

Supplementary Material

This supplement provides details of the calculations used in the manuscript.

1. Calculations for outpatient and inpatient mortality risks

The risks of death among hospitalized and non-hospitalized cases were calculated in order to better account for the impact of antiviral treatment among these two groups. To do so, the case fatality risks for each scenario outlined in Meltzer et al.[22] were separated into an inpatient mortality risk and an outpatient mortality risk. To identify the likely place of death for pandemic influenza, we used vital statistics data on the location of influenza deaths.[64] We assessed the location of death for any fatalities that were listed under the following ICD-10 codes: J09, J10, and J11. Calculations were made for all ages combined, although the proportion of deaths occurring among hospitalized individuals did not vary greatly by age. In 2009-2010, 78% of recorded influenza deaths occurred among hospitalized individuals. The proportions of deaths that occurred among inpatients were similar in 2009 and 2010 (approximately 78% each year), but were larger than in previous years (55-60% deaths occurred among inpatients in 2005-2008). For this analysis, we used data from 2009-2010 since these were the most recent years for which data were available.

The following formulas were used to calculate the risks of death:

OP mortality risk = Proportion of influenza deaths occurring in the community * overall case fatality risk

$$\text{IP mortality risk} = \frac{\text{Proportion of deaths occurring in hospital} * \text{overall case fatality risk}}{(1 - \text{OP mortality risk}) * \text{hospitalization risk}}$$

OP: outpatient

IP: inpatient

High severity scenario

$$\text{OP mortality risk} = 0.22 * 0.005 = 0.0011$$

$$\text{IP mortality risk} = \frac{0.78 * 0.005}{(1 - 0.0011) * 0.04} = 0.09760737$$

Low severity scenario

$$\text{OP mortality risk} = 0.22 * 0.00084 = 0.0001848$$

$$\text{IP mortality risk} = \frac{0.78 * 0.00084}{(1 - 0.0001848) * 0.0105} = 0.06241153$$

2. Antiviral Demand & Impact Calculations

The following equations were used for each attack rate and severity scenario:

a. Antiviral Demand

$$\begin{aligned} \text{Antiviral demand} = & \sum_{a,t} (\text{Infection } AR_{a,t} * \text{Symptomatic} * [\text{seek OP care}_{a,s} * \text{OP flu diagnosis \& prescribed} * \\ & \text{Avg. regimens OP}] * (1 + \text{NonFlu}) * \text{prophylaxis} + \text{Hosp} * \text{IP flu diagnosis} * \text{IP prescribed} * \text{Avg. regimens} \\ & \text{IP} * (1 + \text{NonFlu})) \end{aligned}$$

$$\begin{aligned} \text{Hosp} = & \text{hospitalization risk}_s * \{\text{seek OP care}_{a,s} * \text{OP flu diagnosis \& prescribed} * \text{adherence} * [1 - \text{OP} \\ & \text{mortality risk}_s * (1 - \text{AVE}_{\text{death}})] * (1 - \text{AVE}_{\text{Hosp}}) + (1 - \text{seek OP care}_{a,s} * \text{OP flu diagnosis \& prescribed} * \\ & \text{adherence}) * [1 - \text{OP mortality risk}_s]\} \end{aligned}$$

a = age-group (i.e., 0-9, 10-19, 20-59, ≥60)

t = day index (e.g., $t = 43$ is the 43rd day of the epidemic)

s = severity level (high or low as defined in Table 1)

\sum_a means 'take the sum over all age groups'.

\sum_t means 'take the sum over all days'.

AR = attack rate

= number

Subscripts refer to specific age-groups, days, and severity scenarios.

Definitions of the equation parameters are as follows: 'Infection $AR_{a,t}$ ' refers to the number of influenza infections in age group 'a' on day 't'; 'Symptomatic' = proportion of influenza cases that are symptomatic; 'Seek OP care $_{a,s}$ ' refers to the proportion of symptomatic cases in age-group 'a' that seek medical care during a pandemic of severity type 's'; 'prophylaxis' = multiplier to account for regimens distributed for chemoprophylaxis and which includes regimens saved a course for a personal stockpile; OP = outpatient; IP = inpatient; 'Seek OP care' = proportion of those clinically ill that seek medical care in the community; 'OP Flu diagnosis & prescribed' = proportion of those that seek medical care in the community that are diagnosed as having influenza and that receive antivirals; 'Avg. regimens OP' = average number of regimens prescribed to a outpatient receiving treatment; hospitalization risk $_s$ = per-capita risk of hospitalization among symptomatic influenza cases for pandemic of severity type 's'; 'OP mortality risk $_s$ ' = per-capita risk of death among untreated cases in the community for pandemic of severity type 's'; 'IP Flu diagnosis' = proportion of those hospitalized that are diagnosed as having influenza; 'IP Prescribed' = proportion of diagnosed, hospitalized influenza cases that are prescribed antivirals; 'Avg. regimens IP' = average number of regimens prescribed to an inpatient receiving treatment; 'NonFlu' = regimens distributed to treat people with ILI due to illness other than influenza; and 'adherence' = proportion who adhere sufficiently to the treatment course for it to be effective.

b. Antiviral Impact on Hospitalizations

Hospitalizations averted = $\sum_{a,t} (\text{Infection } AR_{a,t} * \text{Symptomatic} * \text{seek OP care}_{a,s} * \text{OP flu diagnosis \& prescribed} * \text{adherence} * \text{hospitalization risk}_s * [1 - \text{OP mortality risk}_s * (1 - AVE_{\text{death}})]) * AVE_{\text{hosp}}$

Definitions of the equation parameters are as follows (duplicate parameters are defined above):

' AVE_{hosp} ' = reduction in the risk of hospitalization for influenza due to receipt of antivirals; and ' AVE_{death} ' = reduction in the risk of death due to influenza as a result of antiviral treatment (assumed to be the same for inpatients and outpatients).

c. Antiviral Impact on Deaths

Deaths averted = $\sum_{a,t} (\text{Infection } AR_{a,t} * \text{Symptomatic} * [\text{seek OP care}_{a,s} * \text{OP flu diagnosis \& prescribed} * \text{adherence} * (\text{OP mortality risk} * AVE_{\text{death}} + \text{hospitalization risk}_s * [1 - \text{OP mortality risk}_s * (1 - AVE_{\text{death}})]) * AVE_{\text{hosp}} * \text{IP mortality risk}) + \text{Hosp} * \text{IP flu diagnosis} * \text{IP prescribed} * \text{IP mortality risk}_s * AVE_{\text{death}}])$

Hosp = $\text{hospitalization risk}_s * \{\text{seek OP care}_{a,s} * \text{OP flu diagnosis \& prescribed} * \text{adherence} * [1 - \text{OP mortality risk}_s * (1 - AVE_{\text{death}})] * (1 - AVE_{\text{Hosp}}) + (1 - \text{seek OP care}_{a,s} * \text{OP flu diagnosis} * \text{OP prescribed} * \text{adherence}) * [1 - \text{OP mortality risk}_s]\}$

Definitions of the equation parameters are as follows (duplicate parameters are defined above): ' $\text{IP mortality risk}_s$ ' = risk of death among hospitalized cases for pandemic of severity type 's'.