

Centers for Disease Control and Prevention

Influenza Division International Activities



Fiscal Years
2012 & 2013

Acknowledgement

The U.S. Centers for Disease Control and Prevention's (CDC) Influenza Division would like to acknowledge the World Health Organization (WHO) and Regional Offices, the National Influenza Centers and all of our influenza surveillance cooperative agreement partners for their dedication and determination to establish, expand and maintain seasonal and pandemic influenza surveillance, locally and globally. Their notable efforts and contributions have significantly increased laboratory and epidemiologic capacity for the world to respond better to pandemic and other emerging infectious disease threats. Their collective work has contributed to greater global health security.

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Cover Photo Credit

Surveillance officer preparing to perform a nasal swab on a child at a sentinel surveillance site in Abidjan, Cote d'Ivoire. Courtesy of Thelma Williams, MPH, Project Officer, CDC/NCIRD/Influenza Division (Atlanta, GA).

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INFLUENZA DIVISION INTERNATIONAL OVERVIEW



Background

The U.S. Centers for Disease Control and Prevention's (CDC) Influenza Division has a long history of supporting the World Health Organization (WHO) and its global network of National Influenza Centers (NIC). With limited resources, most international assistance provided in the early years was through hands-on laboratory training of in-country staff, the annual provision of WHO reagent kits (produced and distributed by CDC), and technical consultations for vaccine strain selections. The Influenza Division (at that time, the Influenza Branch) also conducted epidemiologic research including vaccine studies and serologic assays and provided international outbreak investigation assistance.

In 1997, the first human cases of influenza A (H5N1) were reported in Hong Kong, and the Influenza Division played a key role in assisting with the outbreak investigations. The re-emergence of fatal human cases of avian influenza A (H5N1) in China in 2003 following the outbreak of SARS, followed by human outbreaks caused by highly pathogenic avian influenza A (H5N1) viruses in Vietnam and Thailand in 2003 and 2004 led to a growing concern that a pandemic of influenza may emerge. These outbreaks highlighted several important gaps that needed to be closed to improve the ability to rapidly identify novel influenza viruses with pandemic potential. These included:

- conspicuous geographic gaps in human influenza surveillance.
- critical gaps in information, laboratory and epidemiologic training and technology transfer for rapid identification and analysis of avian influenza viruses in many affected countries.
- longstanding obstacles and gaps in the sharing of information, resources and specimens between agriculture and human health authorities.

These events fostered the beginning of a larger international program to improve global pandemic preparedness and enhance capacity for laboratory and epidemiologic surveillance of influenza and avian influenza.

In 2004, the U.S. government (Health and Human Services (HHS)/CDC) committed resources and developed a multi-faceted approach to support global capacity for seasonal influenza and pandemic preparedness. Support was made available through cooperative agreements to enhance the existing support to WHO's Global Influenza Program (GIP) and WHO's regional offices. Substantial support was also provided to Ministries of Health in high-risk countries to enhance influenza surveillance and response capabilities. These cooperative agreements, paired with technical assistance, support the provision of training, staffing, direct assistance, supplies and reagents, formed the foundation for CDC's expanded role in international influenza control and prevention. The program accomplishes key goals by building on existing programs and infrastructure including WHO and its regional offices, CDC Global Disease Detection (GDD) sites and International Emerging Infections Program (IEIP) sites, Department of Defense (DOD) international program sites, and by utilizing the assistance of U.S. Embassies.

In April 2009, the first case of pandemic 2009 H1N1 influenza virus infection in the United States was identified. Subsequent cases were quickly identified in Mexico and other states. The influenza virus identified in these early cases was unique and contained a combination of gene segments that had not been previously reported in animals or humans. The 2009 H1N1 pandemic allowed many countries with cooperative agreements to showcase the progress they have made in the last few years. First-time investigations of influenza were conducted in response to the pandemic and labs that previously could not identify influenza virus were able to diagnose pandemic 2009 H1N1 using molecular techniques. Many countries that previously had not reported influenza routinely were able to report consistently and contribute to the global picture of influenza epidemiology during the pandemic. The global surveillance and response capacity built before the pandemic of 2009 was critical to the rapid global response and disease prevention.

