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# Modelling the health-economic impact of the next influenza pandemic in The Netherlands

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## Abstract

To optimally develop or adjust national contingency plans to respond to the next influenza pandemic, we developed a decision type model and estimated the total health burden and direct medical costs during the next possible influenza pandemic in the Netherlands on the basis of health care burden during a regular epidemic. Using an arithmetic decision tree-type model we took into account population characteristics, varying influenza attack rates, health care consumption according to the Dutch health care model and all-cause mortality. Actual direct medical cost estimates were based on the Dutch guidelines for pharmaco-economic evaluation. In the base-case scenario with no preventive measure available and an average influenza attack rate of 30%, 4,958,188 influenza infections, 1,552,687 GP consultations, 83,515 hospitalizations and 173,396 deaths will take place in The Netherlands. The burden is highest in adults aged 20 to 64 years. If minimizing the total mortality and sustaining highest net economic returns is the objective, this group needs to be targeted in interventions.

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**Keywords:** Influenza; Models; Economics; Primary care; Health care sector; Prevention

## 1. Introduction

Recent epidemics of highly pathogenic H5N1 avian influenza with an estimated mortality rate exceeding 50% in Asia [1], a report of probable person-to-person transmission [2] and unusual clinical symptoms making differential diagnosis a complicated task [3] warn the world of the next influenza pandemic to come. Many Western countries have therefore been preparing themselves developing influenza contingency plans. In The Netherlands, for example, a detailed planning of interventions during the different pandemic phases has been developed [4]. Only recently, the Dutch Ministry of Health decided to stockpile 5 million doses of the neuraminidase inhibitor oseltamivir®. A vaccine for H5N1 will not be available in the near future, and even if available there will not be sufficient supply to cover Asian, let alone, other countries. Importantly, the effectiveness of

the neuraminidase inhibitors with regard to H5N1 influenza A is relatively unknown. The use of oseltamivir in five of the ten influenza H5N1 cases reported in Vietnam did not show any obvious effects, and mortality remained 80% [5]. Generic hygienic measures aimed at reduction of transmission such as reducing contact rates and social distance measures might therefore be most important [6].

In any case, health care resource planning will be essential to minimize social disruption in case of an influenza pandemic [7,8]. We therefore developed a decision type model and tried to estimate the total health care consumption in primary and secondary care, and associated mortality as well as the total direct medical costs during the next possible influenza pandemic in The Netherlands. The study was based on estimates of health care consumption during a regular influenza A (H3N2) epidemic [9]. Though much remains uncertain in such predictions, these estimates might provide more insight into the expected health-economic burden to optimally develop or adjust national contingency plans to respond to the next influenza pandemic.

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2. Methods

2.1. Model parameters

The arithmetic decision tree-type model underlying the analyses was developed in an Excel spreadsheet (version

2000, Microsoft) to take into account population characteristics, varying influenza attack rates, health care consumption according to the Dutch health care model and all-cause mortality (see Fig. 1).

In accordance with previous mile-stone studies by Meltzer [7] and Van Genugten et al. [8] we subdivided the patient

