Antiviral treatment for outpatient use during an influenza pandemic: A decision tree model of outcomes averted and cost-effectiveness

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Abstract:

Background: Many countries have acquired antiviral stockpiles for pandemic influenza mitigation and a significant part of the stockpile may be focussed towards community-based treatment.

Methods: We developed a spreadsheet-based, decision tree model to assess outcomes averted and cost-effectiveness of antiviral treatment for outpatient use from the perspective of the healthcare payer in the UK. We defined five pandemic scenarios– one based on the 2009 A(H1N1) pandemic and four hypothetical scenarios varying in measures of transmissibility and severity.

Results: Community-based antiviral treatment was estimated to avert 14% to 23% of hospitalizations in an overall population of 62.28 million. Higher proportions of averted outcomes were seen in patients with high-risk conditions, when compared to non-high-risk patients. We found that antiviral treatment was cost-saving across pandemic scenarios for high-risk population groups, and cost-saving for the overall population in higher severity influenza pandemics. Antiviral effectiveness had the greatest influence on both the number of hospitalizations averted and on cost-effectiveness.

Conclusions: This analysis shows that across pandemic scenarios, antiviral treatment can be cost-saving for population groups at high risk of influenza-related complications.

Introduction

Influenza pandemics are rare, unpredictable events with potentially serious consequences. They are considered to be important public health emergencies by the World Health Organization, and a number of countries, with many having specific pandemic preparedness plans(1-3). Neuraminidase inhibitors (NAI) often feature prominently in pandemic influenza preparedness plans(2) and several high-income countries have acquired NAI stockpiles because pandemic specific vaccines may not be widely available for up to 6 months(4). Clinical trials show NAI effectiveness in modestly reducing duration of symptomatic illness in patients with uncomplicated seasonal influenza(5-14). However, these trials were under-powered to assess NAI impact on secondary outcomes such as hospitalizations(15-17). Two meta-analyses of the extant clinical trial data, examining outcomes based on the intention-to-treat-influenza infected (ITTI) approach, found that early NAI treatment (≤48 hours of symptom onset) was associated with a risk reduction of 59%(18) and 63%(19) for hospital admission in otherwise healthy patients with influenza. Other meta-analyses of trial data that evaluated all outpatients with influenza-like-illness (ILI) using the intention-to-treat (ITT) approach did not find a reduction in hospitalizations in those treated with NAIs(20, 21).

If a future pandemic is severe, hospital capacity may be exhausted and therefore reserved for the severely ill who are most likely to benefit(22). Countries may decide to focus a significant part of their pandemic response plan towards community treatment aimed at averting hospitalizations. Policy makers considering NAI stockpiling for a future pandemic of unknown severity will have to consider both number of hospitalizations averted and the cost-effectiveness of such an intervention. NAI treatment for pandemic influenza has generally been estimated to be cost-effective for higher-income countries(23-25). However, a review identified that previous health economic evaluations often neglected pandemic uncertainty by only evaluating singular, fixed pandemic scenarios(26). Moreover, few models have

incorporated the increased risks of adverse pandemic influenza-related outcomes for patients with at-risk conditions. We present a spreadsheet-based decision tree model that evaluates the impact of community-based NAI treatment in terms of the averted influenza-related hospitalizations and associated cost-effectiveness in a range of pandemic scenarios.