Over the past nine years the program has undergone remarkable growth [see Maps] and has expanded to provide support to over 50 countries, all WHO regional offices and WHO Headquarters. Partnerships have been developed with the DOD, United States Agency for International Development (USAID), Biosecurity Engagement Program (BEP), universities, nongovernmental organizations, private industry and other entities to enhance global surveillance and preparedness. Over 20 staff have been placed in the field [see Map] to provide on-the-ground assistance and support to countries and to WHO, and to augment the GDD Program and DOD field sites.

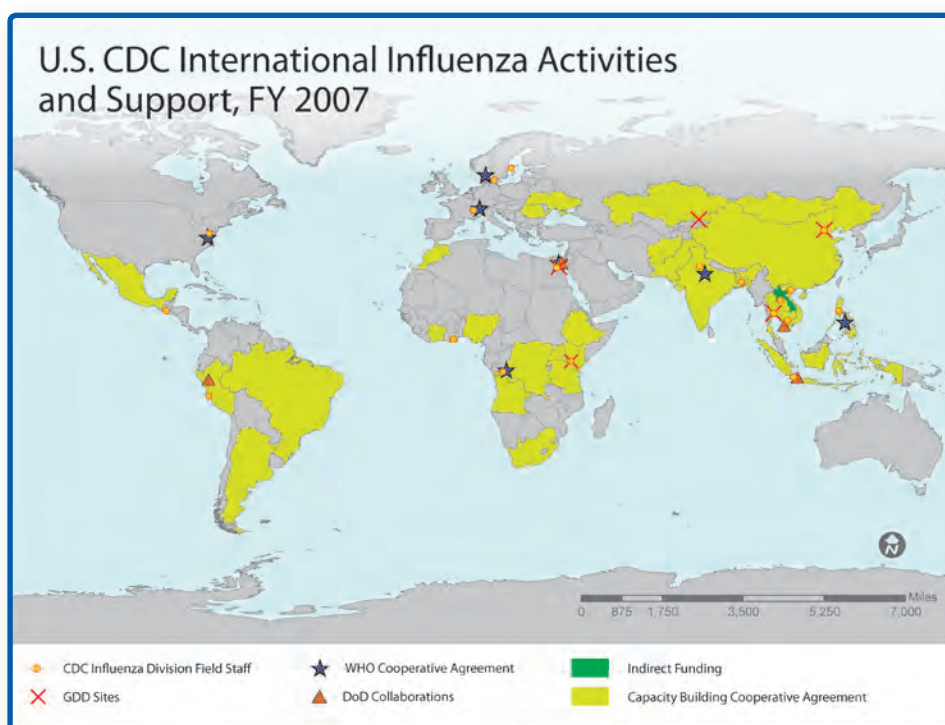
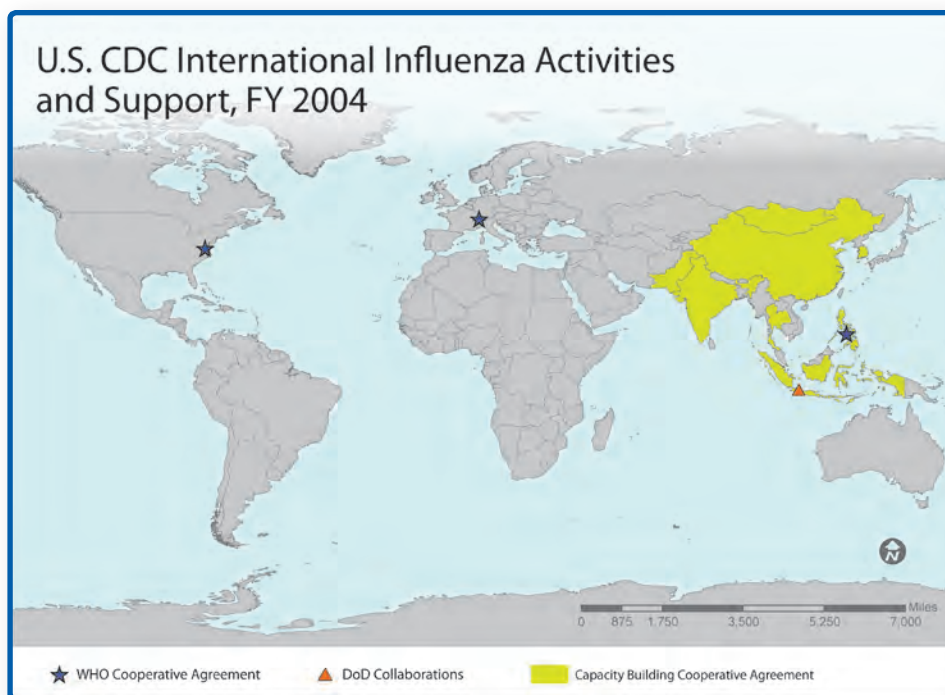
Recognizing that needs vary by countries, the program is designed as a continuum to include: improvements to surveillance, efforts to enhance pandemic preparedness, implementation of burden of disease studies to measure the impact of influenza, and studies to determine the effectiveness of intervention measures such as vaccination. With the data generated through surveillance, each country can determine which populations are most vulnerable to influenza-related morbidity and mortality and who should receive influenza vaccine. Based on surveillance and other analyses, influenza vaccination policy and issues related to vaccine production can be approached on a country-by-country and a regional basis. In 2010, we embarked on placing more emphasis on the development of data to help countries evaluate the need and feasibility of vaccine policy. In 2011, CDC entered a partnership with WHO's Global Action Plan for Influenza Vaccine, towards expanding prevention of global disease and improving health security through greater use of influenza vaccines worldwide.