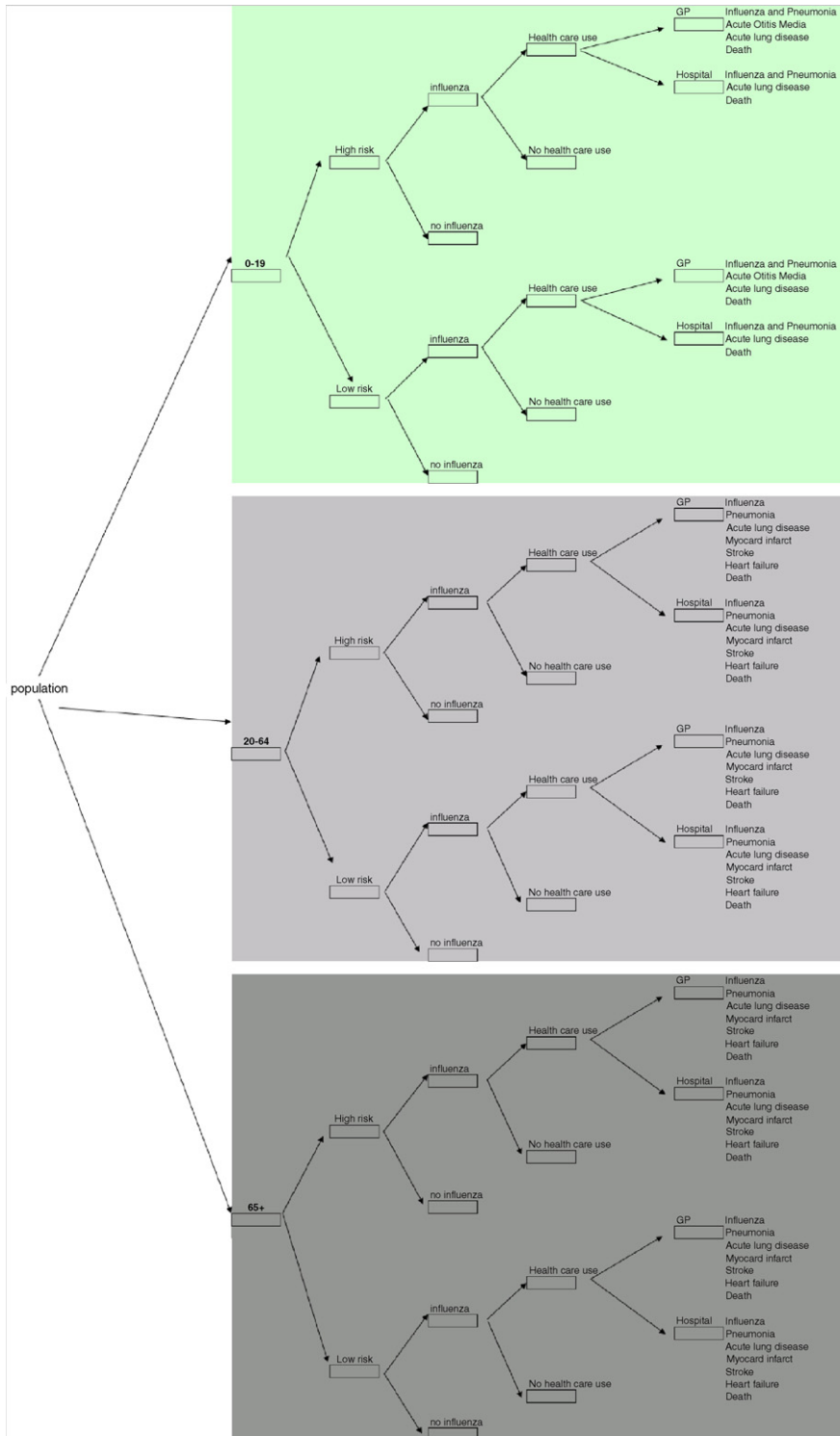


Fig. 1. Model.

Table 1  
Model parameters during influenza A (H3N1) epidemic

Parameter	Unit/ thousand	Category of information <sup>a</sup>
Outpatient visits age group 1-LR	5.8	1
Outpatient visits age group 1-HR	33.9	1
Outpatient visits age group 2-LR	7.5	1
Outpatient visits age group 2-HR	12.8	1
Outpatient visits age group 3-LR	12.1	1
Outpatient visits age group 3-HR	28.3	1
Hospitalizations age group 1-LR	0.113	2
Hospitalizations age group 1-HR	0.340	1
Hospitalizations age group 2-LR	0.333	2
Hospitalizations age group 2-HR	1.00	1
Hospitalizations age group 3-LR	2.3	1
Hospitalizations age group 3-HR	6.5	1
Deaths age group 1-LR	0.038	2
Deaths age group 1-HR	0.113	2
Deaths age group 2-LR	0.800	2
Deaths age group 2-HR	2.400	1
Deaths age group 3-LR	3.900	1
Deaths age group 3-HR	10.800	1

Abbreviations—1-LR: low-risk children (0–19 years); 1-HR: high-risk children; 2-LR: low-risk adults (20–64 years); 2-HR: high-risk adults; 3-LR: low-risk elderly ( $\geq 65$  years); 3-HR: high-risk elderly.

