specific combination of viruses, and other factors; there is much uncertainty in our knowledge about this topic[2]. Coinfection effects have typically been categorized in the following ways:
    a. Viral coinfections can have a **synergistic effect** where the combined impact of the two viruses is greater than the impact of each virus alone, which leads to more severe disease outcomes than would be expected with each virus alone.
    b. Viral coinfections can have an **antagonistic effect** where one virus interferes with the dynamics of the other, resulting less severe outcomes associated with of one of the viruses.
    c. Simultaneous viral infections that **do not interfere with each other**, and there is not much difference in clinical outcomes between the coinfection and the single viral infection.

    When there are two simultaneously circulating viruses that sometimes leads to coinfection, what is the impact of the nature of viral interaction (synergistic vs antagonistic mechanisms) on forecasts? What is the impact on timing and size of the waves of infection?

2. **Navigating uncertainty around avian influenza**: In recent years, there has been an increased rate of spread of highly pathogenic avian influenza (HPAI), caused by Influenza A/H5 virus) worldwide in birds and mammals, with some spillover into humans. H5N1 is a particularly virulent strain of HPAI and has caused 68 infections in the United States since 2022[3] and is circulating while seasonal influenza viruses circulate as well. Outside the United States, more than 950 cases of H5N1 have been reported, with an approximate 50% case fatality percent (i.e., number of fatal cases divided by the total cases * 100%)[4,5], although there is speculation that the total number of cases is higher, which would decrease the case fatality percent. While there is currently no evidence of sustained human-to-human transmission of H5N1, there is significant concern that each avian, mammalian, and human infection provides opportunities for

[2] Babawale, P. I., & Guerrero-Plata, A. (2024). Respiratory Viral Coinfections: Insights into Epidemiology, Immune Response, Pathology, and Clinical Outcomes. *Pathogens*, *13*(4), 316. https://doi.org/10.3390/pathogens13040316
[3] https://www.cdc.gov/bird-flu/situation-summary/index.html
[4] https://www.cdc.gov/media/releases/2025/m0106-h5-birdflu-death.html
[5] https://www.who.int/publications/m/item/cumulative-number-of-confirmed-human-cases-for-avian-influenza-a(h5n1)-reported-to-who--2003-2024--20-december-2024

mutation and potential reassortment (i.e. exchange of genetic material) with the seasonal influenza virus, which could lead to a new strain that causes a pandemic. There is uncertainty around the following: 1) when such a novel strain might emerge, 2) how quickly it could spread, and 3) what the clinical severity of such a strain would be.

Given this, what could the upcoming respiratory season look like under best- and worst-case scenarios?

3. **Understanding the impact of public health interventions**: Decision makers would like to explore the impact of public health interventions on the trajectories of one or more cocirculating viruses and strategize about optimal interventions for the future. Types of interventions include:
    a. Nonpharmaceutical interventions (NPIs) like masking, social distancing, and testing policies that impact viral transmission
    b. Pharmaceutical interventions like immunizations (i.e., vaccines or antibodies) for specific age groups or the general population

In terms of objectives, decision makers are first concerned with minimizing severe disease among those at risk of the most severe outcomes (i.e., infants, young children, and older adults) and then for the overall population.

Part 1: Choosing the Right Starting Model

For Part 1 of this scenario, you will consider various candidate models and go through a series of questions to help you select the most appropriate model, which you will further extend and simulate in Parts 2 and 3.

Part 1 supports Decision-maker Confidence Metric 1, "Confidence in finding and selecting an appropriate starting point for the scenario/problem." Decision makers will evaluate whether material provided includes an appropriate base model with relevant parameters and starting values, among other factors.

To support your modeling for this scenario, you've identified the following three publications with mathematical models of viral coinfection. (These papers are also provided in the supplementary materials for this scenario).

- **Model A**: L. Pinky, H. Dobrovolny, 'Epidemiological Consequences of Viral Interference: A Mathematical Modeling Study of Two Interacting Viruses', Front. Microbiol., 10 March 2022, https://doi.org/10.3389/fmicb.2022.830423. **Note the supplementary file for this publication.**
- **Model B**: M. Ojo et. al., 'Nonlinear optimal control strategies for a mathematical model of COVID-19 and influenza co-infection', Physica A: Statistical Mechanics and its Applications, Volume 607, 1 December 2022, https://doi.org/10.1016/j.physa.2022.128173
- **Model C**: R. Zafarnejad, P. Griffin, M. Ventresca, 'A Joint Compartmental Model for The Co-infection of SARS-CoV-2 and Influenza', medRxiv 2022.08.26.22279281; doi: https://doi.org/10.1101/2022.08.26.22279281

