衞生防護中心
Centre for Health Protection

The Scientific Committee on Advanced Data Analysis and Disease Modelling

A Review of Pandemic Preparedness Plans and Modelling Studies on Pandemic Influenza

衞生防護中心乃衞生署
轄下執行疾病預防
及控制的專業架構

The Centre for Health Protection is a professional arm of the Department of Health for disease prevention and control

Centre for Health Protection
February 2006

Content

LIST OF TABLES **PAGE**

1. Introduction

The Working Group on Investigating Interventions for Influenza Pandemics (WGIIIP) was established under the Scientific Committee on Advanced Data Analysis and Disease Modelling (SCADADM).

WGIIP aims to review, synthesise and recommend effective public health interventions with a view to minimising morbidity, mortality, social and economic disruptions caused by an influenza pandemic; and to assess the feasibility and impact of potential public health interventions in the case of an influenza pandemic, using mathematical modelling and operational research methods.

In this regards, the Surveillance and Epidemiology Branch (SEB) and Emergency Response & Information Branch (ERIB) of the Centre for Health Protection have prepared a review of modelling studies on pandemic influenza and pandemic preparedness plans of different countries respectively.

2. A review of modelling studies on pandemic influenza

2.1 Objectives

This part of the paper aims to systematically review current efforts to address the imminent problem of pandemic influenza by mathematical modelling. This review focused on published modelling works that has so far been done to address different aspects of the problem of pandemic influenza in human. The primary aim is to review on current evidence regarding different intervention strategies that have been assessed by modelling studies, and to identify gap areas that has not yet been or being insufficiently studied for pandemic influenza.

2.2 Methods of the review

2.2.1 Criteria for selecting studies for this review

This review aims to include all published studies focused on the problem of pandemic influenza using mathematical modelling approach.
As we are primarily interested in the problem of pandemic influenza rather than influenza in other problem settings (such as seasonal or sporadic epidemic), we limited our focus only to studies on pandemic influenza.

As we are interested to review on the range of problem areas concerning pandemic influenza that has been addressed by modelling studies, the range of different modelling approaches that had been adopted by different workers, as well as the findings of these studies, we had included all studies addressing the problem using principally a mathematical or statistical modelling approach with no regard of the primary focus of the problem each study was tried to tackle. Also for the same reason, we had set no limit on the type of problem scenario, types of intervention strategies, or types of outcome measures assessed in those studies.

Only original research articles were being included into the review. Review articles, news, editorials, letters, and commentaries were not being included.

The selected papers have been reviewed with special reference to the following aspects:

- Approaches and types of models used
- Reference areas and populations
- Underlying assumptions
- Values of different parameters employed
- Intervention strategies assessed
- Results and conclusions

2.2.2 Search strategy for identification of studies

We searched the following databases using the topic search terms "influenza [mh]" and "pandemic" and either "model*" (for model, modelling) or "simulate*" (for simulate, simulating, simulation) or "mathematic*" (for mathematics, mathematical).

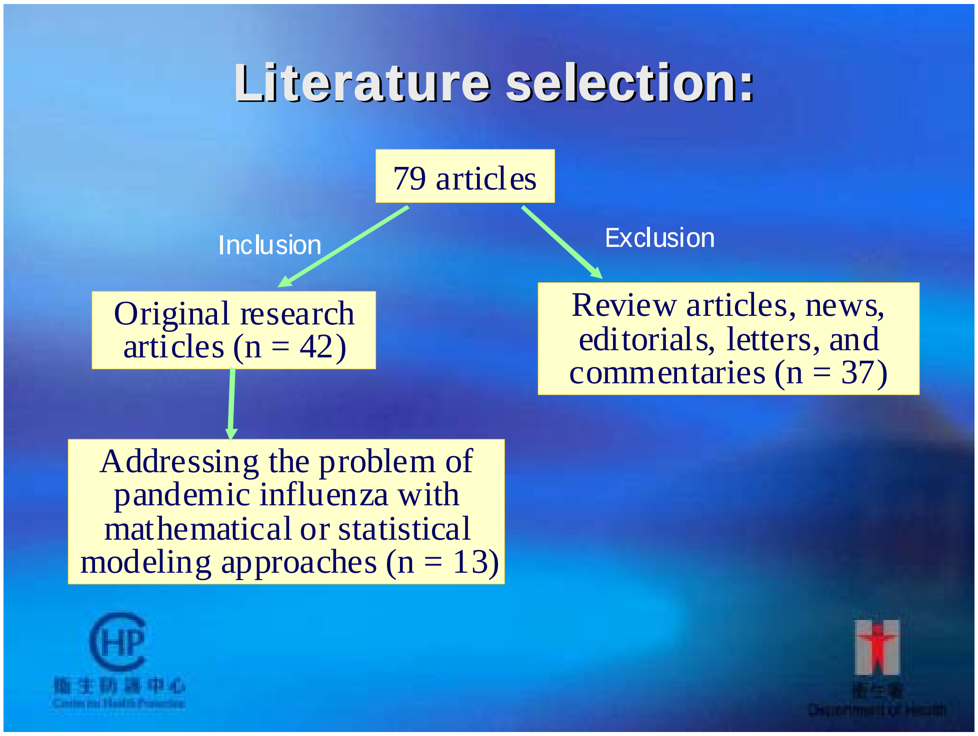
- MEDLINE (1966 to Oct 2005)
- EMBASE (1974 to Oct 2005)
- Cochrane Central Register of Controlled Trials (CENTRAL), published in *The Cochrane Library* (Issue 4, 2005)

We also scanned for studies available in the in the grey literature using the search function in Google.com with combination of search words "influenza pandemic mathematical model" to look for any additional materials that may be relevant for the review.

The reference lists in all identified papers were also scanned in an effort to identify further studies suitable for the review.

A total of seventy-nine articles were identified by the literature search. Forty- two of those were original research articles while the others thirty-seven were review articles, news, editorials, letters, and commentaries. Among the forty-two original research articles, thirteen were tried to address the problem of pandemic influenza with either a mathematical or statistical modelling approach, and were thus included into the review.

Figure 1: Flow diagram of literature selection for the review



2.3 Results

2.3.1 Description of studies

The thirteen papers reviewed fall into five broad categories according to their primary aims and focus. (Table 1) One paper focused on parameter estimation, five on impact estimation, five on assessing effectiveness of intervention strategies, two on assessing economic implication, and one on understanding the global spread of influenza pandemic. Papers sharing a similar focus and fall into the same category were reviewed together for detailed analysis and comparison.

Table 1: Major concentration of different modeling papers included into this review

Parameter estimation	**Impact estimation**	**Intervention strategies**	**Economic implications**	**Global spread**
Mills 2004[i]	**Wilson 2004**[ii] **Wilson 2005**[iii] **Anderson 2003**[iv] **Menon 2005**[v] **Balicer 2005**[vi]	**Ferguson 2005**[vii] **Longini 2005**[viii] **Patel 2005**[ix] **Longini 2004**[x] **van Genugten 2003**[xi]	**Medema 2004**[xii] **Balicer 2005**[6]	**Grais 2003**[xiii]

2.3.2 Group1: Papers focused on parameter estimation

Mills et al 2004 tried to obtain an estimate of the reproductive number for 1918 influenza so as to measure its transmissibility by fitting a deterministic SEIR model to pneumonia and influenza death epidemic curves from 45 US cities.

Using excess pneumonia and influenza mortality data as surrogates for influenza case data, the model result reported a reproductive number with a median less than 3. The estimated proportion of the population with A/H1N1 immunity before September 1918 implies a median basic reproductive number of less than four, suggesting that it is not highly transmissible relative to other influenza subtypes and infectious agents. (Table 2) As a pandemic with an R_0 of 2–4 could in principle be prevented by vaccinating or administering antiviral prophylaxis to 50–75% of the population, this estimate suggested the feasibility of controlling a similar pandemic in the future.

