



The Fogarty International Center MISMS Newsletter

Summer 2010

MISMS Oceania Regional Meeting & Workshop March 15-19, 2010 · Melbourne, Australia

Following the success of previous regional meetings in South America, Asia, Europe, and Africa, the 2010 MISMS Oceania Meeting & Workshop was held early this spring in Melbourne, Australia. Co-hosted by the Melbourne School of Public Health, this meeting brought together epidemiologists, virologists, evolutionary biologists, and public health officials to share and present their latest findings on the epidemiology and virology of influenza in the Pacific region. The meeting's primary aim was to build analytical capacity for epidemiologic and molecular studies of influenza in this region, while identifying potential collaborators and disseminating scientific findings that can inform influenza control strategies.

Over 50 participants from universities and public health institutions across Australia, Asia, Europe, and the United States attended the meeting. MISMS researchers and regional participants presented on a range of topics, including influenza epidemiology, transmission dynamics, phylogenetic and molecular analyses, virus surveillance, and control strategies. Much of the discussion was directed toward the 2009 H1N1 pandemic in the Southern Hemisphere, but sessions were also dedicated to inter-pandemic influenza and the transmission dynamics of the 1918 pandemic, among other diverse research topics.

Speakers included researchers from academic institutions in Australia, Singapore, China, Taiwan, and Hong Kong, members of the defense community, investigators from various foreign health agencies and international organizations, like the WHO, and National Institutes of Health (NIH) staff. A special presentation was also delivered by Jim Bishop, the Chief Medical Officer of the Australia Department of Health & Aging, who outlined Australia's recent control strategies for the 2009 H1N1 pandemic.



MISMS Oceania Meeting, March 2010
Melbourne, Australia

During the three-day workshop that followed, participants received technical training in analyzing various types of virologic and epidemiologic data. Fogarty collaborators Eddie Holmes (Pennsylvania State University), Derek Smith (University of Cambridge), and Andrew Rambaut (University of Edinburgh) led workshops in the analysis of phylogenetic and antigenic data. Fogarty researcher Wladimir Alonso used software he has developed to illustrate space-time analysis, an issue that is of particular relevance when evaluating long-term trends in influenza mortality. Yiming Bao from the US National Center for Biotechnology Information (NCBI, NIH) demonstrated the Influenza Virus Resource, an online tool that makes influenza sequences and publications more widely available to researchers.

Following the workshops, NIH staff led small group discussions on data analysis and demonstrated new techniques using specially-prepared sample data. The workshop also provided a unique networking opportunity that enabled scientists from different geographic and research areas to share their experiences and establish connections that will undoubtedly yield stronger collaborations.



“Historical Influenza Pandemics: Lessons Learned” Meeting & Workshop May 3-7, 2010 · Copenhagen, Denmark

The 2010 MISMS “Historical Influenza Pandemics: Lessons Learned” Meeting & Workshop took place late this spring in Copenhagen, Denmark and was co-hosted by the Epidemiology Department of Statens Serum Institut (SSI) and the Department of Science, Systems, and Models of Roskilde University, Denmark.

This unique meeting brought together an interdisciplinary group of over 50 participants, united by a common interest in the epidemiology of past influenza pandemics. During the conference, public health officials met with researchers from a wide range of disciplines, including epidemiology, clinical medicine, biostatistics, mathematical modeling, social science, law, history, and demography.

At the general scientific meeting (May 3-4), MISMS researchers and guest experts described innovative analytical methodologies, presented their latest findings in historical data, and articulated key lessons for future control strategies. Plenary sessions highlighted new strategies for spatial and temporal analysis, virus surveillance, and control efforts for the 1889, 1918, 1957, 1968, and 2009 influenza pandemics. The medical, political, and legal implications of influenza pandemics on society were also described. The ultimate goal of this exchange was to extract lessons from the past and adapt them to current and future pandemics.