1) (TA1/TA4) **Model Extraction:** First, ingest all three models and implement the following unit tests to ensure that you're able to get them into executable states and can faithfully capture the model structure and parameter values.
    1) For Model A (Pinky), recreate Fig. 5D from the publication with the original model described by equation set 1
    2) For Model B (Ojo), recreate Figure 1 shown below. For this unit test, use the following initial conditions: $S(0) = 1{,}000{,}000\ people;\ I_c(0) = I_f(0) = I_{cf}(0) = 1000$ people. Assume all other compartments start with 0 people in them. Assume all parameters are equal to the values given in Table 2 of the publication (using the minimum value when a range is given). Let $\beta_f = 0.406/\text{day};\ \beta_{cf} = 0.220/\text{day};\ \beta_{fc} = 3/\text{day}$.
    3) For Model C (Zafarnejad), recreate Fig. 2 (main figure, excluding 'deceased' compartments) from the publication.

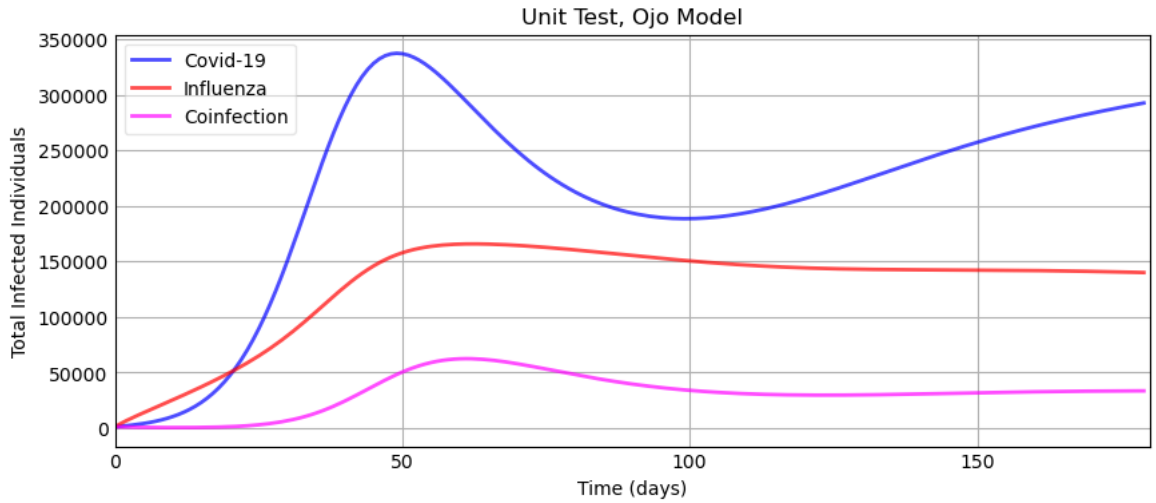

Figure 1. Unit test for Model B (Ojo), describing a case where COVID-19 has a between-host advantage ($R_C > R_F$) but Influenza has a within-host advantage ($\beta_{fc} > \beta_{cf}$), leading to COVID-19 being prevalent, but influenza is not eradicated and in fact stays at a sustained level throughout the simulation.

For baseline modelers, model extraction is defined as the following:

- Writing out or capturing the equations describing the model and drawing out the model structure
- Gathering definitions of all variables and parameters, with units
- Getting model into executable state (you may need to find and install code or write your own code to do this)
- Configuring model (setting initial conditions and parameter values) and running unit test, iterating until you are able to reproduce the required figure, potentially incorporating Model Checks (see below)

For the workbench modelers, model extraction is defined as the following:

- Ingesting the model from source paper into the workbench
- Capturing the set of equations describing the model in the workbench
- Gathering definitions of all variables and parameters with units
- Configuring model (setting initial conditions and parameter values) and running unit test, iterating until you are able to reproduce the required figure, potentially incorporating Model Checks (see below)

(TA2) **Model Checks**: If you are having difficulties reproducing the unit tests, consider implementing common sense model checks on model structure as you diagnose the issue. For example:

- Under the assumption that the total population is constant for the time period considered (i.e. setting natural birth and death rates to 0), demonstrate that population is conserved across all disease compartments, and within demographic groups (if the model is stratified in such a way).
- After setting reinfection parameters to 0 and assuming no immunity waning, ensure that the total susceptible population can only decrease over time,

unvaccinated populations never increase over time, and the total vaccinated population and vaccinated population within each demographic group, can never decrease over time.
    - What other common-sense checks did you implement? Are there others you would have liked to implement but were too difficult?

2) (TA1/TA4) **Model Comparison Based on Summarization**: Do a model comparison based on key differences in assumptions, strengths, limitations, and distinguishing characteristics. Use the template shown in Table 1.