This result was very different from the wide variation of R (from 1.68 to 20) estimated for pandemic influenza from different studies and thus served to provide a more consistent estimate for the likely transmissibility of an influenza that had caused a pandemic.

Table 2: Details of study on parameter estimation

	Aims:	Approaches:	Results:
Mills 2004	• estimating the reproductive number for 1918 pandemic influenza	• by fitting a deterministic SEIR model to pneumonia and influenza death epidemic curves from 45 US cities • mean latent period: 1.9 days • mean infectious period: 4.1 days • CFP: 2% • Mean survival time: 2 weeks	• R: ~ 2-3 (median 2, IC range 1.7, 2.3) • R_0: median less than four

2.3.3 Group 2: Papers focused on impact estimation

Five papers focused on estimating the potential impact of pandemic influenza in the community. All of them based on the model developed by Meltzer et al[xiv], using either the software package FluAid 2.0[xv] or FluSurge 1.0[xvi]. (Table 3)

The Meltzer model was developed initially by the Centers for Disease Control and Prevention for estimating the impact range of pandemic influenza in its first wave in the United States of America using a deterministic model. Generally the model assumes no effective public health interventions to control disease spread (such as quarantine, access to appropriate vaccine, or widespread use of antiviral drugs). Outputs of the FluAid model included estimations for deaths, hospitalizations, outpatient visits, and ill persons not seeking medical care. Specific details about the FluAid software and the various assumptions in the model are detailed on the Centers for Disease Control and Prevention (CDC) Web site[xvii].

Three of the five studies, based respectively on population data from New Zealand, Pacific Island and Israel, focused on estimating the impact on primary care physician consultation, hospitalization and death. Another two studies, based respectively on population data from Australia, New Zealand and England, focused on the impact on critical care resources. (Table 3)

Three studies specified an assumed duration of eight weeks for the first wave of the pandemic. One study used an assumed symptomatic attack rate of 25% as the base case scenario, three studies based on a range of attack rate from 15% to 35% (15%, 25% & 35%), while an assumed attack rate of 10%, 30% & 45% were used in Anderson 2003. (Table 4)

All five studies used local data on population structure, including country-specific population and age distribution data in the model. Resource planning and utilization estimates, however, were less readily available. The default value used in FluAid, based on data from United States, were used for estimating health utilization in all the five studies, these included proportion of the population in the high-risk category for each age group, the death rates, hospitalization rate, and proportion of illness requiring medical consultations. This may not reflect the real situation in the local community under study and lead to bias in their estimation.

As most of the results of these five studies were expressed in terms of absolute numbers of patients involved, they have to be interpreted with respect to local population data in each country. Generally all studies indicated that a large number of people would be affected and hospitalized, and the majority of admission and death would occur in the high-risk groups. All studies indicated that all levels of the medical system would be overwhelmed even in the best case scenario of a mild influenza pandemic. During the peak of the pandemic, up to 40% of all hospital beds would be taken up by patients admitted as a result of influenza and demand of critical care beds and ventilator support would exceed 200% of available capacity. (Table 5)

Basiler 2005 had also included a cost-benefit analysis of using antiviral drug according to five different strategies. The result of this part will be discussed in Section 3.5.

Table 3: Models on impact estimation – Model details

Articles	Modelling methodology employed:	Primary focus:	Geographical area concerned:
Wilson 2004	FluAid (a deterministic model developed by CDC to estimate the impact range of an influenza pandemic in its first wave)	• Primary care physician consultation • Hospitalization • Death	New Zealand
Wilson 2005	FluAid	• Primary care physician consultation • Hospitalization • Death	Pacific Islands
Anderson 2003	Meltzer, Cox and Fukuda model	• Critical Care Resources	Australia and New Zealand
Menon 2005	FLUSURGE 1.0	• Critical Care Resources • hospital admission • occupancy of all ICU beds • occupancy of Level 3 beds (i.e. those with facilities for mechanical ventilation).	England
Balicer 2005	Meltzer's model	• Primary care physician consultation • Hospitalization • Death • Cost-benefit for antiviral drug use	Israel

Table 4: Models on impact estimation – Data source of utilization estimates

			Resource planning and utilization estimates					
Articles	Duration	Influenza attack rate	proportion of the population in the high-risk category for each age group	Death rates	Hospitalizations rate	Proportion of illness requiring medical consultations	Proportion requiring ICU admission	Proportion requiring mechanical ventilation
Wilson 2004	8 weeks	15%-35%	default values (US data)					
Wilson 2005	8 weeks	15%-35%	default values (US data)					
Anderson 2003		10%, 30% & 45%	Extrapolated from overseas data, expert opinion (Meltzer, Cox and Fukuda) and population data		default values (US data)		5%, 15%, and 25% of hosp. admissions (based on CAP data)	25%, 50%, and 75% of ICU admission
Menon 2005	8 weeks	15%-35%	default values (US data)					
Balicer 2005	50 days	25%						

Table 5: Models on impact estimation – Summary of result details

Articles	Incidence rate	Duration	Total Death	Hospitalization	Consultations	ICU Bed requirement	Burden during peak week:
Wilson 2004	15%-35%	8 weeks	1600-3700	6900-16200	325000-759000		42% of all public hospital beds would be required
Wilson 2005	15%-35%	8 weeks	650-1530	3540-8250	241000-563000		15-34% of all hospital beds required for influenza
Menon 2005	15%-35%	8 weeks	36 745			208% of the current combined Level 2 and 3 bed capacity 231% of the current capacity for Level 3 beds	35,738 hospital admission/ week 5569 hospital admission/ day 34% of all hospital beds required for influenza
Balicer 2005	25%	50 days	2,855	10,334	781,921		

2.3.4 Group 3: Papers focused on intervention strategies

Five papers tried to assess the relative effectiveness of a range of different intervention approaches and strategies in different assumed scenario of the pandemic. Four studies employed a spatially explicit stochastic simulation model, one of these also modelled with genetic algorithms and random mutation hill climbing method. The other one study used a static spreadsheet calculation model. (Table 6)

Two studies (Ferguson 2005 & Longini 2005) based on the scenario of a pandemic starting off in a rural area in South East Asia and modelled the possibility of containment at source. Two studies (Patel 2005 & Longini 2004) based on a hypothetical population of 10,000 people constructed based on US Census data 2000, and modelled different strategies of interventions. One paper (van Genugten 2003) based on Netherlands population data and modelled the size of the problem in different intervention scenario. (Table 6 & 7)

A number of intervention strategies had been investigated in these studies, including social distancing measures, quarantine, different approaches of using antiviral drugs, and vaccination. (Table 8)

Measures to increase social distance included school and workplace closure so as to reduce the chance of contact and thus the chance of transmission. Area quarantine involved restriction of all movements in and out of the affected area as a whole, while Household quarantine involved movement restriction for every identified case and contacts to within their household and their neighbourhood. (Table 9)

Antiviral drug may be used in a therapeutic or prophylactic manner. Therapeutic antiviral use refers to the treatment of cases, either non-selectively for all patients or only selectively for patients at high risk. Pre-exposure antiviral prophylaxis can also be used with different coverage. Blanket prophylaxis covers an entire country or region. Targeted antiviral prophylaxis (TAP) offers prophylaxis only to the contacts of index cases in predefined close contact groups. These can either be done for socially targeted groups including households, neighborhood clusters, preschool groups, schools, and workplaces, or for all individuals in a geographically targeted (GTAP) area around the index case. (Table 9)