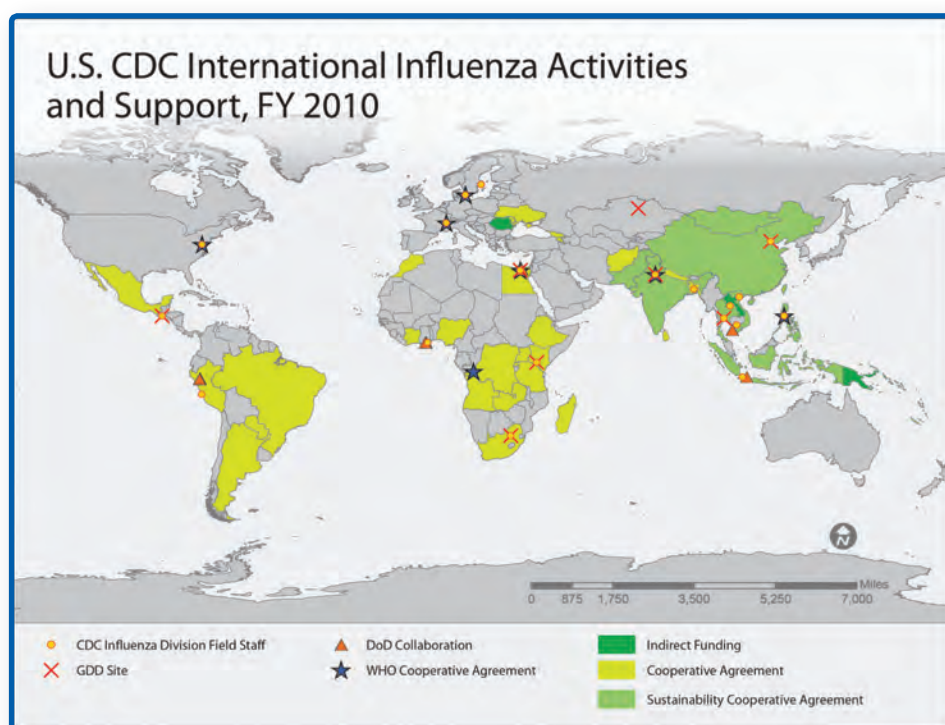
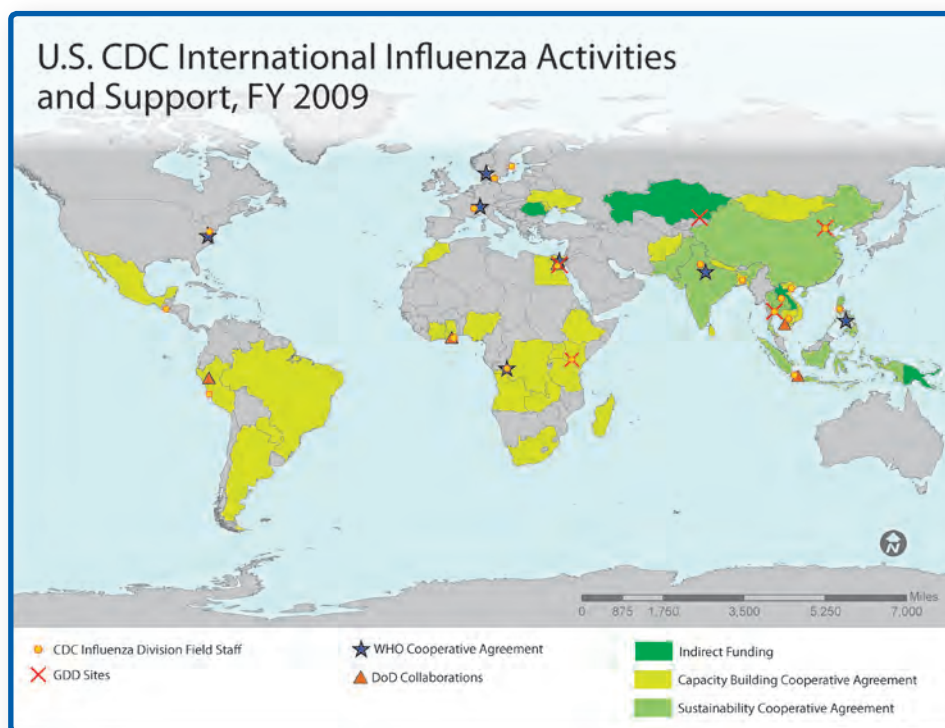
While the response to the 2009 H1N1 pandemic was an opportunity to show recent progress, avian influenza H5N1 outbreaks still pose a significant and ongoing global health threat and a threat to U.S. security. To sustain the gains made in the past years, a broad-based commitment to build and maintain influenza surveillance globally that is sustainable (and eventually self-sustainable) requires dedicated, annualized resources and staffing. It is our hope that these HHS/CDC resources and technical assistance will act as a catalyst for affected countries, neighboring countries and donor countries to commit resources to establish long-term influenza surveillance, prevention and control, and pandemic preparedness activities as high priorities. We also envision that each affected country will utilize the technical assistance and resources available to improve surveillance, develop influenza vaccination policy, make plans for the use of influenza vaccine both annually and during a pandemic, and work closely with regional and international partners to further preparedness.