Methods

We built a decision tree model (Figure 1) to calculate the impact of community-based NAI treatment for five pandemic scenarios. The first scenario is based on the United Kingdom's (UK) A(H1N1)pdm09 experience, with a clinical attack rate (CAR) of 7% and a case hospitalization risk (CHR) of 0.3% and 1.5% among non-high-risk and high-risk patients, respectively (Table 1). The other four scenarios were based on hypothetical pandemics that varied the CAR (20% and 30%) and the CHR (1.05% to 4.0% for non-high-risk patients; 5% to 20% for high-risk patients) (Table 1). The hypothetical scenarios are based on a risk assessment framework developed by the CDC(27, 28). A standardized risk space was defined based on previous influenza pandemics, and hypothetical pandemic scenarios were identified from this risk space to allow easy comparisons to future economic evaluations. The CHRs for the high-risk groups in these four hypothetical pandemics were assumed to be five times the CHR for the non-high-risk group of patients based on estimates from the 2009 A(H1N1) pandemic(29). We also assumed that the percentage of patients seeking outpatient/ambulatory care would increase with the CHR of the pandemic, ranging from 40% among non-high-risk patients in a 2009-type pandemic to approximately 81% among high-risk patients when the CHR is 20% (Table 1). We estimated the number of deaths averted through averting hospitalizations by multiplying the number of hospitalizations averted with an in-hospital mortality risk that was constant across the scenarios.

We did not differentiate between oseltamivir and zanamivir in the definition of NAIs in our model; however, we based our cost and treatment effectiveness estimates on data specific for oseltamivir. We focus on community-based treatment and do not consider NAI prophylaxis. We used NAI effectiveness estimates from an individual participant data (IPD) meta-analysis of clinical trials data on otherwise healthy patients with seasonal influenza(19) based on ITTI analysis (relative risk: 0.37, 95% confidence interval: 0.17 to 0.81) since NAIs are not active against non-influenza respiratory infections(30). To account for NAI prescriptions to patients with non-influenza ILI, we assumed a 'wastage factor' of 40%, i.e. patients with non-influenza ILI would be prescribed 40% of the number of regimens that are prescribed to patients with influenza(31). We assumed that all patients would start NAI treatment ≤48 hours of symptom onset in our main model and then performed a sensitivity analysis varying the promptness of care-seeking within 48 hours of symptom onset from 25% to 75% (percentage of all care-seeking patients who do so ≤48 hours of symptom onset). Based on estimates from 2009, we also assumed that 64% of patients would be compliant with the prescribed regimen(32).

Unit cost data for our model were obtained from secondary sources including the British National Formulary and UK-based reports on the cost of health and social care (Table 1). Briefly, we used a weighted average cost of physician-based consultation of £24.20. This cost was calculated as a weighted average cost of either a conventional primary care consultation or a phone-based consultation with the 2009 National Pandemic Flu Service (NPFS)(33). The weighting of the costs was done using the proportion of assessments routed through each consultation service in 2009. We used a cost of £16 for an NAI prescription, which included the cost of delivery. Costs of hospitalizations ranged from £436 for non-high-risk patients to £1,727 for high-risk patients (Table 1). All costs were inflated to the 2017 British Pound Sterling (£) using the hospital & community health services (HCHS) index(34).

The overall population of 62.28 million was based on the 2009 UK population(35). We performed the analyses from the perspective of the healthcare payer, the UK National Health Service (NHS). Given that we did not undertake a full cost-utility analysis, we chose to measure our outcomes in natural units (deaths and hospitalizations) rather than in standardized units (QALYs)(36). We considered a time horizon of less than one year (one pandemic event), therefore a discounting rate would not apply.

In each pandemic scenario, we compared the number of outcomes averted (hospitalizations and deaths) and total costs associated with NAI treatment compared to no NAI treatment. We assessed cost-effectiveness of community-based NAI treatment by estimating the cost per averted hospitalization. Our primary analysis was performed using the middle values of our input parameters using formulas provided in Appendix 1. To account for uncertainty in parameter estimates, we performed sensitivity analyses by probabilistically varying input parameters along pre-defined probability distributions (Table 1) and using Monte Carlo simulations (5,000 iterations using Latin hypercube sampling) to calculate mean output values and 95% confidence intervals for different combinations of input parameters. The sensitivity analyses were performed using the software @Risk version 7.3 (Palisade Corporation). Further, we also performed two-way sensitivity analysis to assess the impact of varying NAI effectiveness and patient compliance on the outcome (hospitalizations averted).