Speakers included public health officials, researchers from academic and national health institutions in Scandinavia and across the US, Mexico, and greater Europe, and NIH staff. SSI Director Nils Standberg Peterson described the history of the Danish response to pandemics, including the 2009 A/H1N1 virus. Alain-Jacques Valleron (Université Pierre et Marie Curie, Paris, France) presented findings from a multinational study of the 1889 pandemic in Europe, while FIC investigator Lone Simonsen illustrated how an understanding of the signature features of pandemic influenza can help create more effective prevention and control efforts. Presentations

focusing on influenza in Denmark, Sweden, Iceland, France, Italy, Spain, Mexico, Brazil, Canada, and the US demonstrated how centuries-old data taken from libraries and church archives can be used to reveal key epidemiological features of past pandemics.



“Historical Influenza Pandemics: Lessons Learned” Meeting, May 2010
Copenhagen, Denmark

During the technical workshops that followed (May 5-7), guest researcher Lisa Sattenspiel (University of Missouri, USA) led an informative workshop on the geographic spread of influenza. In addition, Fogarty researchers Cécile Viboud, Vivek Charu, Gerardo Chowell, and Wladimir Alonso led practical sessions on time series analysis, the estimation of the reproductive number (R_0) of influenza, and the usage of graphics to effectively represent data. Through subsequent group discussions, participants shared historical data and analytical techniques for investigating past and present influenza epidemiological data.

The conference established an international forum for the study of historical pandemics and linked key insights of ongoing scientific and historical research to the current needs of public health officials. Several scientific connections forged at the meeting have already resulted in new collaborations focused on the analysis of past influenza pandemics and its relevance to present-day public health policy and outcomes.



Guest Researcher Spotlight

The Fogarty International Center's MISMS program utilizes a number of collaborative mechanisms, including the support of visiting fellows who perform research at the NIH Headquarters in Bethesda, Maryland. Recent guest researchers visited from France, Italy, Taiwan, Brazil, Japan, South Korea, South Africa, Australia, Portugal, Denmark, and other parts of the US. Here we spotlight Drs. Tany Tan, from Hong Kong, and Jie He, from Wisconsin, US.

Jie He, PhD, Medical College of Wisconsin

Jie He is currently a postdoctoral fellow at the Midwest Respiratory Virus Program (MRVP) at the Medical College of Wisconsin in Milwaukee, WI. A molecular virologist who received her graduate training from the State Key Laboratory at China CDC in Beijing, she studies the molecular genetics of respiratory viruses, including the development of innovative diagnostic methods.

Spending two weeks at our office in June, Dr. He worked with FIC researcher Martha Nelson, PhD to apply methods in phylogenetic analysis to the study of parainfluenza virus evolution at a genomic level. Moving forward, she hopes to apply these techniques to her research on respiratory virus evolution at MRVP.

While Dr. He describes the atmosphere at Fogarty as open, friendly, and exciting, she also found it to be quite challenging. "I was very impressed by the international cooperation happening [at Fogarty] and [had the opportunity] to see how top researchers can improve global health through collaboration."



Tany Tan, PhD, Fogarty International Center

Tany Tan joined FIC as a post-doctoral fellow in January 2010, and since then, she has worked closely with Martha Nelson on the phylogenetic analysis of influenza sequences from human and swine populations. Through this research, she hopes to trace the transmission patterns of epidemics and gain a better understanding of viral evolution.

Dr. Tan began her foray into the world of public health as a graduate student at the Chinese University of Hong Kong. Since much of her earlier training was based in molecular biology, she knew relatively little about epidemiology, but her work with SS Lee, MD from the Stanley Ho Centre for Emerging Infectious Diseases soon changed that. Under his guidance, Dr. Tan researched the molecular epidemiology and evolutionary biology of the Human Immunodeficiency and Hepatitis C Viruses. As she developed techniques in phylogenetic analysis, she eventually and inevitably found her niche in the field of molecular epidemiology.