The primary difficulty of social targeting (TAP) would be the identification of index cases. Since TAP is aimed at pre-defined close contact groups, identification of potential TAP recipients would be less difficult than in classical contact tracing.
Geographical targeting, also known as ring prophylaxis, may represent an even less resource intensive alternative strategy as a certain percentage of people in an entire locality would be given one course of oseltamivir once an influenza case is identified in the locality. (Table 9)

Options using influenza vaccination included vaccinating defined high risk groups such as persons >65 years of age and healthcare workers, or vaccinating the entire population. Besides using influenza vaccine, one paper also studied the use of Pneumococcal Vaccine to high risk groups for getting influenza. (Table 9)

Ferguson 2005 & Longini 2005 assessed the possibility of containment of the pandemic at source when it first emerges in a rural area in South East Asia. Ferguson 2005 modelled a population of 85 million in a rural area in Thailand and a 100-km wide zone of contiguous neighbouring countries, with explicit inclusion of households, schools and workplaces and modelling of individual movements, with the pandemic seeded by a single infection in the most rural third of the population. Longini 2005 modelled a population of 500,000 in 36 adjacent geographic localities distributed across a space of 5,625 km^2 in rural South East Asia. Social structures, mixing patterns and probability of a person escaping from the area were modelled. (Table 10 & 11)

It is estimated most epidemics will go extinct of R_0 <1.5, and will affect up to 33% or 50% of the population when R_0 =1.5 or 1.8 respectively. Spatially it would be limited mainly to the region around the seeding location in the first 30 days but it may rapidly become country-wide between days 60 and 90. (Table 12)

Both studies assessed the use of antiviral for prophylaxis as a mean for containing the pandemic. Although blanket prophylaxis would be able to eliminate a pandemic virus with an R_0 as high as 3.6, the huge amount of medication for the whole population for up to three weeks makes the approach practically unfeasible and some form of targeted prophylaxis would therefore be needed to minimize drug usage while maximizing the overall effect.

Both paper suggested that the probability of successfully contain the pandemic at its source depends critically on the R_0 of the actual pandemic virus. When R_0 = 1.1, all of the interventions may work well. Generally a containment threshold seems to exist at R_0 = 1.6 – 1.7; below which a high probability of containment could be achieved by 80% social targeting or 90% geographical targeting. For a much higher R_0, however, neither would be consistently effective in containing the epidemic. It is suggested that for containing a pandemic with R_0 < 1.6, an antiviral agent stockpile on the order of 100,000 to one million courses would be sufficient. (Table 13)

When combined with targeted antiviral prophylaxis, other intervention strategies (pre-vaccination, quarantine and social distancing measures) all work towards increasing the threshold of R_0 value that may be successfully contained. For instance, Ferguson 2005 revealed that adding area-based school and workplace closure to a drug-sparing prophylaxis policy increases policy effectiveness significantly to >90% chance of elimination for R_0 = 1.7, while area adding quarantine to GTAP may increase effectiveness to 90% containment at R_0 = 1.8, and adding both may further increases effectiveness to 90% containment at R_0 = 1.9. On the other hand, Longini 2005 suggested that the combinations of targeted antiviral prophylaxis, pre-vaccination and quarantine may even be able to achieve containment for contain strains with an R_0 as high as 2.4.

Generally the probability of effective containment did not vary much if intervention measures can be initiated within 21 days from the appearance of the first symptomatic case. Sensitivity analyses of policy delay revealed that the effectiveness of antiviral prophylaxis alone becomes much lower when the intervention starts 28 days or more after the detection of the first case, and quarantine becomes less effective 42 days after detection of the first case, even with the addition of targeted antiviral prophylaxis.

On the other hand, initiation of TAP in the close contact mixing groups need to be implemented within a very short period of time in order to for the intervention to be effective for achieving a high probability of containment. A sensitivity analysis for delays in initiation of 80% TAP in the close contact revealed that a delay of up to 2 days may still achieve a substantial reduction in the number of cases, while the benefit quickly becomes much reduced for delays of 3-5. (Table 15)

Generally both studies regarded that containment and elimination of an emergent pandemic strain of influenza at the point of origin is feasible using a combination of antiviral prophylaxis and social distancing measures. This conclusion, however, is based on a number of highly optimistic assumptions which may not always be feasible in practice. These included the assumption that there are rapid and sensitive identification of the original case cluster and subsequent contacts and cases, efficient delivery of treatment to targeted groups within 2 – 3 weeks of a case arising, effective delivery of prophylactic antivirals to a high proportion of the population based on sufficient stockpiles of drug in the order of 3 million or more courses of oseltamivir, and highly ordered population and international cooperation with the involved containment strategies in such a period of disaster. It also has to be reminded that it may means a very different story when we translate the finding from an isolated rural setting to the situation of a well mixed urban population like Hong Kong.

Using a similar approach, Longini 2004 studied the idea of containment by targeted antiviral prophylaxis and vaccination using a discrete-time, stochastic simulation model with a hypothetical population of 2000 person with age distribution and household size according to US Census Bureau data. Families, social mixing groups and contact patterns were individually modeled, with the pandemic seeded with 12 initial infective persons with an agent similar to Asian pandemic influenza A virus (H2N2) of 1957-1958. (Table 10 & 11)

Results of this study were similar to the last two studies based on actual population structure in South East Asia. Targeted antiviral prophylaxis in just schools and preschools or just in families would not be very effective, while those covering 80% of the exposed persons and maintained for up to 8 weeks would be able to reduce the overall attack rate from an average of 33% to 2% and thus contain the pandemic, representing a potentially effective measure for containing influenza until adequate quantities of vaccine are available. (Table 13)

Longini 2004 also looked at the effect of delay in initiating antiviral prophylaxis using a sensitivity analysis and gave a similar finding to the former two studies. The result suggested that the intervention remains effective in achieving substantial reduction in morbidity & mortality with a delay of up to four days, after which the effect would decline rapidly. A much shorter interval, however, seems to exist for the effective containment of the pandemic. The probability of successfully preventing the pandemic remained above 50% only for a delay of up to 2 days, after which the intervention may fail to have the pandemic contained. (Table 15)

Patel 2005 used a similar hypothetical, structured population consisting of five 2,000 person communities with detailed family and social structures for finding the optimal vaccine distributions strategies during a pandemic, with the pandemic seeded with 12 initial infective persons with an agent similar to either the Asian pandemic strain (H2N2) in 1957–1958 or the Hong Kong pandemic strain (H3N2) in 1968–1969. Three types of modelling approaches including stochastic epidemic simulations, genetic algorithms, and random mutation hill climbing were used. (Table 10 & 11)

What constitutes an optimal vaccine distribution strategy depends on the nature of the spread of the influenza agent, the objective for control, and also the amount of vaccine available. In face of limited quantities of available vaccine, the study suggested that optimal vaccine distributions strategies for different age groups were more effective in minimizing the impact of the pandemic when compared to random mass vaccination.

For a pandemic influenza virus similar to the Asian (H2N2) strain, vaccinating first preschool children followed by adults and finally elderly groups helps to minimize the illness attack rate, while starting first with elderly followed by preschool children and finally young and middle-aged adults would work best in minimizing the overall number of deaths. In fact we may be able to effectively to stop the epidemic even if we only have sufficient stock to cover 20% of the population by directing all the available stocks for vaccinating 98% of school children.

For a pandemic virus similar to the Hong Kong (H3N2) strain, however, the model suggested to start with school-age children and young adults when stock is insufficient, then proceed to cover pre-school children, middle-age adults, and finally older adults when more stock is available. We would only be able to stop the epidemic when sufficient vaccines were available to cover ~40% of the population. (Table 14)

Whereas a number of logistic problems may need to be considered before the benefit of antiviral prophylaxis or vaccination can be actualized, all suggested effects of different approaches of vaccination should still be regarded purely theoretical in view of the absence of any candidate vaccine potentially useful for the job.