<sup>a</sup> 1: derived from the PRISMA data; 2: estimated indirectly from the PRISMA data assuming similar distributions of deaths and hospitalizations as recorded in the elderly (ratio hospitalization:death = 1:3, ratio low risk/high risk = 1:3).

population into children 0–19 years of age ( $N=3,593,132$  in 2004), adults 20–64 years of age ( $N=10,379,439$ ) and elderly aged 65 years and older ( $N=2,220,002$ ). Further, we subdivided these age groups according to the presence or absence of risk-elevating medical conditions as mentioned in the influenza immunization guidelines by the Dutch Health Council (high-risk medical conditions in children: 7%, adults: 12% and elderly: 40%).

The attack rates during pandemic influenza were estimated to vary from 20% to 50% with a most likely average of 30% [10]. We used the average age-specific attack rates as estimated by Glezen [11] on the basis of the three epidemics in the 20th century (children: 38%, adults: 30% and elderly: 20%, all persons: 30%) and used multiplication factors to estimate the outcomes based on the health outcomes during the 1999–2000 influenza A (H3N2) epidemic with an average influenza attack rate of 9%.

The probabilities of the complications and associated health care use (33% of influenza cases needs health care) in the model were based on data from the Dutch Prevention of Influenza, Surveillance and Management (PRISMA) study (Table 1) [9]. This influenza vaccine effectiveness case-control study was nested in a primary care cohort of approximately 75,000 persons recommended for influenza vaccination, and was conducted during the 1999–2000 influenza A (H3N2) epidemic. The major (possibly) influenza-related complications recorded were: pneumonia, acute otitis media, acute lung disease, myocardial infarction, stroke, heart failure and death from any cause. The distribution of these compli-

cations was estimated for each subgroup. For example, of all low-risk children that consulted the GP, we estimated that most would have acute otitis media (77%) and the remainder influenza or pneumonia (23%). In high-risk children, 29% would consult the GP for exacerbations of the asthma, 55% for acute otitis media and 16% for influenza or pneumonia. In low- and high-risk adults and elderly, the most common reason for encounter was acute respiratory disease (48%, 58%, 44% and 24%, respectively). In low- and high-risk adults and elderly, sudden cardiac death was responsible for 12%, 14%, 18% and 23%, respectively, of all complications recorded in primary care. We observed no deaths in high-risk children in the PRISMA study, but assumed similar ratios for hospitalization and deaths as in adults and elderly (3:1) to occur during a pandemic.

Initially a 1-year time horizon was used to predict short-term impact in terms of costs and burden of disease. We further adapted the model to be able to use the model to explore the (long-term) survival impact of influenza. Each health state or co-morbid condition is associated with a specific expected longevity. Based on national statistics and previously published national predictions of future burden of disease, health care resource use and expenditures, health state specific (long-term) estimates for the above outcomes were obtained. For the calculation of the age- and co-morbidity-adjusted life expectancy we used complication-specific reduction factors. The age-adjusted life expectancy for children was 71 years, 40 years for adults and 12 years for elderly persons on average. A reduced life expectancy is used because of the theoretical impact of co-morbidity of these complications on life expectancy. Reduction factors have been used to indicate the reduction in survival after certain complications. Complications that result in reduced survival were COPD (reduction factor 0.75), heart failure (0.50), myocardial infarction (0.50), stroke (0.75) and diabetes mellitus (0.75) [12].