Through record-breaking blizzards, the Washington DC Cherry Blossom Festival, and the MISMS Oceania Conference in Australia, Dr. Tan has not had a dull moment since joining FIC. Recently returning from Hong Kong, Dr. Tan helped forge new research collaborations in Southern China. During her trip, she also had the opportunity to study seasonal influenza epidemics and the impact of the 2009 A/H1N1 pandemic in subtropical regions.



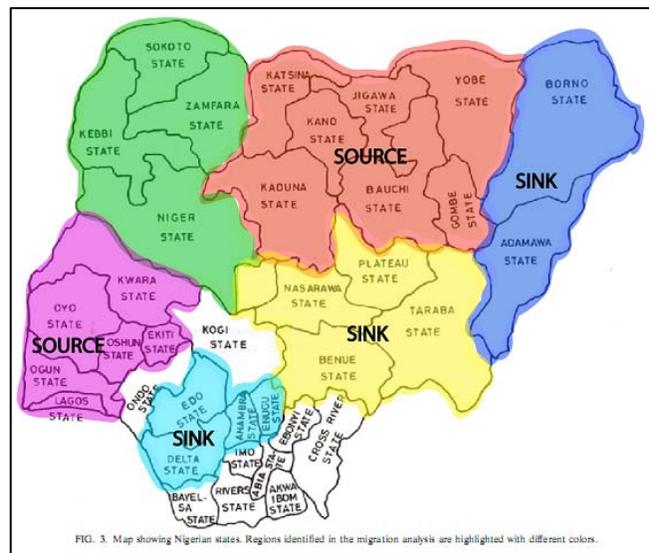
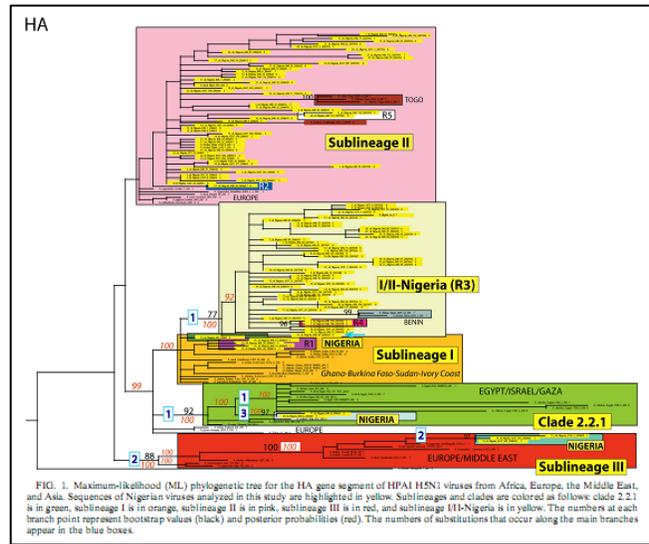
Study Highlights

MISMS collaborators published a breadth of articles on influenza viruses over the years. Articles focus on topics as diverse as influenza evolutionary dynamics, the disease burden and transmission of influenza, and the effectiveness of control strategies. A selection of recent articles is found below.