Table 1. Model Comparison Template

Model	**Distinguishing characteristics**	**Assumptions**	**Strengths**	**Limitations of Model or Approach** (as described in paper)
A (Pinky)				
B (Ojo)				
C (Zafarnejad)				

3) (TA2) **Structural Model Comparison**: Now perform structural model comparison between the models. By structural model comparison, we seek to understand how compartments and transition pathways overlap or diverge between models. Feel free to create diagrams and/or use equations in your response.

4) (TA4) **Gap Analysis:** Referring to the high-level decision maker objectives you have been given, what are the key gaps (if any) between each of these existing models and your modeling needs? Also determine what needs to be changed for each model to make it completely suitable for supporting the decision-maker objectives described in the *Decision-maker Priorities* section above and in *Part 3: Addressing Decision-maker Priorities*.

   For this question, also consider a fourth modeling approach, which is to begin with an SIR-type model for 1 virus (see https://en.wikipedia.org/wiki/Compartmental_models_in_epidemiology#Variations_on_the_basic_SIR_model or the epidemiological modeling literature for a starting point), and extend that into a 2-virus coinfection model. Rank each model in terms of their relevance and fit-for-purpose in this context, *given decision-maker objectives and priorities*. Use the template shown in Table 2.

Table 2. Gap Analysis Template

Approach or Model	**Gap Analysis:** What needs to be added or changed, to make model/approach completely suitable for supporting decision-maker objectives?	**Rank relevance and fit-for-purpose with reasoning** (1 = most suitable; 3 = least suitable)
Model A (Pinky)		
Model B (Ojo)		
Model C (Zafarnejad)		
Extend Single Virus SIR-type Model		

5) **Model Selection**: Based on Q1-4, select the model you think is the most appropriate ***starting point*** for supporting decision makers, and explain your reasoning. Note that there is no single right answer – this question is about selecting a model and providing reasoning or evidence for your choice.

6) **Find Parameters:** Ensure your chosen model in Q5 can support two cocirculating viruses – RSV and COVID-19. If your model parameters don't reflect RSV and COVID-19 disease dynamics, find relevant parameter values and fill in the following information about sources and quality (see Table 3). You may use any of the papers provided above or others that you find online.

   If relevant, you may include multiple rows for the same parameter (e.g. you find different values or ranges from different reputable sources), with a 'summary' row indicating the final value or range of values you decide to use. If there are required parameters for your model that you can't find sources for in the literature, you may find data to calibrate your model with, or make reasonable assumptions on what sensible values could be (with rationale).

Table 3. Parameter Table Template

Parameter	Parameter Definition	Parameter Units	Parameter Value or Range	Uncertainty Characterization	Sources	Modeler Assessment on Source Quality

Part 1: Decision-maker Panel Questions

How confident are you that the modeling team selected a model and associated information appropriate for the decision-making questions under consideration? Select a confidence level on a 7-point scale.

1	2	3	4	5	6	7
Very Low	Low	Somewhat Low	Neutral	Somewhat High	High	Very High

Metric Explanation: Decision makers will evaluate whether results include an appropriate model, with relevant parameters, starting values, etc.

The decision-maker confidence score should be supported by the answers to the following questions:

- Did modelers clearly communicate key differences between the chosen model and other candidate models? What kinds of information were provided to help you understand the differences? What kinds of information would you have wanted?
- Are results traceable to sources and did modelers assess source quality?
- Is the model chosen for the scenario appropriate/fit-for-purpose for the given problem?
- Were assumptions and data associated with models clearly communicated?

Part 2: Developing/Updating the Model

Part 2 supports Decision-maker Confidence Metric 2: "Confidence in developing an appropriate model and associated parameter space to sufficiently explore the scenario/problem."

This part involves modifying the model. There is no single right answer for making these modifications – you may approach them in any justifiable way you'd like.

Consider that you will need to find additional parameters for your extended/updated models at various points. We encourage you to incorporate iterative validation steps throughout the process, including model checks (see Q1 in Part 1).

Decision makers will evaluate whether this was done in a logical way based on reasonable assumptions, and whether the final model can support the questions asked in the scenario.

