

MISMS Newsletter

November 2006



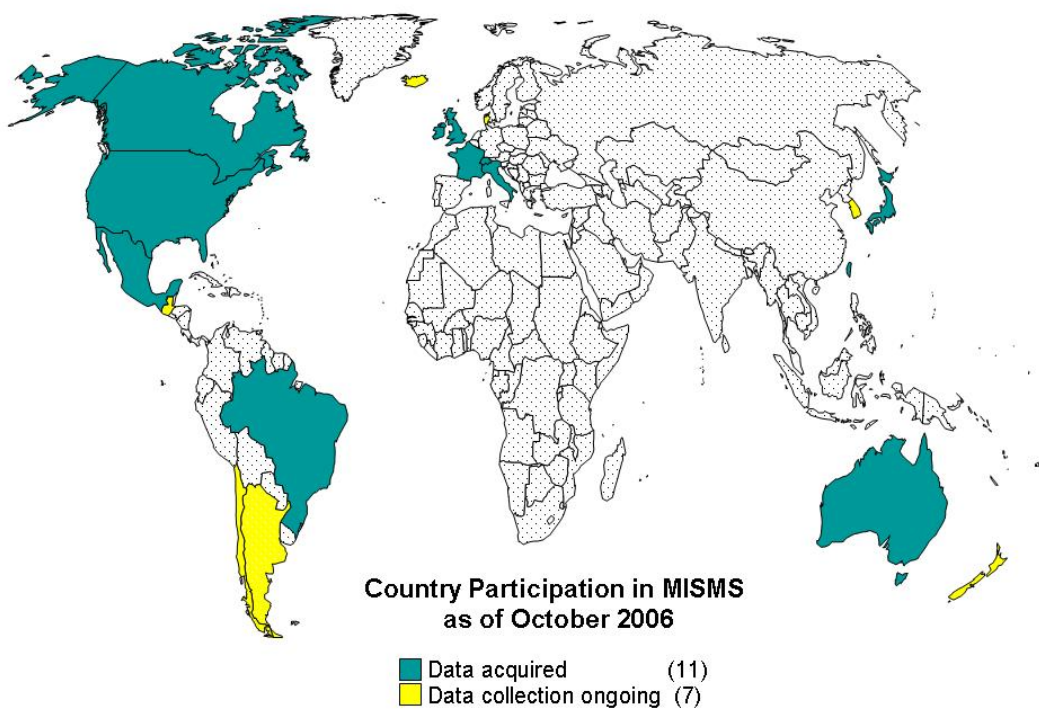
INTRODUCTION

The Multinational Influenza Seasonal Mortality Study (MISMS) is an international collaborative effort to analyze national and global mortality patterns associated with influenza virus circulation.

MISMS has 4 specific aims:

1. To describe synchrony in seasonal variations of various causes of mortality associated with influenza, by state, country, and region
2. To describe long-term temporal trends and inter-annual variations in influenza mortality patterns, both within and amongst countries, and their association with changes in circulating subtypes of influenza virus, antigenic characteristics, population factors, and vaccine coverage
3. To explore the seasonal patterns and burden of influenza mortality in tropical countries, and understand the global circulation of influenza viruses - to achieve this goal, new methods for estimating mortality impact in tropical countries need to be developed
4. To develop a world map of influenza mortality burden and seasonal patterns

COUNTRY DATABASE PROGRESS



Technical assistance can be provided to new and on-going MISMS participants. Collaborators are welcome to email or visit the Fogarty International Center to receive technical assistance in the analysis of their data. Past visitors to the center have included researchers from Italy, Japan, Brazil and Taiwan, for periods ranging from 1 month to 1 year.