INFLUENZA VIRUS EVOLUTIONARY DYNAMICS AND PATTERNS

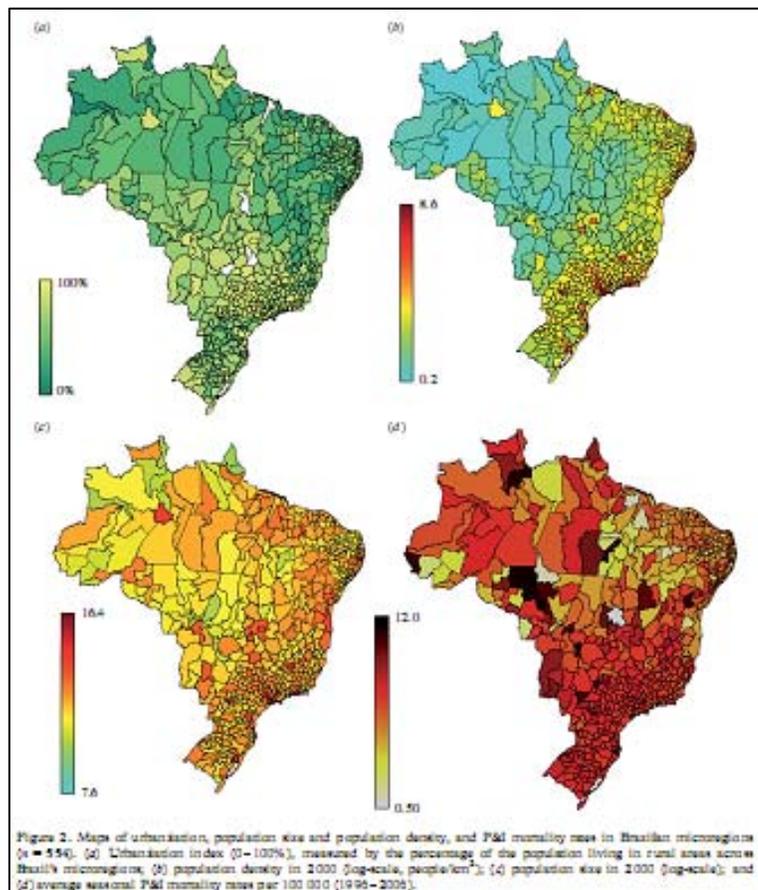
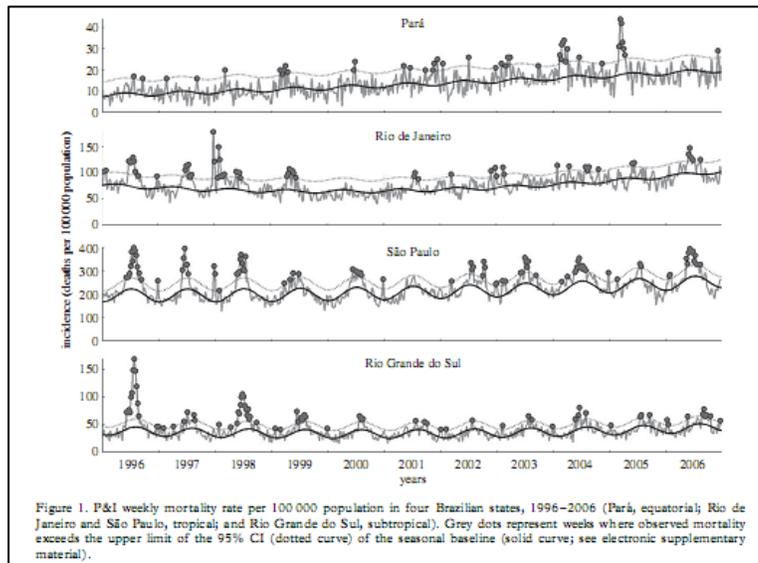
Fusaro A, Nelson MI, Joannis T, Bertolotti L, Monne I, Salviato A, Capua I, Holmes EC, Cattoli G (Apr 2010) Evolutionary dynamics of multiple sublineages of H5N1 influenza viruses in Nigeria, 2006-2008. *J Virol.* 84(7): 3239-47.

Highly pathogenic A/H5N1 avian influenza (HPAI H5N1) viruses have seriously affected the Nigerian poultry industry since early 2006. Previous studies have identified multiple introductions of the virus into Nigeria and several reassortment events between cocirculating lineages. To determine the spatial, evolutionary, and population dynamics of the multiple H5N1 lineages cocirculating in Nigeria, we conducted a phylogenetic analysis of whole-genome sequences from 106 HPAI H5N1 viruses isolated between 2006 and 2008 and representing all 25 Nigerian states and the Federal Capital Territory (FCT) reporting outbreaks. We identified a major new subclade in Nigeria that is phylogenetically distinguishable from all previously identified sublineages, as well as two novel reassortment events. A detailed analysis of viral phylogeography identified two major source populations for the HPAI H5N1 virus in Nigeria, one in a major commercial poultry area (southwest region) and one in northern Nigeria, where contact between wild birds and backyard poultry is frequent. These findings suggested that migratory birds from Eastern Europe or Russia may serve an important role in the introduction of HPAI H5N1 viruses into Nigeria, although virus spread through the movement of poultry and poultry products cannot be excluded. Our study provides new insight into the genesis and evolution of H5N1 influenza viruses in Nigeria and has important implications for targeting surveillance efforts to rapidly identify the spread of the virus into and within Nigeria.