Results

In a 2009-like pandemic scenario, we estimated that in our base-case model (no NAI treatment) there would be 28,773 hospitalizations in the overall population. We estimated that 1.9 million regimens of NAIs would be dispensed for outpatient treatment. NAI treatment would have averted 4,034 (14%) hospitalizations in a population of 62.28 million (65 hospitalizations averted/million population) at a cost of £7,110 per hospitalization averted

(Table 2). The cost to avert one hospitalization was £2,238 in high-risk populations and £20,473 in the non-high-risk population (Table 2).

In the 20% CAR-Severity 1 scenario (CHR: non-high-risk=1.05%; high-risk=5.25%), we estimated that 287,734 hospitalizations would occur. 8.07 million regimens of NAIs would be dispensed, averting 57,281 (19.9%) hospitalizations at a cost per averted hospitalization of £1,008 in the overall population and £5,497 in the non-high-risk population. NAI treatment was seen to be cost-saving in the high-risk population.

In the 20% CAR- Severity 2 scenario (CHR: non-high-risk=4%; high-risk=20%), we estimated that over 1.09 million hospitalizations would occur. 9.34 million NAI regimens would be dispensed, averting 250,478 (22.9%) hospitalizations in the total population at a cost per averted hospitalization of £1,079 in the non-high-risk population. NAI treatment was seen to be cost-saving in the overall population and in the high-risk population.

In the 30% CAR- Severity 1 scenario, (CHR: non-high-risk=1.05%; high-risk=5.25%), we estimated that over 430,000 hospitalizations would occur. 12.1 million NAI regimens would be dispensed, averting 85,922 (19.9%) hospitalizations at a cost per averted hospitalization of £1,008 in the overall population and £5,497 in the non-high-risk population. NAI treatment was seen to be cost-saving in the high-risk population.

In the fourth pandemic scenario, (CHR: non-high-risk=4%; high-risk=20%), we estimated that over 1.6 million hospitalizations would occur. 14.01 million NAI regimens would be dispensed, averting 375,717 (22.9%) hospitalizations in the overall population at a cost per averted hospitalization of £1,079 in the non-high-risk population. NAI treatment was seen to be cost-saving in the overall population and in the high-risk population.

We found that varying the proportion of care-seeking patients who do so within 48 hours of symptom onset, while keeping all other variables constant, lowered the percentage of averted

hospitalizations in the overall population from 14.0% (assuming 100%) to 3.5% (assuming 25%) in the 2009-like pandemic scenario (Table 2, Supplemental Table 1).

Our sensitivity analyses revealed that using just the middle values of input parameters in a simple multiplicative model without probability distributions was likely to overestimate the number of hospitalizations averted and underestimate the cost per averted hospitalization. For the 2009-like pandemic scenario, multiplying the middle values of input parameters (Table 2) overestimated the overall number of averted hospitalizations by 28% and underestimated the overall cost per-averted hospitalization by 34% when compared to the mean estimated from the Monte Carlo simulation (Supplemental Table 2). Similar differences in estimates were observed in the other scenarios as well.

The sensitivity analyses, based on a 2009-like pandemic scenario, indicated that NAI effectiveness had the greatest impact on both the total number of hospitalizations averted, as well as on the cost per hospitalization averted (see Figure 2 for 2009 scenario). When the NAI effectiveness was varied from 19% to 83%, the resulting overall proportion of averted hospitalizations ranged between 6% and 15%, at a cost per averted hospitalization of £6,936 to £19,338. The percentage of care-seeking patients who were prescribed NAI, the proportion of NAI prescriptions to non-influenza patients, and NAI treatment compliance were in the top three influential parameters for one or both outcomes (Figure 2). In our two-way sensitivity analysis we varied the treatment compliance level along with NAI effectiveness beyond the 95% confidence intervals of our input parameter (from 90% effectiveness to 10% effectiveness). Increased compliance levels were consistently associated with an increased number of averted hospitalizations across NAI effectiveness estimates (Figure 3). The impact of prescribing NAIs to non-influenza ILI patients had a considerable effect on the cost per averted hospitalization. For the 2009-like pandemic scenario, this ranged from £7,983 per

averted hospitalization (wastage factor=30%) to £11,032 per averted hospitalization (wastage factor=70%).