MISMS Newsletter

November 2006

FUTURE PLANS

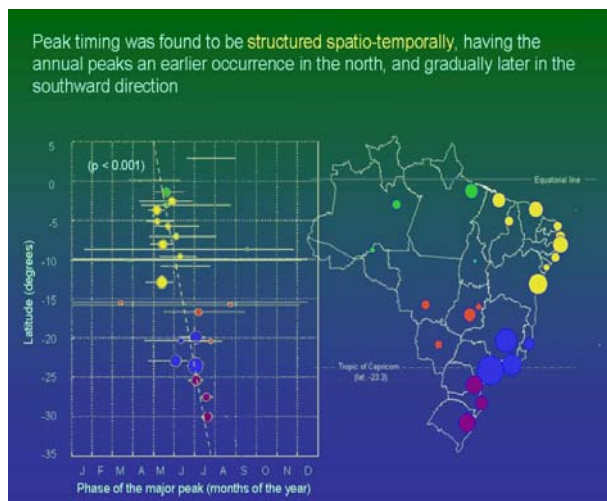
Collaborators are encouraged to share their findings at the upcoming Options for the Control of Influenza VI conference to be held in Toronto from June 17-23, 2007. Abstracts are due by March 1, 2007. The conference website is: <http://www.optionsviconference.com/Index.html>.

Regional MISMS meetings are planned in early 2007 in South America, Asia, Toronto, and possibly one additional site. These meetings will include opportunities for collaborators to present country-specific data, a presentation of the regional/multinational modeling efforts, policy relevant findings, and workshops and sessions on data and analytical methods. In addition, MISMS hopes to increase the number of active collaborators worldwide in order to allow for regional analysis and improved statistical modeling. If you are interested in attending any of these meetings, please contact richardst@mail.nih.gov for more information.

STUDY HIGHLIGHTS

Collaborators in the MISMS project have published a number of articles and presented at international meetings. Below is a sample of the manuscripts that have been published.

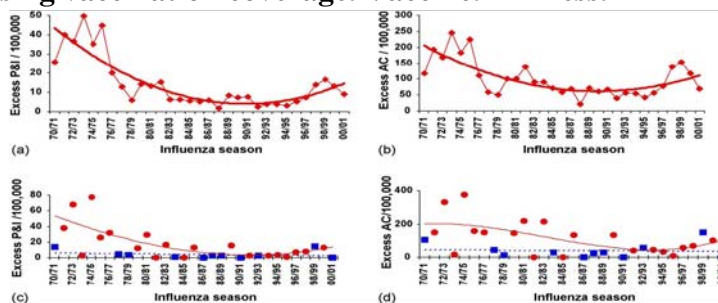
Alonso WJ, Viboud C, Simonsen L, Hirano EW, Daufenbach LZ and Miller M. (2006) Seasonality of Influenza in Brazil: Traveling Waves from the Equator to the Sub-Tropics. Am J Epidemiol. In Press.



- Of the ~19 million deaths in Brazil from 1979-2001, 4.0% were due to pneumonia and 0.03% were due to influenza
- The seasonality of influenza in Brazil follows a semi-annual pattern, peaking in the winter month of June with a second smaller peak during summer (January)
- Based on timing of pneumonia and influenza mortality peaks, influenza was found to travel from the less populated North to the densely populated South
- The Southward wave indicates that environmental forces (temperature, humidity) may play a more important role than population factors (density, size, traveling patterns) in driving the timing of influenza epidemics in Brazil

Rizzo C, Viboud C, Montomoli E, Simonsen L and Miller MA. (2006) Influenza-related mortality in the Italian elderly: No decline associated with increasing vaccination coverage. Vaccine. In Press.

- On average, 99 excess all-cause deaths per 100,000 elderly persons occur during the influenza season
- The most severe seasons were characterized by a predominance of A(H3N2) viruses
- Although influenza vaccination rates in the elderly increased from <5% in 1970 to ~60% in 2001, there was no associated decline in age adjusted excess mortality



Seasonal excess mortality rates among elderly ≥ 65 years of age, for individual seasons 1970–2001, Italy. P&I (left panels) and AC (right panels) excess death rates are indicated. (a and b) Unadjusted rates (red square) and (c and d) age-adjusted rates stratified by virus subtypes (red dots: A/H3N2; blue squares: B or A/H1N1). The red curve represents a 3-year moving average of all seasons (a and b) and A/H3N2-only seasons (c and d).