Actual direct medical cost estimates were based on the Dutch guidelines for pharmaco-economic evaluation [13] and the Dutch medical economics guideline [14]. We estimated the costs from a societal perspective and included average costs for general practitioner visits, hospitalization and death. During an influenza-like illness, persons of all ages consult their general practitioner 1.9 times on average according to questionnaire data with an average of €20.20 per consultation. Since no other data are available that describe the average number of prescriptions per consultation in the three age groups, we conservatively assumed one prescription with a median net payment of €9 as observed in the PRISMA study. Data from the PRISMA study were used to estimate median costs associated with a hospitalization. The average unit costs for hospitalizations were determined by calculating the weighted average unit costs for hospitalisation for the indications stroke, pneumonia, myocardial infarction, acute lung disease, heart failure, stroke multiplied by the weighted average price per bed for general and academic hospitals (€4252). Further, it was recorded that 35% of all hospitalized patients required intensive care for one or more days

(unit cost €2370); 83% of patients were brought to the hospital by ambulance (unit cost €306) and that 12% needed additional diagnostic research (unit cost €33). The average unit costs for hospitalization for the various indications plus the additional components resulted in a total average unit cost per hospitalization of €5362. The costs of death were determined by the use of several health care components by patients. Since there are no published data available on the costs of death, we have tried to give an impression on the components that have to be taken into account, i.e. general practitioner visit, consulting specialist, first aid, diagnostics, stay at an intensive care unit and at a general ward and transport to the hospital with an ambulance (€2391).

### 3. Results

In the base-case scenario of a possible pandemic no preventive measure is available and the average influenza attack rate is assumed to be 30% with estimated group-specific attack rates in low-risk and high-risk children, adults and elderly of 38%, 62%, 29%, 38%, 14% and 32%, respectively.

In all, 4,958,188 influenza infections, 1,552,687 GP consultations, 83,515 hospitalizations and 173,396 deaths will take place in The Netherlands.

Absolute figures for GP consultations (965,798), hospitalizations (47,761) and deaths (132,860) are expected to be highest in adults aged 20–64 years. Among children, many GP consultations are to be expected (458,744) and these persons account for the lowest rates of hospitalizations and deaths (8440 and 2746, respectively). Among the elderly, 128,135 GP consultations, 27,313 hospitalizations and 37,790 deaths would occur. With a time-horizon of 1 year, the average numbers of life-years lost during a pandemic are estimated at  $(173,396 \times 40)/52 = 133,208$ . The remaining life expectancy analysis showed that 2,716,293 future life-years are lost during a pandemic.

Overall, the total direct medical costs in one year are estimated at €843,679,580. The costs are higher for adults (€569,002,321), than for elderly (€214,127,301) and children (€60,549,958). In a total population of 16 million inhabitants, this means that from a direct medical cost perspective any preventive measure that has a real-life effectiveness of preventing 50% of deaths during a pandemic (which equals a reduction of 1,358,147 life-years), would be cost-effective at a maximum incremental cost of €20,000/life-year gained when the costs of the measure per inhabitant would be €1697 or lower.

### 4. Discussion

Our data indicate substantial loss of life, health care consumption and economic losses during the next pandemic in The Netherlands. Absolute hospitalization, mortality and economic cost figures are highest for the group aged between

20 and 64 years and considerable, though lowest, among children.

The observation that mortality figures might be highest in the under 65s during a pandemic is in agreement with recent observations by Simonsen et al. [15]. They found that the proportion of total deaths among the under 65s was more than 40% in the last three pandemics, and even 95% during the Spanish pandemic of 1918–1919. Our observations are also in agreement with those from Meltzer who observed a high proportion of total number of deaths among the under 65s [7]. Van Genugten and colleagues used a scenario model and estimated more than 95% of deaths to occur among the elderly [8]. However, in their model input for mortality figures was estimated on the basis of excess figures for deaths due to influenza and pneumonia. In younger persons, influenza may cause death through secondary complications that are not directly attributed to influenza and pneumonia, such as cardiovascular complications, as observed in the PRISMA study [9].