Chowell G, Viboud C, Simonsen L, Miller M, Alonso WJ (Jun 2010) The reproduction number of seasonal influenza epidemics in Brazil, 1996-2006. Proc Biol Sci. 277(1689): 1857-66.

The transmission dynamics of influenza in tropical regions are poorly understood. Here we explore geographical variations in the reproduction number of influenza across equatorial, tropical and subtropical areas of Brazil, based on the analysis of weekly pneumonia and influenza (P&I) mortality time series in 27 states. The reproduction number (R) was low on average in Brazil (mean = 1.03 (95% CI 1.02-1.04), assuming a serial interval of 3 days). Estimates of the reproduction number were slightly lower for Brazil than for the USA or France (difference in mean R = 0.08, $p < 0.01$) and displayed less between-year variation ($p < 0.001$). Our findings suggest a weak gradient in the reproduction number with population size, where R increases from low population in the North to high population in the South of Brazil. Our low estimates of the reproduction number suggest that influenza population immunity could be high on average in Brazil, potentially resulting in increased viral genetic diversity and rate of emergence of new variants. Additional epidemiological and genetic studies are warranted to further characterize the dynamics of influenza in the tropics and refine our understanding of the global circulation of influenza viruses.



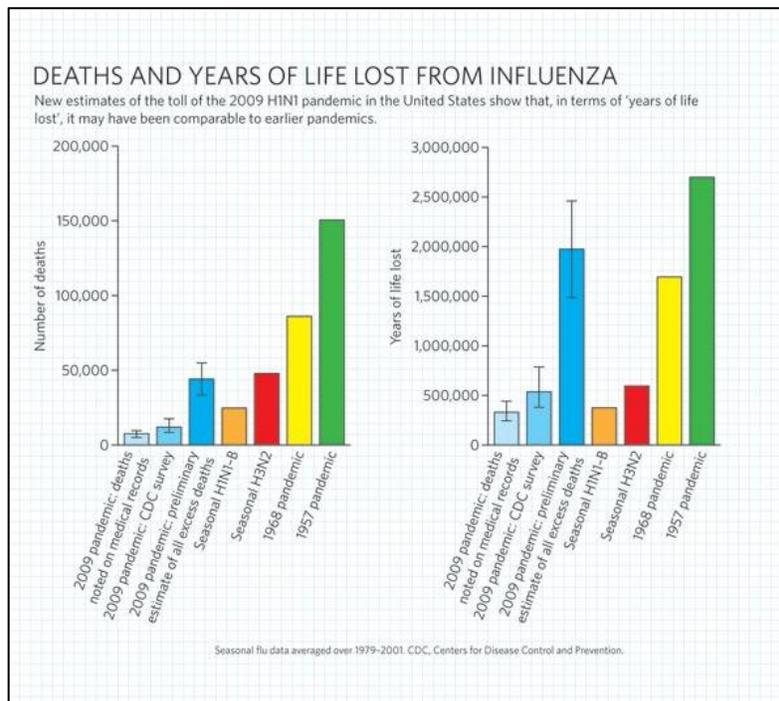
MORTALITY IMPACT OF PANDEMIC INFLUENZA

Viboud C, Miller M, Olson D, Osterholm M, Simonsen L (Mar 2010) Preliminary estimates of mortality and years of life lost associated with the 2009 A/H1N1 pandemic in the US and comparison with past influenza seasons. PLoS Curr Influenza. RRN1153.