MISMS Newsletter

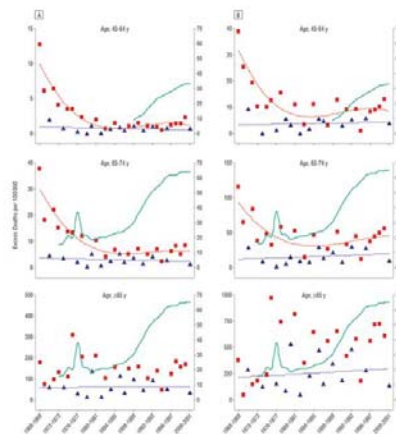
November 2006

STUDY HIGHLIGHTS, cont.

Simonsen L, Reichert TA, Viboud C, Blackwelder WC, Taylor RJ and Miller MA. (2005) Impact of influenza vaccination on seasonal mortality in the US elderly population. Arch Intern Med. 165 3 265-72.

- For people aged 65-74 years, excess age adjusted mortality rates due to influenza in A(H3N2)-dominated seasons fell between 1968 and the early 1980s but remained relatively constant thereafter
- Age-adjusted mortality rates for persons 85 years or older remained flat from 1968-2001
- Increasing flu vaccination coverage did not correlate with declining mortality rates
- All-cause excess mortality for persons 65 years or older never exceeded 10% of all winter deaths

Age-adjusted estimates of seasonal excess pneumonia and influenza (A) and all-cause (B) mortality rates among persons 45 to 64, 65 to 74, and 85 years or older

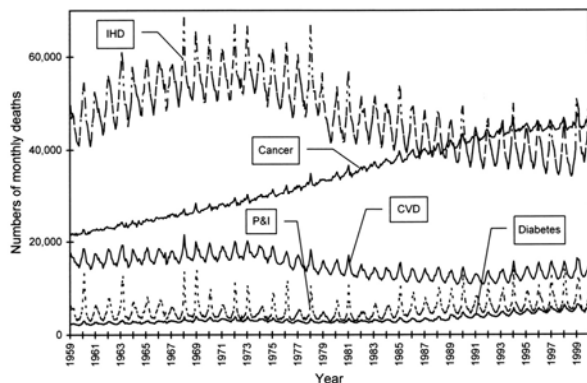


Simonsen, L. et al. Arch Intern Med 2005;165:265-272.

ARCHIVES OF
INTERNAL MEDICINE

Copyright restrictions may apply.

Reichert TA, Simonsen L, Sharma A, Pardo SA, Fedson DS and Miller MA. (2004) Influenza and the winter increase in mortality in the United States, 1959-1999. Am J Epidemiol. 160 5 492-502.



Monthly numbers of deaths attributed to five classes of disease in the United States during the period 1959–1999. Numbers of deaths for the individual disease classes differed greatly, and deaths in all classes except cancer showed regular increases during the winter season. IHD, ischemic heart disease; P&I, pneumonia and influenza; CVD, cerebrovascular disease.

- Peak months of mortality for ischemic heart disease, cerebrovascular disease, and diabetes mellitus coincided with peaks in pneumonia and influenza deaths
- Excess mortality in cardiovascular disease, heart disease, pneumonia, influenza, and all-causes was higher in seasons dominated by the more lethal H2N2 and H3N2 viruses
- An age shift towards younger deaths was found in deaths from cardiovascular disease, heart disease, pneumonia, influenza, and all-causes in the decade following the 1968/69 pandemic