Discussion

Main finding of this study

We found that community-based NAI treatment would avert a significant proportion of hospitalizations and deaths, particularly in high-risk patients, across the pandemic scenarios we explored in this analysis. However, a substantial number of hospitalizations and deaths would continue to occur even with community-based NAI treatment. The proportion of hospitalizations averted by NAIs could be an important consideration while planning for conditions when hospital capacity could be exceeded. Community-based NAI treatment was seen to be cost-saving for the overall population in a pandemic with a high CAR and high severity, and cost-saving for patients at high risk of complications from influenza across all the pandemic influenza scenarios tested. The value of NAI treatment for population groups not at high risk and for milder pandemic scenarios will have to be determined by careful review under country-specific willingness-to-pay thresholds and the desire to reduce the number of hospitalizations and potential hospital capacity issues.

What is already known on this topic

NAI treatment for pandemic influenza has generally been shown to be cost-effective, when compared to no NAI treatment(23-25, 37). Previous studies have found that NAI effectiveness is, by far, the most influential factor affecting the numbers of outcomes averted and the associated cost-effectiveness(23, 31). Results from our sensitivity analysis support this finding. A study based in the United States that used a similar model(31) showed slightly lower proportions of hospitalizations averted due to NAI treatment when compared to ours, but the difference could be because of the lower level of treatment effectiveness assumed in

the U.S. study. The U.S. study further found that while NAI treatment averted many hospitalizations, large numbers of hospitalizations would remain(31), which is similar to what we have found.

What this study adds

We found that variations in NAI prescription rate, treatment compliance and healthcare-seeking behaviour (to include the choice to seek care and the promptness in care-seeking) impacted considerably on the outcomes, suggesting that even with a drug of fixed effectiveness, factors relating to healthcare-seeking and healthcare delivery could significantly influence the total number of hospitalizations and deaths averted. These data indicate that a successful pandemic stockpiling strategy must be linked to operational procedures which optimise timely access to antivirals, widespread treatment implementation, and high levels of compliance in targeted groups.

One recognised limitation of some previous economic analyses of NAI treatment has been that entire populations have been modelled homogenously without accounting for the increase in the likelihood of influenza-related care-seeking and complications in patients with underlying at-risk conditions(23, 24). In our model, we vary the propensity to seek care and CHR by patients' at-risk status. The significance of this is that countries with limited resources could consider obtaining smaller antiviral stockpiles to target at-risk population groups and avert a higher number of hospitalizations and deaths for each antiviral course dispensed than if they adopted a treat-all approach.

The CAR was an important factor in determining the number of NAI regimens that would be needed for community-based treatment. Our model showed that a highly transmissible, but low severity pandemic would require a larger NAI stockpile than a pandemic with lower transmissibility and higher severity. However, across all pandemic scenarios, the number of

NAI regimens dispensed for outpatient treatment was well below the UK's published national NAI stockpile size of almost 40 million courses of the drug(38).

We have adopted a simple and transparent approach to model building in which we account for important epidemiological factors, population healthcare-seeking behaviour and service utilization rates in a range of pandemic scenarios. Our analyses are UK-focussed, but the spreadsheet tool is easily adaptable to represent other healthcare systems. While the epidemiological parameters are unlikely to change drastically by country, input parameters relating to healthcare utilization and costs will need to be replaced with country-specific ones. We provide the simple version of the spreadsheet tool (without the sensitivity analysis) in Appendix 2. We used updated NAI effectiveness estimates from seasonal influenza data, although observational data from the 2009 A(H1N1) pandemic in a high-severity (high risk of hospitalization) population suggest similar estimates of NAI effectiveness (≤48 hours from symptom onset)(39). We assumed NAI effectiveness is the same in patients with and without at-risk conditions. While there is some evidence to suggest that the level of effectiveness against hospitalization is similar for both groups (39), there is also evidence that suggests a reduction in NAI effectiveness in patients with at-risk conditions(40).