See also Nature commentary "Portrait of a year-old pandemic":

<http://www.nature.com/news/2010/100421/full/4641112a.html>

The on-going debate about the health burden of the 2009 influenza pandemic and discussions about the usefulness of vaccine recommendations has been hampered by an absence of directly comparable measures of mortality impact. Here we set out to generate an "apples-to-apples" metric to compare pandemic and epidemic mortality. We estimated the mortality burden of the pandemic in the US using a methodology similar to that used to generate excess mortality burden for inter-pandemic influenza seasons. We also took into account the particularly young age distribution of deaths in the 2009 H1N1 pandemic, using the metric "Years of Life Lost" instead of numbers of deaths. Estimates are based on the timely pneumonia and influenza mortality surveillance data from 122 US cities, and the age distribution of laboratory-confirmed pandemic deaths, which has a mean of 37 years. We estimated that between 7,500 and 44,100 deaths are attributable to the A/H1N1 pandemic virus in the US during May-December 2009, and that between 334,000 and 1,973,000 years of life were lost. The range of years of life lost estimates includes in its lower part the impact of a typical influenza epidemic dominated by the more virulent A/H3N2 subtype, and the impact of the 1968 pandemic in its upper bound. We conclude that the 2009 A/H1N1 pandemic virus had a substantial health burden in the US over the first few months of circulation in terms of years of life lost, justifying the efforts to protect the population with vaccination programs. Analysis of historic records from three other pandemics over the last century suggests that the emerging pandemic virus will continue to circulate and cause excess mortality in unusually young populations for the next few years. Continuing surveillance for indicators of increased mortality is of key importance, as pandemics do not always cause the majority of associated deaths in the first season of circulation.



A Selection of Recent MISMS Publications

For the full list of MISMS publications, visit <http://origem.info/FIC/Bibliography.html>

Influenza virus evolutionary patterns

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Pandemic influenza

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Influenza vaccine benefits and control strategies

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Influenza transmission dynamics

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Influenza disease burden in the tropics and temperate climates

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- Gordon A, Videia E, Saborio S, López R, Kuan G, Reingold A, Balmaseda A, Harris E (Nov 2009) Performance of an influenza rapid test in children in a primary healthcare setting in Nicaragua. PLoS One. 4(11): e7907.

Announcements

Join us at the 2010 “Options for the Control of Influenza VII” Conference!

September 3-7, 2010, Hong Kong Convention and Exhibition Center, Hong Kong, China

For more information, visit: <http://www.controlinfluenza.com/>

The Options conference series is held approximately every three years and is the largest meeting that brings together scientists working on all aspects of influenza, from basic science to healthcare policy. Options for the Control of Influenza will celebrate its 25-year anniversary since its inception and first meeting in Keystone, Colorado in 1985. The influenza situation today is far more complex and demanding with the advent of the first pandemic declared in 25 years. Options has a history of strong scientific content, and the 2010 meeting will continue this tradition of answering the call for the latest scientific information on ALL aspects of influenza. The goal of Options VII is to showcase recent advances in the basic science and control and prevention of influenza. All attendees are invited to experience the heritage and cultural diversity of Hong Kong.

Save the Date: A Practical Short Course on Mathematical Modeling of Infectious Diseases: Preparedness and Response for the 2009 Influenza Pandemic

September 8-9, 2010, The University of Hong Kong Telemedicine Center, Faculty of Medicine Building, Hong Kong, China

For more information, visit: <http://sph.hku.hk/shortcourse/>

Mathematical modeling of infectious diseases has been extensively used to inform policymaking of epidemic control in recent decades (e.g. SARS, foot and mouth disease, influenza). In particular, infectious disease modeling has played a key role in advising countries on their influenza pandemic preparedness planning as well as public health response to the 2009 influenza A/H1N1 pandemic. In this short course, we will give introductory lectures on the mathematical and statistical techniques used in the research of influenza pandemic preparedness and research. We have also invited key members of national public health agencies from China, Hong Kong, Singapore, and the United States to share with us their experience and insights from the 2009 influenza pandemic.