7) (TA2) **RSV and COVID-19 Coinfection Model:** You may need to update the model you selected in Part 1 to answer questions in Part 3 related to decision-maker priorities about RSV and COVID-19 cocirculating during the upcoming school year. Make the following modifications to your model.
    - **Model edits to include hospitalizations and deaths**: In order to prepare for the questions in Part 3, your model should be able to represent hospitalizations and deaths for RSV and COVID-19 separately. If needed, modify your model to support this.
    - **Model edits to include vaccination coverage**: If your model doesn't include vaccination for RSV or COVID-19 separately, modify your model to include this. To prepare for the types of vaccine-related interventions described in Part 3, your model should be able to represent the fraction of the population that has been vaccinated, and its impact on infections, hospitalizations, and deaths.
    - **Model edits to include age stratification**: If your model doesn't include age stratification for RSV, stratify your model accordingly. At minimum you should include 3 age groups. To support the age-specific interventions of interest to decision makers (described in Part 3), at least one age group should represent infants under the age of 2, and at least one age group should represent the population above 60 years of age. The following variables or compartments should be stratified, if they exist in your model: $Susceptible$, $Vaccinated_{RSV}$, $Infected_{RSV}$, and $Hospitalized_{RSV}$. You may use real contact data to inform your stratification parameters and draw from any reasonable sources (see below).
    - **Update parameters**: Find reasonable parameter values for your updated model and create a table similar to the Table 3 template above. You may draw from any reasonable sources (e.g. authoritative public health or medical organizations, or other peer-reviewed and evidence-based sources). Some helpful sources may include the following:

i. *Contact matrix data*: "Projecting social contact matrices in 152 countries using contact surveys and demographic data", https://doi.org/10.1371/journal.pcbi.1005697
ii. *Simple example of age-stratification*: Ram, V., Schaposnik, L.P. A modified age-structured SIR model for COVID-19 type viruses. *Sci Rep* **11**, 15194 (2021). https://doi.org/10.1038/s41598-021-94609-3
iii. *Surveillance of RSV*: https://www.cdc.gov/rsv/php/surveillance/index.html
iv. *RSV-Net*: https://www.cdc.gov/rsv/php/surveillance/rsv-net.html
v. *Preliminary Estimates of RSV Burden for 2024-2025*: https://www.cdc.gov/rsv/php/surveillance/burden-estimates.html
vi. *Weekly RSV Vaccination Dashboard*: https://www.cdc.gov/rsvvaxview/data/index.html
vii. *'Maternal Respiratory Syncytial Virus Vaccination and Receipt of Respiratory Syncytial Virus Antibody (Nirsevimab) by Infants Aged <8 Months — United States, April 2024'*: https://www.cdc.gov/mmwr/volumes/73/wr/mm7338a2.htm#:~:text=To%20determine%20maternal%20and%20infant,communicating%20the%20importance%20of%20immunization
viii. *Vaccination Trends*: https://www.cdc.gov/respiratory-viruses/data/vaccination-trends.html
ix. *CDC study shows effectiveness of RSV immunization for infants*: https://www.cdc.gov/media/releases/2024/s0307-rsv-immunization.html
x. *Kriss JL, Black CL, Razzaghi H, et al. Influenza, COVID-19, and Respiratory Syncytial Virus Vaccination Coverage Among Adults — United States, Fall 2024. MMWR Morb Mortal Wkly Rep 2024;73:1044–1051. DOI*: http://dx.doi.org/10.15585/mmwr.mm7346a1
xi. *COVID Data Tracker*: https://COVID.cdc.gov/COVID-data-tracker/#datatracker-home
xii. *COVID-19 Death Data and Resources*: https://www.cdc.gov/nchs/nvss/COVID-19.htm

8) (TA2) **RSV and COVID-19 Coinfection Model, Version 1 – With Antagonistic Viral Interactions**: If your model from Q7 doesn't include a measure of antagonistic interaction between COVID-19 and RSV, build upon it to include some type of antagonistic or competitive viral interaction, while still including some level of coinfection. Some examples of antagonistic interactions could include the following:
   - Within a host, being infected with one virus (V1) suppresses the ability to then become coinfected with a second virus (V2).
   - Once coinfected with two viruses V1 and V2, one virus dominates the other and becomes the sole virus that can then be spread onto others. This might be due to one virus inhibiting viral replication of the other virus or modulating the host's immune response to the other virus.