Limitations of this study

This study is subject to limitations. We used a decision tree model (not a transmission dynamic model) and assumed no effect of NAI treatment on transmission. There is evidence to suggest that NAI treatment, at a population level, is likely to have minimal impact on influenza transmission(41). However, decision tree models are known to be limited, especially in their ability to describe the change in influenza attack rates in different risk groups over the course of a pandemic(37). A comparison of static and dynamic models of NAI treatment for pandemic influenza concluded NAI treatment was seen to be cost-effective

with both modelling paradigms; although the associated cost-effectiveness ratios were seen to differ(37). Due to a lack of evidence specific to hospitalization, we did not consider benefits of NAI treatment >48 hours of symptom onset. NAI treatment has, however, been shown be beneficial even when started beyond 48 hours from symptom onset(12). The use of NAIs may be associated with additional costs to the healthcare system due to possible adverse effects of NAIs(21) but we have not considered these costs in our model since most side effects are known to be minor(19). Finally, we have assumed that the multiplier for high-risk patients remains constant between severity scenarios resulting in a CHR as high as 20%. CHRs of 20%, even for high-risk patients, may be unlikely.

Conclusions

Our analyses shows that NAI treatment in outpatients can be cost-saving, particularly for population groups at high risk of influenza-related complications. Model-based estimates like these of the potential hospitalizations, deaths and costs associated with different pandemic scenarios can help countries consider different treatment options and inform stockpiling decisions while developing pandemic preparedness plans. NAI stockpiling decisions are also influenced by other costs to the healthcare system related to storage and maintenance of the NAI stockpile. Currently, the shelf-life for the 75 mg hard capsules of oseltamivir phosphate that comprise most of the NAI stockpile is estimated to be 10 years if stored as per instructions(42). However, influenza pandemics cannot be predicted, and NAI stockpiles could remain unused at the end of their shelf-life, or they may be rendered ineffective or less relevant by the development of antiviral drug resistance or newer, more effective influenza antiviral therapies. Additionally, evidence suggests that in-hospital NAI treatment may also be associated with protective effects(43, 44) and NAI treatment has been shown to be cost-effective if the benefits of NAI usage are confined only to those treated in hospital(45). If a pandemic treatment policy was pursued which combined community use of NAIs to prevent

hospital admission and NAI treatment of hospitalised patients to reduce mortality, then cost-effectiveness and stockpile strategies across both scenarios would need to be considered. Future research in optimizing NAI distribution to risk groups during a pandemic will further inform the cost-effectiveness of stockpiling.

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447 **Table 1: Input parameters used to estimate the number of outcomes averted by**
448 **neuraminidase inhibitors (NAI) treatment and the cost per averted hospitalization**