The last study in this group (van Genugten 2003) compared sizes of the potential problem in Netherlands under different intervention scenario using expert consultation and a static spreadsheet calculation model. Scenario addressed included no intervention, using influenza vaccination, Pneumococcal vaccination, and therapeutic use of neuraminidase inhibitors. Based on a non-intervention scenario of having > 10,000 influenza-related hospitalizations and >4,000 deaths, the model predicted a 60%, 25% and 59% reduction in hospitalization respectively for using influenza vaccine, pneumoccoccal vaccine and therapeutic use of antiviral; and a similar reduction in mortality. (Table 7, 8 & 13)

Details regarding some of the parameters quoted in these modes were tabulated in Table 16 and 17.

Table 6: Models assessing intervention strategies – Model details

Articles	Modelling methodology	Setting	Geographical area
Ferguson 2005	• a spatially explicit stochastic simulation	Pandemic	SE Asia (Thailand)
Longini 2005	• a discrete-time, stochastic simulation model	Pandemic	Rural SE Asia
Patel 2005	• stochastic epidemic simulations • genetic algorithms(GA) • random mutation hill climbing (RMHC)	Pandemic	A hypothetical population based on US Census data 2000
Longini 2004	• stochastic epidemic simulations	Pandemic	A hypothetical population based on US Census data 2000
van Genugten 2003	• A scenario analysis including expert consultation and a static spreadsheet calculation model	Pandemic	Netherlands

Table 7: Models assessing intervention strategies – Modelling approaches & strategies

Articles	Intervention approaches	Intervention strategies
Ferguson 2005	Containment in its earliest stage at source	• targeted mass prophylactic use of antiviral drugs
Longini 2005	Containment in its earliest stage at source	• home quarantine • targeted antiviral prophylaxis • vaccination
Patel 2005	Optimal vaccine distributions strategies of limited quantities of available vaccine among different age groups so as to minimize the impact of the epidemic	• vaccination
Longini 2004	Targeted antiviral prophylaxis to contain influenza	• targeted antiviral prophylaxis • vaccination
van Genugten 2003	Comparing size of problem in different intervention scenario	• nonintervention scenario • Influenza vaccination • Pneumococcal vaccination • Therapeutic use of neuraminidase inhibitors

Table 8: Models assessing intervention strategies – Different intervention strategies examined by each study

Articles	social distancing measures	quarantine	antiviral drugs			vaccines	
			Blanket prophylaxis	Targeted prophylaxis	Treatment	Influenza	Pneumococcal
Ferguson 2005	+		+	+		-	
Longini 2005		+ HQ		+ TAP/ GTAP*		+	
Patel 2005						+	
Longini 2004				+		+	
van Genugten 2003					+	+	+

Table 9: Detailed explanation of different control strategies

Measures to increase social distance	• school and workplace closure • potentially infectious contacts may be displaced into other settings • population contact rates may change spontaneously or as a result of policy during severe epidemics
Quarantine zones (Area quarantine)	• movements in and out of the affected area are restricted
Household quarantine (HQ)	• The first case in a locality triggers a quarantine policy • Policy applied to every case and a certain percent of susceptible people • Movement restriction to within their household and their neighborhood cluster • contact probabilities within household and household clusters are doubled for quarantined people
Blanket prophylaxis	• of an entire country or region
Targeted antiviral prophylaxis (TAP)	• carried out by treating identified index cases, i.e., the first symptomatic illness in a mixing group • and offering prophylaxis only to the contacts of these index cases in predefined close contact groups (households, neighborhood clusters, preschool groups, schools, and workplaces0 • Index cases are therapeutically treated the day after onset of illness • prophylaxis of contacts begins at the same time • both with a single course of oseltamivir • A susceptible individual may receive subsequent courses if exposed to further index cases
Socially targeted antiviral prophylaxis	• prophylaxing individuals in the same household, school or workplace as a newly diagnosed symptomatic case • assumes prophylaxis of 90% of household members and 90% of pupils or colleagues in 90% of the schools or workplaces with detected cases

Geographically targeted antiviral prophylaxis (ring prophylaxis) (GTAP)	• prophylaxing the whole population in the neighbourhood of the household in which a case is detected • assumes 90% of people within 5, 10 or 15 km of a detected case are prophylaxed
Therapeutic Use of Neuraminidase Inhibitors	• taken within 48 hours after onset of symptoms • continued for 5 days
Influenza vaccination	1. vaccination of risk groups including persons >65 years of age and healthcare workers 2. vaccination of the total population
Pneumococcal Vaccination	• influenza risk groups (including those >65 years of age)

Table 10: Models assessing intervention strategies – Details of model setting and assumptions

Articles	Detailed setting and assumptions:
Ferguson 2005	• 85 million people residing in Thailand + in a 100-km wide zone of contiguous neighbouring countries • incorporates households, schools and workplaces • day-to-day movement and travel were also modeled • start with a single infection in the most rural third of the population
Longini 2005	• a population of 500,000 people • partitioned into 36 geographic localities • distributed across a space of 5,625 km2 yielding a density of 89/km2 (approximately the population density of rural SE Asia) • age and household size distributions of the population based on the Thai 2000 census • Many of the mixing group sizes and distributions are based on a social network study of the Nang Rong District in rural Thailand • Estimated daily probability that a person will leave (i.e., escape) the area is on the order of 10^{-3}
Patel 2005	• a hypothetical, structured population of 10 000 individuals • consists of five 2000 person communities each containing four neighborhoods, one high school, one middle school, and two elementary schools • age and family structure approximate information from the US Census 2000 • 2 sets of age-specific illness attack rates: 1. similar to the Asian pandemic in 1957–1958 caused by influenza A(H2N2) 2. similar to the Hong Kong pandemic in 1968–1969 caused by influenza A(H3N2) • vaccination of the population occurs before the influenza pandemic begins • number of vaccination doses is limited over the range of 10–90% of the population

	• Influenza is introduced into the population by randomly assigning 12 initial infectives in each of the five communities
Longini 2004	• Stochastically generated populations of 2000 persons • Age distribution and household size according to US Census Bureau data • Family size of 1-7 persons • Mixing groups considered including households, day-care centers, playgroups, and schools • close contacts of suspected index influenza cases take antiviral agents prophylactically • agent similar to Asian pandemic influenza A virus (H2N2) of 1957-1958 • influenza introduced by randomly assigning 12 initial infective persons • assume start of targeted antiviral prophylaxis in the close mixing group within 1 day after the first symptomatic illness • assume antiviral agents will reduce the length of illness for 1 day • assume non-compliant rate after 1 day = 5% • assume stopping of antiviral upon recovery • assume stopping of antiviral at the termination of the epidemic • assume vaccination taking place early enough before the influenza season • assume one dose of vaccine is given

Table 11: Models assessing intervention strategies – Details of model components

Articles	Population size & structure	Area	Community structures incorporated	Day-to-day movement	Infection seed
Ferguson 2005	• 85 million	• Thailand • + 100-km wide zone of contiguous neighbouring countries	• Households • Schools • workplaces	• Modeled	• a single infection in the most rural third of the population •
Longini 2005	• 500,000	• SE Asia • 36 geographic localities • distributed across a space of 5,625 km2 • yielding a density of 89/km2	• Mixing group sizes and distributions based on a social network study of the Nang Rong District in rural Thailand	• Estimated daily probability that a person will leave (i.e., escape) the area is on the order of 10^{-3}	
Patel 2005	• A hypothetical, structured population of 10 000 individuals	• Hypothetical	• Five 2000 person communities each containing four neighborhoods, one high school, one middle school, and two elementary		• randomly assigning 12 initial infectives in each of the five communities