Setting priority for preventive measures in pandemic planning is guided by the objectives to be reached. Objectives can range from minimizing the total mortality to sustaining highest net economic returns. The data indicate that both objectives can be reached if the group aged between 20 and 64 years is targeted in interventions. Our model does not take into account virulence factors or transmission factors. However, most persons who suffered from avian influenza are currently under 65 years and transmission is highest among the group with highest contact rates, i.e. those under 65 years. Moreover, if large numbers of working-age persons are affected, as for example in many countries in which HIV is epidemic, social disruption is inevitable.

### References

- [1] World Health Organisation, Department of Communicable Disease Surveillance and Response. Avian Influenza: Assessing the Pandemic Threat, 2005 [available from: <http://www.who.int/csr/disease/influenza/>].
- [2] Ungchusak K, Auewarakul P, Dowell SF, Kitphati R, Auwanit W, Puthavathana P, et al. Probable person-to-person transmission of avian influenza A (H5N1). *N Engl J Med* 2005;352:333–40.
- [3] De Jong MD, Bach VC, Phan TO, VO MH, Tran TT, Nguyen BH, et al. Fatal avian influenza A (H5N1) in a child presenting with diarrhea followed by coma. *N Engl J Med* 2005;352:686–91.
- [4] Dutch Health Council. Use of antiviral drugs and other means during an influenza pandemic. The Hague: Gezondheidsraad; 2005 [no. 2005/05].
- [5] Tran TH, Nguyen TL, Nguyen TD, et al. Avian influenza A (H5N1) in 10 patients in Vietnam. *N Engl J Med* 2004;350:1179–88.
- [6] Ferguson NM, Cummings DA, Cauchemez S, Fraser C, Riley C, Meeyai A, et al. Strategies for containing an emerging influenza pandemic in Southeast Asia. *Nature* 2005;437:209–14.
- [7] Meltzer MI, Cox NJ, Fukuda K. The economic impact of pandemic influenza in the United States: priorities for intervention. *Emerg Infect Dis* 1999;5:659–71.
- [8] Van Genugten ML, Heijnen MA, Jager JC. Pandemic influenza and healthcare demand in the Netherlands: scenario analysis. *Emerg Infect Dis* 2003;9:531–8.

- [9] Hak E, Buskens E, Van Essen GA, De Bakker DH, Grobbee DE, Tacken MA, et al. Clinical effectiveness of influenza vaccination in persons younger than 65 years with high-risk medical conditions: the PRISMA study. *Arch Intern Med* 2005;165:274–80.
- [10] Nguyen-Van-Tam JS, Hampson AW. The epidemiology and clinical impact of pandemic influenza. *Vaccine* 2003;21:1762–8.
- [11] Glezen WP. Emerging infections: pandemic influenza. *Epidemiol Rev* 1996;18:64–76.
- [12] Hoogenveen RT, Gijzen R, van Genugten MLL, Kommer GJ, Schouten JSAG, de Hollander AEM. Dutch DisMod: constructing a set of consistent data for chronic disease modelling. Bilthoven: RIVM, editor; 2000.
- [13] College voor Zorgverzekeringen. Dutch guidelines for pharmacoeconomic research. Amstelveen, the Netherlands: College voor Zorgverzekeringen; 1999.
- [14] Oostenbrink J, Koopmanschap MA, Rutten FFH. Handleiding voor kostenonderzoek; methoden en richtlijnrijzen voor economische evaluaties in de gezondheidszorg. Amstelveen: College voor zorgverzekeringen; 2004.
- [15] Simonsen L, Clarke MJ, Schonberger LB, Arden NH, Cox NJ, Fukuda K. Pandemic versus epidemic influenza mortality: a pattern of changing age distribution. *J Infect Dis* 1998;178:53–60.