Parameter	**Value**	**Range** (probability distribution)	**Source**
Total population	62280000	Fixed	(35)
Clinical attack rate (CAR)			
2009 pandemic	7%	Fixed	Box A1, page 31 of (46)
Transmissibility scenario 1	20%	Fixed	(28)
Transmissibility scenario 2	30%	Fixed	(28)
% Seeking outpatient care (non-high-risk)*			
2009 pandemic	40%	32% to 43% (Uniform)	(47)
Severity 1	60%	Fixed	(28)
Severity 2	70%	Fixed	(28)
% Seeking outpatient care (high-risk)			
2009 pandemic	51.2%	43.2 to 54.2 (Uniform)	Assumed from (48)
Severity 1	71.2%	Fixed	Assumed in line with: (48) and (28)
Severity 2	81.2%	Fixed	Assumed in line with: (48) and (28)
% of high-risk individuals	30%	27% to 33% (Uniform)	(49)
Case hospitalization risk (non-high-risk)			
2009 pandemic	0.30%	0.27% to 0.33% (Uniform)	From Annex G, page 171 of (50)
Severity 1	1.05%	Fixed	(28)
Severity 2	4.00%	Fixed	(28)
Case hospitalization risk (high-risk)			
2009 pandemic	1.50%	1.35% to 1.65% (Uniform)	Assumed from page 10 of (29) that at-risk groups would have an increased risk of hospital admission by five times
Severity 1	5.25%	Fixed	Assumed in line with: (28) and (29)
Severity 2	20.00%	Fixed	Assumed in line with: (28) and (29)
% of care-seeking patients prescribed NAI	73%	60% to 85% (Triangular)	(32)
Prescription of NAIs for non-influenza ILI as a % of those receiving NAIs for influenza	40%	30% to 50% (Uniform)	Assumed from (31)

NAI (any time) compliance (as a %)	64%	55% to 70% (Uniform)	(32)
Effectiveness of NAI treatment (<48 hours from symptom onset) on hospitalization (risk reduction) (Intention-to-treat-infected)	63%	83% to 19% (Triangular)	Assumed for pandemic influenza from (19)
Mortality risk (in-hospital)			
2009 Pandemic	5.3%	Fixed	(51)
Severity 1	5.3%	Fixed	Assumed to be fixed between scenarios
Severity 2	5.3%	Fixed	Assumed to be fixed between scenarios
Costs Before being input into the model, all costs listed below were inflated to the 2017 UK Pound Sterling (£) (The hospital & community health services (HCHS) index)			
Cost of GP consultation	£ 37		(52) and (55)
Cost of telephone consultation	£ 22		(52) and (55)
Average (weighted) outpatient consultation cost	£24.2	£22 to £37 (Truncated log normal)	
Cost of NAI (+delivery)	£ 16	Fixed	(53)
High-risk patients: Cost of Hospitalization due to influenza (per patient)	£1,727	£1,263 to £2,075 (Truncated log normal)	(54) and (55)
Low-risk patients: Cost of Hospitalization due to influenza (per patient)	£436	£307 to £504 (Truncated log normal)	(54) and (55)

*This includes consultations made through the National Pandemic Flu Service (NPFS) telephone line

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Table 2: Outpatient NAI treatment for averting outcomes and the cost per averted hospitalization

	NAI regimens dispensed to pandemic influenza patients	NAI regimens dispensed to non-influenza ILI patients	Total NAI regimens dispensed	Total Hospitali-zations	NAI costs (£)	Total costs (£)	Hospitali-zations averted (%)	Incremental cost per averted hospitalization (£)	Deaths averted, No.
2009 A(H1N1) pandemic									
High-risk patients									
No NAI treatment	NA	NA	NA	19,618	NA	56,713,354	NA	NA	NA
NAI treatment	488,833	195,533	684,367	16,662	12,397,546	63,330,048	2,956 (15.1)	2,238	157
Non-high-risk patients									
No NAI treatment	NA	NA	NA	9,155	NA	37,976,039	NA	NA	NA
NAI treatment	891,102	356,441	1,247,543	8,077	22,599,693	60,043,645	1,078 (11.8)	20,473	57
Total population									
No NAI treatment	NA	NA	NA	28,773	NA	94,689,393	NA	NA	NA
NAI treatment	1,379,935	551,974	1,931,910	24,739	34,997,239	123,373,693	4,034 (14.0)	7,110	214
20% CAR- Severity 1									
High-risk patients									
No NAI treatment	NA	NA	NA	196,182	NA	456,499,003	NA	NA	NA
NAI treatment	1,942,239	776,896	2,719,135	155,069	49,258,106	425,367,141	41,113 (21.0)	CS	2,179
Non-high-risk patients								-	
No NAI treatment	NA	NA	NA	91,552	NA	188,534,796	NA	NA	NA
NAI treatment	3,819,010	1,527,604	5,346,613	75,383	96,855,827	277,409,315	16,168 (17.7)	5,497	857