衛生防護中心 Centre for Health Protection

衛生署 Department of Health

			schools		
Longini 2004	• Stochastically generated populations of 2000 persons • Age distribution and household size according to US Census Bureau data	• Hypothetical	• Households • day-care centers • playgroups • schools	•	• by randomly assigning 12 initial infective persons
van Genugten 2003		• Netherlands			

Table 12: Models assessing intervention strategies – Results of spatial spread

Articles	Size & time frame:				Spatial spread:	
Ferguson 2005	For R_0:	Peak at:	Over by:	% population infected:	first 30 days	limited to the region around the seeding location
	<1.5			most epidemics go extinct	between days 60 and 90	rapidly became country-wide
	=1.5	day 150	day 200	33%		
	=1.8	day 100		50%		

Table 13: Models assessing intervention strategies – Results of different antiviral strategies

Articles	Main results:	
Ferguson 2005	Blanket prophylaxis	• able to eliminate a pandemic virus with an $R_0 \geq 3.6$ • require enough drug to prophylax everyone for up to three weeks (at least two courses per person) • practically unfeasible
	Targeted prophylaxis	• needed to minimize drug usage while maximizing effect
	Social targeting	• only has a ≥90% probability of eliminating the pandemic strain when R0 ≤ 1.25 if only initiated after 20 or more cases • (detection and decision-making delays could easily mean 20–30 cases had arisen before policy initiation)
	Geographic targeting	• A 5-km ring policy, with a two-day delay from case onset to prophylaxis, is able to contain pandemics with an R0 of 1.5 • at the cost of an average of 2 million courses
	Social distancing (SD) measures	• combined area-based school and workplace closure and a drug-sparing prophylaxis policy increases policy effectiveness significantly (>90% chance of elimination for R0 = 1.7)
	Area quarantine (AQ) strategy	• AQ + GTAP: increase policy effectiveness (to 90% containment at R0 = 1.8) • SD + AQ + GTAP: further increases policy effectiveness (90% containment at R0 = 1.9)
Longini 2005a	• If $R_0 < 1.60$: a prepared response with targeted antivirals would have a high probability of containment • In this case, an antiviral agent stockpile on the order of 100,000 to one million courses would be sufficient • If prevaccination occurs, then targeted antiviral prophylaxis could be effective for containing strains with an R_0 as high as 2.1 • Combinations of targeted antiviral prophylaxis, pre-vaccination and quarantine could contain strains with an R_0 as	

	high as 2.4 • When $R0 = 1.1$: all of the interventions work well • if $R0 \leq 1.4$: Both 80% TAP and 90% GTAP would be effective in containing pandemic influenza at the source (300,000 - 350,000 courses of oseltamivir would be needed) • If $R0 \geq 1.7$, then neither 80% TAP nor 90% GTAP is consistently effective in containing the epidemic • a containment threshold exists somewhere between $R0 = 1.4$ and 1.7 (roughly at $R0 = 1.6$) • if implemented within 21 days of the first case and if $R0 \leq 1.4$, would have a high probability of success for containing an emergent influenza strain at the source in a rural SE Asian population. • Such interventions would be effective for $R0$ as high as 1.7 in the presence of pre-vaccination with a low efficacy vaccine. • For higher values of $R0$, localized household quarantine would have to be implemented, possibly in combination with targeted antiviral prophylaxis to contain the pandemic at the source. • the current WHO stockpile of 120,000 courses could possibly be sufficient to contain a pandemic if the stockpile were deployed at the source of the emerging strain within two to three weeks of detection. • up to one million courses could be needed to deal with the multiple outbreak foci •
Longini 2004	• Targeted antiviral prophylaxis (TAP) has potential as an effective measure for containing influenza until adequate quantities of vaccine are available. • TAP for up to 8 weeks is nearly as effective as vaccinating 80% of the population. • TAP < 80% would not be very effective in containing the epidemic (but still result in modest reductions in influenza cases and deaths) • TAP in just schools and preschools or just in families would not be very effective • Vaccinating 80% of the children aged less than 19 years is almost as effective as vaccinating 80% of the population

		Epidemic	illness attack rate	influenza death rate
	In the absence of intervention	Not contained	33% (95% CI: 30, 37)	0.58 deaths/1,000 persons (95% Cl: 0.4, 0.8)
	targeted antiviral prophylaxis (80% of the exposed persons maintained prophylaxis for up to 8 weeks)	Contained	2% (95% Cl: 0.2, 16)	0.04 deaths/1,000 persons (95% CI: 0.0003, 0.25)

		influenza-related hospitalizations	Deaths	Doses needed
van Genugten 2003	nonintervention scenario	> 10,000	>4,000	
	influenza vaccination scenario	Reduction of >6,000 (>60%).	Reduction of >2,200 (>55%)	for the total population: 15.6 million doses for at risk groups: 3.6 million doses
	pneumoccoccal vaccination scenario	prevent 2,600 (25%)	prevent 2,600 (25%) 140 (3.5%) of the deaths	requires 2.8 million doses
	Therapeutic use of neuraminidase inhibitors scenario	Prevent 5,000 (59%)	Prevent 2,000 deaths	require 4.7 million prescriptions

Table 14: Models assessing intervention strategies – Results of different vaccination strategies

<table>
<tr><td>Articles</td><td></td></tr>
<tr><td>Longini 2005</td><td>

Pre-vaccination of the population with a low efficacy vaccine:
greatly enhances the effectiveness of TAP and GTAP, even with just 50% coverage
With pre-vaccination, both 80% TAP and 90% GTAP are effective at containing the epidemic when $R0 = 1.7$, but not at higher levels of $R0$. (Pre-vaccination essentially lowers the reproductive number)
Local household quarantine is effective at containing the epidemic if $R0 \leq 2.1$, but is not as effective at $R0 = 2.4$.
However, a combination of 80% TAP plus quarantine is effective at an $R0$ as high as 2.4, while adding pre-vaccination makes TAP plus quarantine even more effective.
pre-vaccination of populations at risk for a newly emergent influenza strain would be prudent, even if the vaccine provided only moderate protection.

</td></tr>
<tr><td>Patel 2005</td><td>

optimal vaccine distributions are highly effective, especially when compared to random mass vaccination (given 30% coverage, optimal vaccine distributions is 84% more effective than random vaccination)
optimal vaccine distribution strategy is sensitive to the nature of the spread of the influenza agent, the objective for control, and also the amount of vaccine available

for Asian-like pandemic influenza:
<table>
<tr><td>Vaccination coverage:</td><td>for minimizing the illness attack rate:</td><td>for minimizing the overall number of deaths:</td></tr>
<tr><td>10%</td><td>only school children should be vaccinated</td><td>vaccinating only older adults</td></tr>
<tr><td>20%</td><td>able to vaccinate 98% of school children
effectively able to stop the epidemic</td><td>vaccinating mainly school-aged children
effectively able to stop the epidemic</td></tr>
<tr><td>>20%</td><td>begin with vaccinating preschool children, followed by young and middle aged adults, and finally older adults</td><td>begin to vaccinate the older adults, followed by preschool children and finally young adults and middle-aged</td></tr>
</table>
</td></tr>
</table>

		adults

for a Hong Kong-like pandemic influenza:

Vaccination coverage:	for minimizing the illness attack rate:	for minimizing the overall number of deaths:
10%	• vaccinate school-age children and young adults	• vaccinating only older adults
Increasingly > 10%	• start with school-age children and young adults, then pre-school children and middle-age adults, and finally older adults	• then give vaccine to school-children, young adults, and middle-age adults relatively evenly
~40%	• effectively able to stop the epidemic	•

* in the Hong Kong-like influenza setting, we are unable to stop the epidemic early with high vaccine coverage in one of the age groups because the virus spreads more homogeneously than it does in the Asian-like influenza setting