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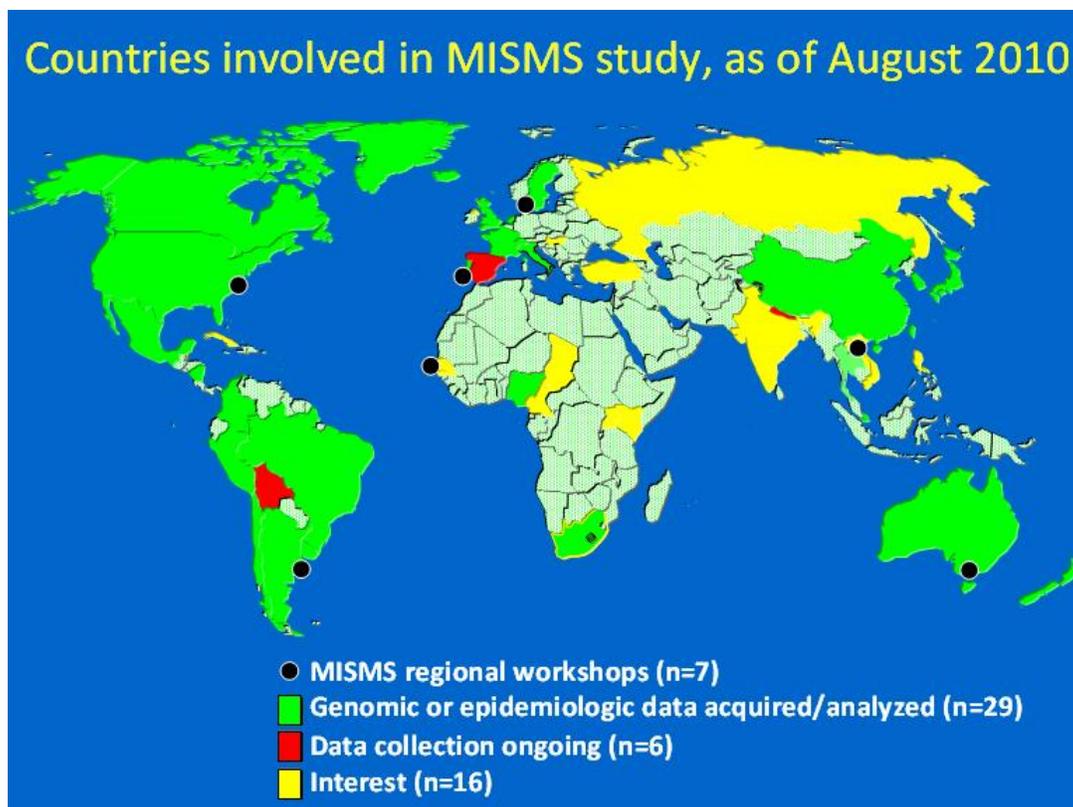
MISMS Overview

Originally called the Multinational Influenza Seasonal Mortality Study, MISMS was initiated in 2001 to analyze national and global mortality patterns associated with influenza virus circulation. The focus of MISMS has since expanded to include evaluating the interaction between the epidemiology, ecology, and evolutionary dynamics of influenza, including natural selection, reassortment, migration, and antigenic change.

MISMS has two specific aims:

1. To analyze the transmission patterns of influenza viruses, quantify time trends and geographical variations in age-specific disease burden, and evaluate control strategies.
2. To understand the interaction between the health impact and the antigenic, genomic, and evolutionary characteristics of influenza viruses in human, avian, and swine populations.

Global map of MISMS participants and regional meetings:



For more information about MISMS, our publications, and our upcoming meetings, visit our website: <http://origem.info/misms>