MISMS Newsletter

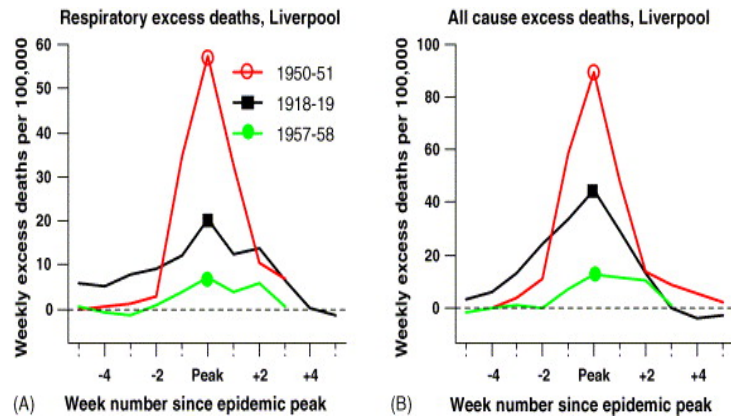
November 2006

STUDY HIGHLIGHTS, cont.

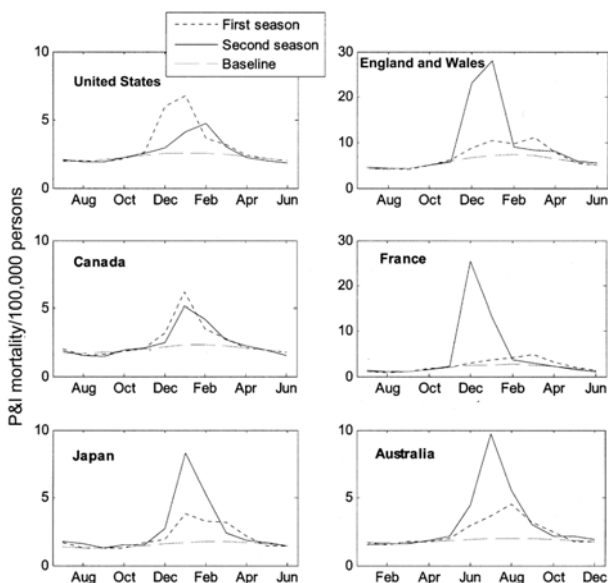
Viboud C, Tam T, Fleming D, Miller MA and Simonsen L. (2006) 1951 influenza epidemic, England and Wales, Canada, and the United States. *Emerg Infect Dis.* 12 4 661-8.

Viboud C, Tam T, Fleming D, Handel A, Miller MA and Simonsen L. (2006) Transmissibility and mortality impact of epidemic and pandemic influenza, with emphasis on the unusually deadly 1951 epidemic. *Vaccine.* In Press.

- Excess death rates from pneumonia and influenza and all-causes were substantially higher for the 1951 epidemic than for the 1957 and 1968 epidemics in England and Canada
- In Liverpool, the 1951 epidemic had higher mortality impact than 1918 pandemic
- Age-specific patterns of deaths in England and Canada were typical of interpandemic seasons but transmissibility was similar to that of pandemics
- In contrast, the 1951 epidemic was not particularly severe in the United States but the reasons for this difference are unclear



Viboud C, Grais RF, Lafont BA, Miller MA and Simonsen L. (2005) Multinational impact of the 1968 Hong Kong influenza pandemic: evidence for a smoldering pandemic. *J Infect Dis.* 192 2 233-48.



- The influenza-related excess mortality was estimated in 6 countries (US, Canada, England, France, Japan, and Australia) by age for 1967-1978
- In North America, majority of flu-related deaths in 1968/69 and 1969/70 occurred during the first pandemic season, whereas in Europe and Asia most deaths occurred during the second pandemic season
- Researchers hypothesize that persons in Europe and Asia had higher pre-existing neuraminidase immunity from A/H2N2 era which protected them against the first H3N2 virus
- Second pandemic season coincided with a drift in the neuraminidase antigen which resulted in higher mortality in Europe and Asia