Table 15: Models assessing intervention strategies – Effects of delay in initiating intervention

<table>
<tr><th>Articles</th><th>Delay</th><th>Effect of delay</th></tr>
<tr><td>Ferguson 2005</td><td></td><td>• GTAP: A 5-km ring policy, with a two-day delay from case onset to prophylaxis, is able to contain pandemics with an R0 of 1.5</td></tr>
<tr><td>Longini 2005</td><td></td><td>Effects of delays in initiation of TAP in the close contact mixing groups:
• delay of up to 2 days: substantial reduction in the number of cases is still achieved
• delays of 3-5 days: much less benefit</td></tr>
<tr><td>Longini 2004</td><td>Delay of 2-5 days for 80% TAP for 8 weeks</td><td>
<table>
<tr><th></th><th>Overall effectiveness</th><th>Epidemic prevention potential</th></tr>
<tr><td>1 day</td><td rowspan="4">Still substantial benefit in reducing morbidity & mortality</td><td rowspan="2">> 50% probability of preventing the epidemic</td></tr>
<tr><td>2 days</td></tr>
<tr><td>3 days</td><td rowspan="3">Fails to prevent the epidemic</td></tr>
<tr><td>4 days</td></tr>
<tr><td>5 days</td><td>< 50 % reduction in morbidity & mortality</td></tr>
</table>
</td></tr>
</table>

Table 16: Models assessing intervention strategies – Summary of parameters 1

Articles	R_0 (days)	Tg (days)	Mean latent period	Mean infectious period	Overall Infection attack rate	age-specific illness attack rates	% symptomatic	% ascertained	% contact covered with TAP
Ferguson 2005	1.8 (1-2)	2.6			50-60%		50%		
Longini 2005a					33% (R_0 = 1.4)			Varying in SA	• For household (preschool) index cases: all other household (preschool) members • For index cases in a school or workplace: only a certain % in that mixing group would receive prophylaxis.
Patel 2005			1.9	4.1					
Longini 2004	1.7		1.9	4.1	33%	0-4: 36 5-18: 62 19-64: 25 >64: 21	67%	80%	80%

Table 17: Models assessing intervention strategies – Summary of parameters 2

Articles	AVE_s	AVE_D	AVE_{SD}	AVE_I	VE_S	VE_I	Remarks:
Ferguson 2005							AVE: Antiviral efficacy AVE_s: Antiviral efficacy for susceptibility to infection AVE_D: Antiviral efficacy for symptomatic disease given infection AVE_{SD}: Antiviral efficacy for symptomatic disease given exposure to infection, $AVE_{SD} = 1-(1-AVE_s)(1-AVE_D)$ AVE_I: Antiviral efficacy for infectiousness VE_s: Vaccine efficacy for susceptibility VE_I: Vaccine efficacy for infectiousness
Longini 2005a					0.3	0.5	
Patel 2005					0.7	0.8	
Longini 2004	0.3	0.6	0.72	0.8	0.7	0.8	

2.3.5 Group 4: Papers focused on economic implications

Two papers focused at the economic aspect of intervention for the problem of pandemic influenza. One paper looked at the compared the cost-benefit of different strategies of stockpiling antiviral drugs while the other looked at the cost-benefit of different vaccine manufacturing scheme for influenza pandemic. (Table 18)

Balicer 2005 used the Metlzer model developed by CDC to estimate the health burden of pandemic influenza in Israel and examined the cost-benefit ratio of using antiviral drugs. Five different strategies of using antiviral drugs, including therapeutic use, long-term preexposure prophylaxis and short-term, epidemiologically directed postexposure prophylaxis were compared. As long as the estimated annual pandemic risk remains >1 pandemic every 80 years, prepandemic stockpiling of oseltamivir is found to be cost-saving to the economy when it is used either solely as a therapeutic measure or as short-term prophylaxis for exposed contacts (ring prophylaxis or targeted prophylaxis). Besides the benefit of life saving, investments of every $1 in antiviral agents can be expected to yield a substantial economic return of as much as $3.68. When indirect costs of preventable deaths were also considered, the cost-benefit ratios would be increased to as much as 6. (Table 19)

Medema 2004 used a simulation model combining a vaccine production model with a cost-effectiveness model of influenza intervention strategies. It compared the costs and benefits of different intervention scenarios based on either egg-based or cell culture-based vaccine manufacturing scheme during an influenza pandemic. Compared to the assumed egg-based vaccine intervention, the cell culture-based intervention strategy was able to achieve a wider vaccine coverage, fewer influenza cases, fewer PCP consultations for influenza treatment, fewer influenza-related hospitalizations, fewer excess deaths, and fewer discounted years per life lost. Although incurring a higher intervention strategy costs, there will be a lower medical care costs and total direct costs. (Table 19)

Table 18: Models assessing economic implications – Modelling approaches and settings

	Model approach	Model setting
Medema 2004	• A simulation model combining a vaccine production model with an cost-effectiveness model of influenza intervention strategies • To compare the costs and benefits of different intervention scenarios based on different vaccine manufacturing scheme (Egg-based and Cell culture-based vaccine manufacturing)	• assumed an 2004 pandemic strain emerges 1 January 2004 • an average 1918–1919 attack rate of 35% in a single wave • with a case fatality rate of 1.87% • Health economic parameters based on average data from elderly in the United Kingdom in recent annual influenza epidemics • increased absenteeism of health care workers, societal disruption by the pandemic, and health economical consequences of influenza are not taken into account • total population estimated at 1 billion • assumed a seed preparation time for vaccination production of 3 months • assumed eggs are readily available for vaccine manufacture • assumed a 7.5g monovalent vaccine given in two doses and should be administered within 6 months after emergence of the "2004 pandemic" virus
Balicer 2005	• Estimation of health-related impact of pandemic influenza by using Meltzer's model (FluAid) • Cost-benefit analysis of using antiviral drug according to five different strategies.	• Assuming pandemic influenza on the Israeli population • Impact estimated using the Meltzer model • Direct costs to the healthcare system and overall costs to the economy (value of lost workdays) calculated but not the potential value of lost lives

Table 19: Models assessing economic implications – Essential findings

	Intervention strategies	Essential findings:
Medema 2004	1. No intervention 2. Egg-based vaccine manufacture 3. Cell culture-based vaccine manufacture	Compared to the assumed egg-based vaccine intervention, the cell culture-based intervention strategy results in: • a wider vaccine coverage, fewer influenza cases, fewer PCP consultations for influenza treatment, fewer influenza-related hospitalizations, fewer excess deaths, and fewer discounted years per life lost • a higher intervention strategy costs, but a reduction of medical care costs, and total direct costs • The years per life lost gained are €2.56 million • the cost per life year gained is €3198 • The cost per case, hospitalization and death averted are, respectively, €234, €2612 and €12,530.
Balicer 2005	1. Therapeutic antiviral use 2. Long-term preexposure prophylaxis 3. Short-term, epidemiologically directed postexposure prophylaxis	• prepandemic stockpiling of oseltamivir is cost-saving to the economy over a wide range of treatment strategies • investments in antiviral agents can be expected to yield a substantial economic return of >$3.68 per $1 invested, while saving many lives • This favorable cost-benefit ratio can be achieved if stockpiled antiviral drugs are administered either solely as a therapeutic measure or as short-term prophylaxis for exposed contacts (ring prophylaxis or targeted prophylaxis) • Investment in stockpiling remains cost-saving to the economy as long as the estimated annual pandemic risk remains >1 pandemic every 80 years

2.3.6 Group 5: Papers focused on global spread

One paper looked at the impact of airline travel on the geographic spread of pandemic influenza. Assuming the Hong Kong influenza pandemic strain of 1968–1969 returned in 2000, the study examined its likely pattern of global spread under contemporary air travel volumes using a series of simulations of an SEIR epidemic model coupled with air transportation data for 52 global cities. The model predicted that the pandemic would spread concurrently to cities in both the northern and southern hemispheres thereby exhibiting less of the characteristic seasonal swing. In addition, after recognition of pandemic onset in the focal city, the pandemic would to all major cities in the world within a period 180 days, almost four months earlier than what it takes for 300 days in 1968, thus giving a very short time lag for public health intervention. (Table 20)

This finding may have special relevance for the situation in Hong Kong. If we assume the pandemic to be emerged in some remote area of South East Asia, the time before its spread to Hong Kong from its first emergence would then be in the order of days or at best a couple of weeks, thus giving an extremely short window period for any possible preparations.