9) (TA2) **RSV and COVID-19 Coinfection Model, Version 2 – With Synergistic Viral Interactions**: If your model from Q7 doesn't include a measure of synergistic interaction between COVID-19 and RSV, build upon it to include some type of synergistic or cooperative viral interaction. Some examples of synergistic interactions could include the following:
    - Infection with one virus enhances likelihood of infection by a second virus by boosting viral entry.
    - Coinfection leads to increased viral replication and load between the two viruses, which could lead to exacerbation of clinical outcomes and symptoms (e.g. increased probability of severe disease, hospitalization, or death, or slower recovery rate/longer symptomatic timeframe, etc.)
10) (*Optional*, TA2) **Influenza and COVID-19 Coinfection Model, Synergistic Viral Interactions**: Now create a separate Influenza and COVID-19 coinfection model. You may repurpose one of your models from Q7-9 with updated parameters or develop a different model. Ensure your parameters reflect COVID-19 and seasonal influenza disease dynamics (i.e., assume influenza virus types A & B, with A subtypes H1N1 and H3N2) and create a table similar to the Table 3 template. You may draw from any reasonable sources (e.g. authoritative public health or medical organizations, or other peer-reviewed and evidence-based sources). Assume that viral interactions are only synergistic. Your model may be stratified or unstratified. You will be doing a horizon scan with this model in Part 3. Some helpful sources for parameterization (in addition to the links above in Q7) may include the following:
    - *Preliminary Estimated Influenza Disease Burden 2024-2025 Influenza Season*: https://www.cdc.gov/flu-burden/php/data-vis/2024-2025.html
    - *FluView Interactive*: https://www.cdc.gov/fluview/overview/fluview-interactive.html
    - *Weekly Influenza Vaccination Dashboard*: https://www.cdc.gov/fluvaxview/dashboard/index.html
    - *Influenza Vaccination Coverage, United States, 2023–24 Influenza Season*: https://www.cdc.gov/fluvaxview/coverage-by-season/2023-2024.html

11) (TA2) **Final Model Checks**: You need to demonstrate that the final 2-3 models you've created (Q8, Q9, optionally Q10), are structurally sound and make sense from a mechanistic perspective. Implement common sense model checks on model structure and parameter space. For example:
    - Under the assumption that the total population is constant for the time period considered (i.e. setting natural birth and death rates to 0), demonstrate that population is conserved across all disease compartments, and within each demographic group.
    - After setting reinfection parameters to 0 and assuming no waning immunity, ensure that the total susceptible population can only decrease over time, unvaccinated populations never increase over time, and the total vaccinated population and the vaccinated populations within each demographic group can never decrease over time.

- What other common-sense checks did you implement? Are there others you would have liked to implement but were too difficult?

Part 2: Decision-maker Panel Questions

How confident are you that the modeling team appropriately modified the model and its parameter space to sufficiently explore the scenario/problem? Select confidence level on a 7-point scale.

1	2	3	4	5	6	7
Very Low	Low	Somewhat Low	Neutral	Somewhat High	High	Very High

Metric Explanation: The scenario involves updating or modifying a model. Decision makers will evaluate whether this was done in a sensible way and whether the final model can support all the questions asked in the scenario.

The decision-maker confidence score should be supported by the answers to the following questions:

- Did modelers clearly explain the changes being made and key differences between the original and updated models? Did the modifications/extensions the modelers made make sense and were they reasonable to you?
- Are you confident that the starting model was updated in ways that make sense? Is the final model structurally sound?
- As the model was updated, was the parameter space being explored reasonable and broad enough/complete enough to support the questions required by the scenario?

Part 3: Addressing Decision-maker Priorities

For Part 3 of this scenario, you will utilize everything you have built in Parts 1 and 2 to answer various decision-maker questions aligned to the priorities described in the scenario background. As with the other parts, there are multiple reasonable approaches.

Part 3 supports Decision-maker Confidence Metric 3: "Confidence in understanding model results and tradeoffs between potential interventions." Decision makers will be asked about their confidence in understanding model output, effectiveness of various interventions under consideration, and how uncertainty factors into the process and the conclusions that can be made.

12) (TA3) **RSV and COVID-19 Baseline Forecasting, Antagonistic Viral Interaction**: The decision makers you are supporting would like to first understand what the next five months of the school year (October 2025 through February 2026) will look like when RSV and COVID-19 are cocirculating, assuming there are no medical countermeasures or NPIs in place. Begin with your model from Q8 (*RSV and COVID-19 Coinfection Model, Version 1 – With Antagonistic Viral Interactions*), and create a 5-month forecast.
    - Assume that your total population N is the size of your municipality (1 million people), and assume that everybody starts off in the susceptible compartment except for 100 people in each of the single-virus infected compartments ($I^i_{RSV}(0) = I_{C19}(0) = 100\ people$, where i refers to age groups).
    - Initial conditions for all other compartments (including the coinfected population) are 0.
    - If there is uncertainty in outcomes, ensure this is communicated in the forecast.

    For RSV, which age group has the worst outcomes with respect to number of hospitalizations and deaths? When do COVID-19 and RSV activity peak? Do the peaks align or are they staggered?

13) (TA3) **RSV and COVID-19 Baseline Forecasting, Synergistic Viral Interaction:** Now repeat Q12, but use your model from Q9 (*RSV and COVID-19 Coinfection Model, Version 2 – With Synergistic Viral Interactions*). How do your results differ from Q12? Do the results make sense given the different nature of viral interactions?