Total population								-	
No NAI treatment	NA	NA	NA	287,734	NA	645,033,798	NA	NA	NA
NAI treatment	5,761,249	2,304,500	8,065,748	230,452	146,113,933	702,776,456	57,281 (19.9)	1,008	3,036
20% CAR- Severity 2									
High-risk patients									
No NAI treatment	NA	NA	NA	747,360	NA	1,544,470,684	NA	NA	NA
NAI treatment	2,215,026	886,010	3,101,036	568,740	56,176,380	1,251,387,276	178,620 (23.9)	CS	9,467
Non-high-risk patients									
No NAI treatment	NA	NA	NA	348,768	NA	339,398,172	NA	NA	NA
NAI treatment	4,455,511	1,782,204	6,237,716	276,910	112,998,465	416,924,159	71,858 (20.6)	1,079	3,808
Total population									
No NAI treatment	NA	NA	NA	1,096,128	NA	1,883,868,856	NA	NA	NA
NAI treatment	6,670,537	2,668,215	9,338,751	845,650	169,174,845	1,668,311,434	250,478 (22.9)	CS	13,275
30% CAR- Severity 1									
High-risk patients									
No NAI treatment	NA	NA	NA	294,273	NA	684,748,504	NA	NA	NA
NAI treatment	2,913,359	1,165,344	4,078,702	232,603	73,887,160	638,050,710	61,670 (21.0)	CS	3,269
Non-high-risk patients									
No NAI treatment	NA	NA	NA	137,327	NA	282,802,193	NA	NA	NA
NAI treatment	5,728,514	2,291,406	8,019,920	113,075	145,283,741	416,113,973	24,252 (17.7)	5,497	1,285
Total population									
No NAI treatment	NA	NA	NA	431,600	NA	967,550,697	NA	NA	NA
NAI treatment	8,641,873	3,456,749	12,098,622	345,678	219,170,901	1,054,164,684	85,922 (19.9)	1,008	4,554
30% CAR- Severity 2									
High-risk patients									

No NAI treatment	NA	NA	NA	1,121,040	NA	2,316,706,026	NA	NA	NA
NAI treatment	3,322,538	1,329,015	4,651,554	853,111	84,264,570	1,877,080,913	267,929 (23.9)	CS	14,200
Non-high-risk patients									
No NAI treatment	NA	NA	NA	523,152	NA	509,097,257	NA	NA	NA
NAI treatment	6,683,267	2,673,307	9,356,574	415,364	169,497,697	625,386,237	107,788 (20.6)	1,079	5,713
Total population									
No NAI treatment	NA	NA	NA	1,644,192	NA	2,825,803,283	NA	NA	NA
NAI treatment	10,005,805	4,002,322	14,008,127	1,268,475	253,762,267	2,502,467,151	375,717 (22.9)	CS	19,913

CAR: Clinical Attack Rate; CS: Cost Saving; NA: Not Applicable

Fig. 1: Decision analytical model tree comparing outcomes in 'NAI treatment' and 'no NAI treatment' groups for patients with symptomatic pandemic influenza

Fig. 2: Probabilistic sensitivity analysis. (A) shows the impact of various parameters on total hospitalizations averted, and (B) shows the impact of various parameters on cost-effectiveness (2009-like pandemic scenario). The width of the bars indicate the change in the output from several replications when each parameter is varied over its range. NAI: Neuraminidase inhibitors; ILI: Influenza-like illness

Fig. 3: Impact of varying treatment compliance on hospitalizations averted at different NAI effectiveness estimates.

This plot is based on a 2009-like influenza pandemic where the number of hospitalizations in the base-case scenario was estimated to be 24,739; NAI: Neuraminidase inhibitor