Table 18: Models assessing economic implications – Modelling approaches and settings

	Model approach	Model setting
Medema 2004	• A simulation model combining a vaccine production model with an cost-effectiveness model of influenza intervention strategies • To compare the costs and benefits of different intervention scenarios based on different vaccine manufacturing scheme (Egg-based and Cell culture-based vaccine manufacturing)	• assumed an 2004 pandemic strain emerges 1 January 2004 • an average 1918–1919 attack rate of 35% in a single wave • with a case fatality rate of 1.87% • Health economic parameters based on average data from elderly in the United Kingdom in recent annual influenza epidemics • increased absenteeism of health care workers, societal disruption by the pandemic, and health economical consequences of influenza are not taken into account • total population estimated at 1 billion • assumed a seed preparation time for vaccination production of 3 months • assumed eggs are readily available for vaccine manufacture • assumed a 7.5g monovalent vaccine given in two doses and should be administered within 6 months after emergence of the "2004 pandemic" virus
Balicer 2005	• Estimation of health-related impact of pandemic influenza by using Meltzer's model (FluAid) • Cost-benefit analysis of using antiviral drug according to five different strategies.	• Assuming pandemic influenza on the Israeli population • Impact estimated using the Meltzer model • Direct costs to the healthcare system and overall costs to the economy (value of lost workdays) calculated but not the potential value of lost lives

2.4 Conclusions and recommendation

Modelling studies have helped to understand the problem of pandemic influenza from a number of different aspects and evaluate some potential solutions to the imminent problem which may otherwise difficult to assess.

- Based on pneumonia and influenza death epidemic data from 45 US cities, the reproductive number for 1918 influenza had been estimated to have a median of less than 3.

- Findings form the two studies about possibility of containment and elimination of an emergent pandemic strain of influenza at the point of origin in an isolated rural setting had regarded that containment, though depended critically on the actual $R_{0,}$ is theoretically feasible using a combination of antiviral prophylaxis and social distancing measures.

- This conclusion, however, should only be taken with caution as it is based on a number of highly optimistic assumptions which may not in practice be feasible, and that it may means a very different story when we translate the finding from an isolated rural setting to the situation of a well mixed urban population like Hong Kong.

- Given that all detection and tracing works and initiation of TAP need to be implemented within a very short period of time in order to for it to be effective, and that these implementation probably has to be done in some rural parts of some Asian countries, such suggested feasibility should at best be regarded as mainly theoretical, or significant planning and investment would actually be required before we can make such feasibility into reality.

- Available studies assessing intervention effectiveness focused mainly on the feasibility of containment at source. Although being highly important and having huge potential impact, such approach may not be the only or even the best solution to the imminent problem.

- For the situation in Hong Kong, investigation of other possible approach to the problem may be advisable and becoming more relevant when such initial attempt to contain the pandemic has proved difficult to be actualized or giving the expected results in reality.

- One option may involve looking into the different ways and their relative effectiveness for preventing invasion into an area once it failed to be contained at source and begin to spread to other countries. Also important would the logistics of implementing these procedures and the likely consequence of any delay given the contemporary dense pattern of travel across most international boarders, meaning that the time before its spread to Hong Kong from its first emergence would probably be in the order of days or at best a couple of weeks, thus giving an extremely short window period for the actual implementation of any possible preparations even if any of these may deemed to be effective.

- Another approach that may worth considering in greater detail included the different ways for minimising R once invasion from an outside source into a city occurred. Although some of the available studies already looked at some aspect of the issue, they had focused mainly on the effect of antiviral drug or vaccination.

- As influenza has a very short generation time and a substantial proportion of transmission actually occurring before the onset of case-defining symptoms, measures that generally reduce contacts between persons, regardless of infection status, may be our most powerful protection against a pandemic until adequate vaccine and antiviral medicines can be produced, at which point mass-vaccination and prophylaxis may be more effective than targeted approaches. As antiviral medication stockpiles and vaccine production capacity would remain insufficient at present, and possibly in the foreseeable future, to provide the any broad coverage even in wealthy countries, control measures based on case identification, isolation, and social distancing measures may proved to be even more practical and may worth to be evaluated in greater detail.

- All five studies focused on impact estimation yielded very coherent conclusions that all levels of the medical system would be overwhelmed even in the best case scenario of a mild influenza pandemic. As the load on different sectors of the health care system may be stretched in different period to different amount, understanding the dynamics of the pandemic may helps to better prepare for the changing requirement of resources. Detailed simulation of the optimal logistics of intervention (e.g. quarantine, social distancing, antiviral distribution, etc) may also contribute to a more practical way to implementation and actualize some of the very optimistic findings of other modelling studies.

3. Comparing Pandemic Influenza Preparedness Plans in Seven Economies

In order to facilitate better preparedness in Hong Kong for pandemic influenza and to identify gaps in strategies which the current preparedness plan, this study compared the government preparedness plans of human pandemic influenza among seven economies.

3.1 Methodology

Pandemic influenza plans were found at http://www.who.int/csr/disease/influenza/nationalpandemic/en. There are 2 main selection criteria for choosing the specific country plan for the study. First, in order to have an overall worldwide perspective, it was decided that at least 1 plan would be selected from each of the continents among the plans listed at the website. Second, only plans in English were chosen for comparison. As a result, a total of 7 countries were selected for the study. Specifically, 3 countries in Asia (Hong Kong, Singapore, Australia), 2 countries in America (USA, Canada), 1 country in Europe (UK) and 1 country in Africa (South Africa) were included in the comparison.

There were 11 areas for comparison among the countries' pandemic preparedness. These included the activation level, the basic planning assumption as well as the 9 major public health responding categories for each of these countries. Specifically, the 9 public health measures were as followed:

- Surveillance
- Investigation and control measures
- Infection control measures
- Laboratory support
- Provision of medical service
- Antiviral stockpiling
- Vaccination
- Port health measures
- Communication

These public health measures areas were based on the WHO recommendation for the planning preparedness activities for an influenza pandemic.

Most defined contingent response systems of the compared countries are based on WHO recommendation with variation of details. In the countries studied, all have developed five activation levels or above except Hong Kong and South Africa. Hong Kong has three response levels. South Africa has not mentioned about the level of activation.

There is great similarity in the 11 areas (see above) covered by the Australia, Canada, Hong Kong, Singapore, UK and US contingency plans. However, detail implementation and logistics are usually omitted therefore it is hard to evaluate the comprehensiveness and effectiveness of the public health measures.

With the exception of South Africa, all the compared countries had contingency action elements suggested by the WHO proposal. Little has been mentioned on the selected areas by South Africa. It would be hard to justify the absence of those public health measures if it is not mentioned. Information being not accessible to the public due to administrative reason has to be considered.

The contingency plan of Canada has been the most explicit and perhaps comprehensive in describing its action. For example, it mentioned the use of health workers and workforce in the post-pandemic / recovery phase. In addition, Canada has planned in providing home supplies (food etc) for needed group during the pandemic situation.