14) (TA3, TA4) **Value of Information and Decision-maker Interventions for RSV and COVID-19**: The decision makers you are supporting are considering various vaccination strategies to manage RSV and COVID-19 infections over the next five months of the school year (October 2025 through February 2026). They would like to explore the impact of the interventions using the models you have developed, in a Value of Information framework (see Figure 2). As described in the Decision-maker Priorities section, the main objective for decision makers is minimizing hospitalizations and deaths for vulnerable age groups first, and then for the overall population.

    The three intervention options being considered are:

- *Option 1*: Vaccinating up to 35% of the susceptible population for COVID-19, at a constant daily vaccination rate over the course of the five months. Use realistic vaccine effectiveness figures from authoritative sources like the CDC:
    i. https://www.cdc.gov/COVID/php/surveillance/vaccine-effectiveness-studies.html
    ii. https://COVID.cdc.gov/COVID-data-tracker/#vaccine-effectiveness
- *Option 2*: Vaccinating up to 40% of the 60+ years age group for RSV, at a constant daily vaccination rate over the course of the five months. Use realistic vaccine effectiveness figures from authoritative sources like the CDC: https://www.cdc.gov/rsv/hcp/vaccine-clinical-guidance/older-adults.html .
- *Option 3*: Vaccinating up to 40% of infants under 2 years of age, with nirsevimab, at a constant daily rate over the course of the five months. Use realistic vaccine effectiveness figures from authoritative sources like the CDC:
    i. https://www.cdc.gov/media/releases/2024/s0307-rsv-immunization.html
    ii. https://www.cdc.gov/mmwr/volumes/73/wr/mm7309a4.htm

You want to measure the impact of each intervention against the baseline forecasts (Q12-13) in terms of Average Treatment Effect (ATE) for infections, hospitalizations, and deaths. ATE is defined as the difference (measured as root mean square error) between mean outcomes with and without an intervention/treatment. You will compute a separate ATE for each of the outcomes.

You are unsure whether RSV and COVID-19 interact in an antagonistic or synergistic manner. The literature on this topic has mixed conclusions and conflicting studies; therefore, you want to explore the three intervention options with both of the interaction models you developed in Part 2 (Q8 and Q9). How does the impact of interventions differ between the two interaction models, and what is the optimal intervention choice for each interaction model? As described in the scenario background, the main objective for decision makers is minimizing hospitalizations and deaths for vulnerable age groups first and then for the overall population. The optimal intervention choice(s) will prioritize this objective. Based on your simulations, form a recommendation for which intervention(s) to prioritize.

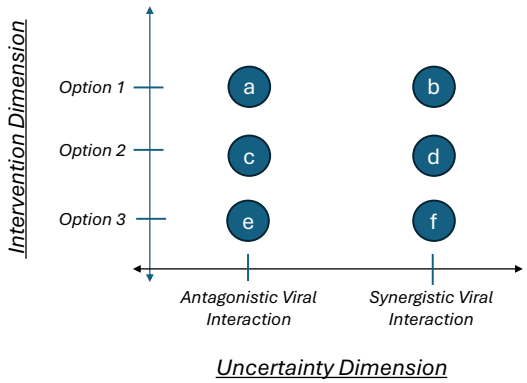

Figure 2. Value of information framework for Question 14.

(*Optional*, TA3) **Seasonal Influenza and COVID-19 Forecasting**: Now decision makers would like to understand what the next five months of the school year (October 2025 through February 2026) will look like when the dominant viruses cocirculating are seasonal influenza and COVID-19. Begin with your model from Q10 (*Influenza and COVID-19 Coinfection Model, Synergistic Viral Interactions*), and create a five-month forecast. Recall that we are assuming circulation of the seasonal influenza caused by influenza virus types A&B, with A subtypes H1N1 and H3N2.

- Assume that your total population N is the size of your municipality (1 million people), and assume that everybody starts off in the susceptible compartment except for 100 people in each of the single-virus infected compartments ($I_{Flu}(0) = I_{C19}(0) = 100\ people$).
- Initial conditions for all other compartments (including the coinfected population) are 0.
- If there is uncertainty in outcomes, ensure this is communicated in the forecast.

When do influenza and COVID-19 activity peak? Do the peaks align or are they staggered? How do peak timing and sizes here compare with the Q13 forecast *(RSV and COVID-19 Baseline Forecasting, Synergistic Viral Interaction*)?