The attack rates of patient infected with influenza during pandemic were assumed to be 15 to 35%. Nevertheless, Hong Kong had adopted 15% as its assumption attack rate.

Although isolation, quarantine and social distancing were mentioned in all the plans, most of them inferred that enforcement decision would be based on WHO recommendation when pandemic occur. Only in Singapore's plan has stated explicitly about enforcement of quarantine.

Table 21: Summary of Avian Flu Preparedness Plans

Key areas of preparedness as recommended by WHO	Canada	UK	Hong Kong	USA	Singapore	South Africa	Australia
I) Surveillance a) Information sharing with involved counties. b) Maintain a close liaison with WHO	a) b)	a) b)	a) b)	a) b)	a) b)	a) b)	a) b)
II) Vaccine Programs a) seasonal flu b) preparation for avian flu vaccination	a) b)	a) b)	a) b)	a) b)	a) b)	a)	a) b)
III) Antivirals stockpiling for avian flu a) as treatment to priority groups b) as prophylaxis to priority groups	a) b)	a) b)	a) b)	a) b)	a) b)		a) b)
IV) Public Health Measures a) Designated flu / fever clinics b) Laboratory capability on avian flu screening c) Surge capacity – plans for enlisting community support	a) b) c)	a) b) c)	a) b) c)	a) b) c)	a) b) c)		a) b) c)
V) Communication a) Medical professional (e.g. regular update materials on all aspects of influenza) **b)** Use of Internet Site	a) b)	a) b)	a) b)	a) b)	a) b)	a) b)	a) b)

Key areas of preparedness as recommended by WHO	Canada	UK	Hong Kong	USA	Singapore	South Africa	Australia
VI)Infection control measures **a) guidelines for clinical setting** **b) general guidelines for public** **c) specific training for essential service workers**	a) b)	a) b)	a) b) c) in the pipeline (ICB)	a) b)	a) b)		a) b)
VII) Planning assumptions **a) Attack rate**	a) 35%	a) 25%	a) 15%	a) 35%	a) 25%	a) 25%	a) 25%
VIII) Level of activation	Phase 0-5	5 level	3 tier	Phase 0-5	6 level	Not mentioned	Phase 0-6

Table 22: Summary of Avian Flu Preparedness Plans: Remarks

Canada	UK	Hong Kong
i)Implement strategy to deploy recovered HCW (presumably immune case) ii) It has plans for providing food and essential life-support needs to persons confine to home.	i) Mandatory quarantine and curfews are generally not considered necessary and are not currently covered by public health legislation. ii) Websites will be used as a central component in managing the surge in public information requests.	i) In anticipation of mass fatalities, a mortuary response operation plan has been in place. ii) Plans to mobilize community resources(volunteer private doctors and social welfare sector) to support the system iii) Risk Communication through public health promotion activities and talks to different sector of the society.

USA	Singapore	Australia
	i) May consider about imposing Curfew in Black Level. ii) Ring Fencing *prophylaxis*: (*close contacts*, health care workers attending to patients (10 days prophylaxis. But discontinued if the virus has infected persons beyond the 1st ring of contacts.	i) In the event of a more widespread outbreak of avian influenza amongst humans occurring in any country, Australians may be advised to defer all non-essential travel to affected areas. Under these circumstances, all travellers arriving in Australia from affected areas may be required to undergo additional disease screening and quarantine measures. ii) Australia has secured a contractual commitment from the Australian and an international supplier for up to 50 million doses of a pandemic vaccine (subject to the vaccine's development and production).

3.2 Authors' comment

A summary of the comparison was described as above. One of the main differences between the plans was the number of activation levels. Among the plans, the Canadian plan was the most comprehensive and it had included detailed arrangement in the recovery period. Details regarding the logistic arrangements for isolation and quarantine were not mentioned in most plans. In summary, Hong Kong is of the same standard as other developed countries in the preparedness of pandemic influenza.

Centre for Health Protection
February 2006

4. References

i. Mills CE, Robins JM, Lipsitch M. Transmissibility of 1918 pandemic influenza. Nature. 2004 Dec 16;432(7019):904-6.

ii. Wilson N, Mansoor O, Baker M. Estimating the impact of the next influenza pandemic on population health and health sector capacity in New Zealand. N Z Med J. 2004 Mar 11;118(1211):U1346.

iii. Wilson N, Mansoor O, Lush D, Kiedrzynski T. Modeling the impact of pandemic influenza on Pacific Islands. Emerg Infect Dis. 2005 Feb;11(2):347-9.

iv. Anderson TA, Hart GK, Kainer MA; ANZICS Database Management Committee. Pandemic influenza-implications for critical care resources in Australia and New Zealand. J Crit Care. 2003 Sep;18(3):173-80.

v. Menon DK, Taylor BL, Ridley SA; Intensive Care Society, UK. Modelling the impact of an influenza pandemic on critical care services in England. Anaesthesia. 2005 Oct;60(10):952-4.

vi. Balicer RD, Huerta M, Davidovitch N, Grotto I. Cost-benefit of stockpiling drugs for influenza pandemic. Emerg Infect Dis. 2005 Aug;11(8):1280-2.

vii. Ferguson NM, Cummings DAT, Cauchemez S, Fraser C, Riley S, Meeyai A, Iamsirithaworn S, Burke DS. Strategies for containing an emerging influenza pandemic in Southeast Asia. Nature doi:10.1038/nature04017

viii. Longini IM Jr, Nizam A, Xu S, Ungchusak K, Hanshaoworakul W, Cummings DA, Halloran ME. Containing pandemic influenza at the source. Science. 2005 Aug 12;309(5737):1083-7. Epub 2005 Aug 3.

ix. Patel R, Longini IM Jr, Halloran ME. Finding optimal vaccination strategies for pandemic influenza using genetic algorithms. J Theor Biol. 2005 May 21;234(2):201-12. Epub 2005 Jan 20.

x. Longini IM Jr, Halloran ME, Nizam A, Yang Y. Containing pandemic influenza with antiviral agents. Am J Epidemiol. 2004 Apr 1;159(7):623-33.

xi. van Genugten ML, Heijnen ML, Jager JC. Pandemic influenza and healthcare demand in the Netherlands: scenario analysis. Emerg Infect Dis. 2003 May;9(5):531-8.

xii. Medema JK, Zoellner YF, Ryan J, Palache AM. Modeling pandemic preparedness scenarios: health economic implications of enhanced pandemic vaccine supply. Virus Res. 2004 Jul;103(1-2):9-15.

xiii. Grais RF, Ellis JH, Glass GE. Assessing the impact of airline travel on the geographic spread of pandemic influenza. Eur J Epidemiol. 2003;18(11):1065-72. Erratum in: Eur J Epidemiol. 2004;19(4):395.

xiv. Meltzer M, Cox N, Fukuda K: The economic impact of pandemic influenza in the United States: Priorities for intervention. Emerg Infect Dis 5:659-671, 1999

xv. Meltzer MI, Shoemake HA, Kownaski M, Crosby R. FluAid 2.0: A manual to aid state and local-level public health officials plan, prepare, and practice for the next influenza pandemic (Beta test version). Atlanta: Centers for Disease Control and Prevention; 2000.

xvi. Zhang X, Meltzer MI, Wortley P. FLUSURGE 1.0. A Manual to Assist State and Local Public Health Officials and Hospital Administrators in Estimating the Impact of an Influenza Pandemic on Hospital Surge Capacity (Beta Test Version). Atlanta, GA: Centers for Disease Control and Prevention, U.S. Department of Health and Human Services, 2004 [WWW document]. http://www.cdc.gov/flu/flusurge.htm.

xvii. Centers for Disease Control and Prevention (National Vaccine Program Office). FluAid. [cited 2004 Jul 15]. Available from: http://www2a.cdc.gov/od/fluaid/default.htm