15) (*Optional*, TA3, TA4) **Horizon Scanning with Avian Influenza and COVID-19 Coinfection**: The decision makers you support would like you to perform a horizon scan to better understand the extreme bounds of possible outcomes over the next five months of the school year. They are interested in the possible emergence of a new strain of influenza A/H5 HPAI which is transmissible from human-to-human and could dominate over seasonal influenza. For this question and Q17, you may make a simplifying assumption that while this new influenza strain is cocirculating with COVID-19, seasonal influenza is not also circulating. Current seasonal influenza vaccines do not provide protection against human infection with H5N1[6] and therefore we expect they will not be effective against this hypothetical new strain either. Consider the following parameters of this hypothetical new strain:

- *Case Fatality Percent:* The first avian influenza H5N1 death in the United States occurred in January 2025[7], and there have been 68 cases in the United States since 2022[8], resulting in a 1.5% fatality percentage. Although the number of cases will very likely increase further by the time we get to the time period described in this scenario, let us consider the 1.5% figure as the lower bound on the case fatality percent for this new strain. For the upper bound, consider global data from the WHO[9]**Error! Bookmark not defined.**
- *Transmissibility*: For a best-case scenario/lower bound on transmissibility for the new strain, assume a similar transmissibility level as seasonal influenza. For the worst

[6] https://www.cdc.gov/bird-flu/prevention/hpai-interim-recommendations.html
[7] https://www.cdc.gov/media/releases/2025/m0106-h5-birdflu-death.html
[8] https://www.cdc.gov/bird-flu/situation-summary/index.html
[9] https://www.who.int/publications/m/item/cumulative-number-of-confirmed-human-cases-for-avian-influenza-a(h5n1)-reported-to-who--2003-2024--20-december-2024

case/upper bound on transmissibility, assume 14x the transmissibility of seasonal influenza.

- Assume other parameters (e.g. recovery rate, hospitalization rate, etc.), are similar to those for seasonal influenza.

Figure 3 and Table 4 summarize the horizon scan analysis. For this question you can use the coinfection model developed in Q10 and replace the parameters for seasonal influenza with updated values corresponding to the hypothetical new HPAI strain.

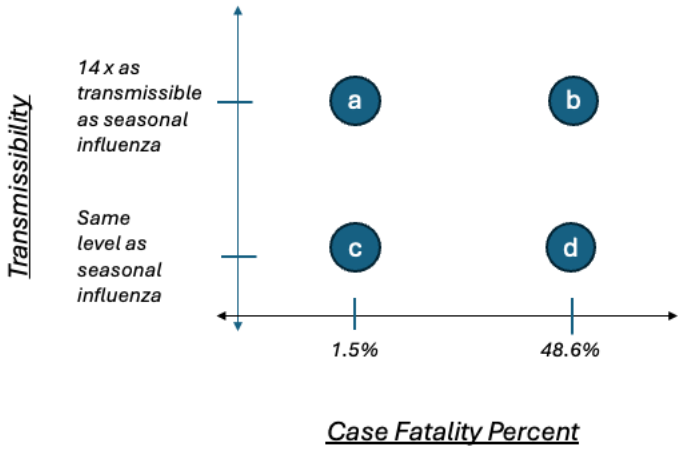

Figure 3. Horizon scanning framework for Question 16.

Table 4. Parameters for Question 16 (Horizon Scanning)

	Case Fatality Percent	
Transmissibility	*Outcome a* • Low case fatality percent (1.5%) • High transmissibility $transmissibility_{new} = \mathbf{14} * transmissibility_{seasonalflu}$	*Outcome b* • High case fatality percent (48.6%) • High transmissibility $transmissibility_{new} = \mathbf{14} * transmissibility_{seasonalflu}$
	Outcome c • Low case fatality percent (1.5%) • Low transmissibility $transmissibility_{new} = transmissibility_{seasonalflu}$	*Outcome d* • High case fatality percent (48.6%) • Low transmissibility $transmissibility_{new} = transmissibility_{seasonalflu}$

Comment on the results of your horizon scan and the uncertainty involved. How do the range of potential outcomes compare against the forecasts you produced in Q15 (with seasonal influenza and COVID-19 cocirculating)?

16) (*Optional*, TA3, TA4) **Optimizing Intervention Strategies for Avian Influenza and COVID-19 Coinfection:** For each of the horizon scan outcomes *a-d* you simulated in Q16, what are the most optimal intervention strategies that you would recommend to decision makers? *The goal of the intervention strategies* would be to get avian influenza and COVID-19 outcomes to be comparable to the forecasts you predicted in Q15 (with seasonal influenza and COVID-19) in terms of total hospitalizations and deaths over the five-month timeframe. In other words, as an optimization constraint, let the total hospitalizations and deaths when the new avian influenza strain and COVID-19 are cocirculating (sum over the entire five-month timeframe) be *no greater than* the totals when seasonal influenza and COVID-19 are cocirculating.

Consider the following intervention strategies and determine the optimal parameter(s) for each of them. Because we expect that current seasonal influenza vaccines will not be effective against this hypothetical new avian influenza strain, we only focus on NPIs for this question.

- *Option 1*: Implement a masking policy over the five-month timeframe, which decreases transmission for both viruses by a factor $\left(1 - m_{compliance} * m_{effectiveness}\right)$ where $m_{compliance}$ is the proportion of people who are likely to comply with the policy and wear masks correctly and consistently, and $m_{effectiveness}$ describes how effective masks are for blocking transmission. Assume $m_{effectiveness}$ = 80%. Find the minimum mask compliance $m_{compliance}$ required to meet the intervention goal.
- *Option 2*: Implement a combination of masking and social distancing mandates. Let the social distancing policy begin in October 2025 at the start of the five-month period, and let the masking policy begin one month after that. Once begun, both policies will continue through the end of the five-month timeframe. Each mandate individually lowers the transmission rate of both influenza and COVID-19 by *X*% when correctly executed. Assume 60% of the population is compliant with the social distancing policy, and 40% of the population is compliant with the masking policy. Find the minimum decrease in transmission *X*% required to meet the intervention goal.
- *Option 3*: Assume that by fall 2025, there will some at-home testing available for the new avian influenza strain, but it won't be as accessible as COVID-19 tests. Now consider a testing campaign that emphasizes at-home testing before gathering with friends and family, with the expectation that people will self-quarantine if they test positive for a particular virus. Testing has an impact by decreasing transmission of a particular virus by factor $\left(1 - test_{access} * test_{effectiveness}\right)$ where $test_{access}$ refers to the proportion of the population that has access to testing and would responsibly self-quarantine based on test results, and $test_{effectiveness}$ refers to how sensitive tests are. Assume $test_{access,avian\ flu}$=15% of the population, and $test_{access,C19}$=30% of the population. For $test_{effectiveness,C19}$ use values cited in evidence-based

publications; one recent study[10] cited sensitivity numbers ranging anywhere from 52% up to 90%, depending on symptomatic or asymptomatic cases, and clinician vs. self-collected rapid testing among patient populations. Assume the avian influenza tests have comparable sensitivity to COVID-19 tests. Let this policy kick in automatically once cumulative hospitalizations (for avian influenza and COVID-19 combined) for a given timepoint exceeds your prior projection of cumulative hospitalizations for seasonal influenza and COVID-19 combined, at the same timepoint. Assume once the policy kicks in, it continues throughout the rest of five-month simulation period. Find the minimum value for $test_{effectiveness,avian\ flu} = test_{effectiveness,C19}$ required to meet the intervention goal.

- *Option 4*: Keeping the upcoming holiday season in mind and knowing the difficulty in enforcing public health interventions during that time period, focus on aggressive interventions starting at the beginning of October with the hope that they can expire at some point around the holidays and still enable you to meet your intervention goal. Implement an aggressive NPI campaign (with testing, social distancing, and masking components) starting in October, which collectively is expected to decrease transmission by $Y\%$. Assume interventions simultaneously expire at some time t. Find the earliest intervention end time t, and minimum decrease in transmission $Y\%$ required to meet the intervention goal. Are you able to let the interventions expire by the Thanksgiving holidays (week of November 24th, 2025), or by the winter holidays (assume this begins on the week of December 22nd, 2025)? You may find that there are multiple valid answers, in which case plot and describe the tradeoffs between disease transmission decrease and earliest possible end date, and provide a recommendation for the best answer.

Finally, is there one or more of these strategies (once optimized) that you would recommend over the others, and why?

[10] https://www.idsociety.org/covid-19-real-time-learning-network/diagnostics/how-accurate-is-a-patients-home-rapid-test-result/#/+/0/publishedDate_na_dt/desc/

Part 3: Decision-maker Panel Questions

With what degree of confidence do you feel that you understand the modelers' results and the potential tradeoffs between the interventions they implemented in their model(s)? Select confidence level on a 7-point scale.

1	2	3	4	5	6	7
Very Low	Low	Somewhat Low	Neutral	Somewhat High	High	Very High

Explanation: Based on the information presented to you by the modelers, determine your confidence in being able to assess effectiveness of all interventions considered in the scenario and understand how uncertainty factors into model results and their implications.

The decision-maker confidence score should be supported by the answers to the following questions:

- Did simulation results make sense? If results did not match your intuition or expectations, did modelers explain the reason(s)? Did their explanations make sense?
- Do you understand the effects of interventions on trajectories? Was the effectiveness of interventions communicated?
- Is it clear how to interpret uncertainty in the results? Do you understand the key drivers of uncertainty in the results?