This program has implications beyond influenza. The capacity being developed for laboratory and epidemiologic surveillance of severe respiratory disease has served as the basis for capacity for the diagnosis and investigation of other infectious diseases, particularly other respiratory pathogens.

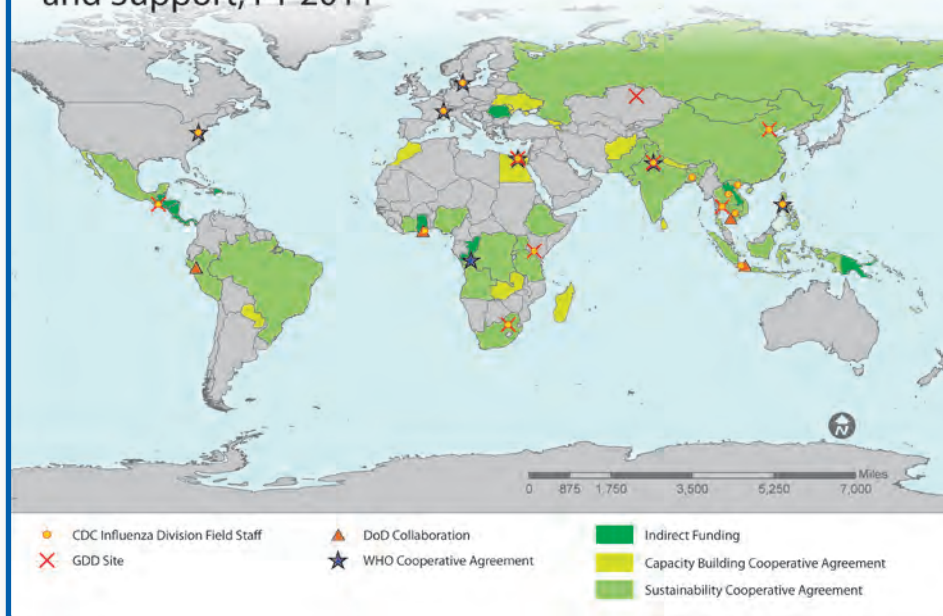
Laboratory equipment and training has enabled the diagnosis and investigation of other diseases. Likewise, through the implementation of a global rapid response training program, CDC has provided training and materials for thousands of people in all WHO regions. These courses have enabled the trained teams to participate in outbreaks not only for the recent pandemic but for other respiratory diseases and many other pathogens including Rift Valley fever, dengue, cholera, Ebola and rabies. Evidence shows that the technical assistance provided by the Influenza Division is assisting countries in increasing their capacity necessary for compliance with the new International Health Regulations 2005 (IHR). The generic approach, with a focus on influenza and avian influenza, contributes greatly to global capacity for laboratory, epidemiology and overall preparedness for emerging and re-emerging infectious diseases. Efforts are underway to plan for the sustainability of the gains that have been made. This report is the fifth update on the Influenza Division's international activities and encompasses fiscal years 2012 and 2013.

Maps

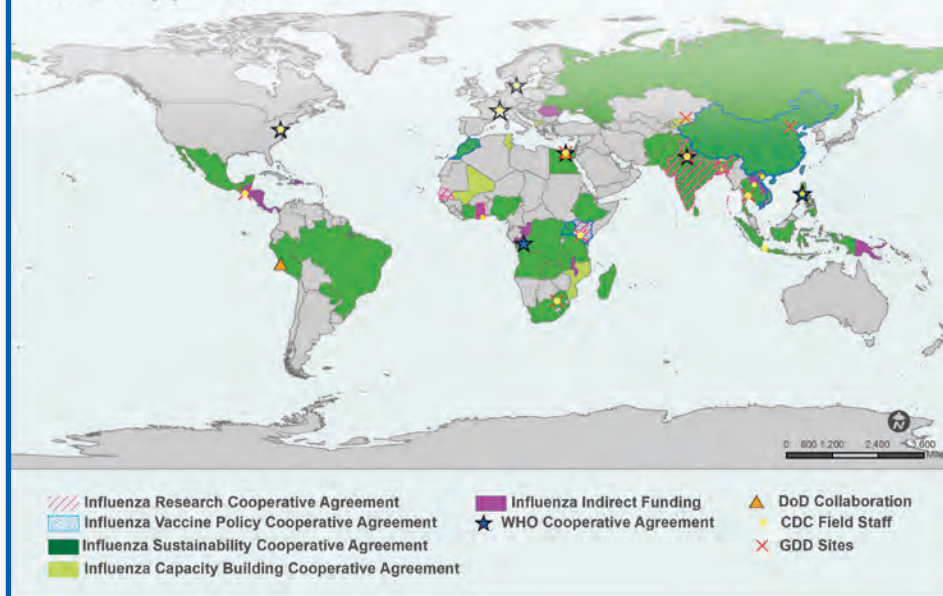




U.S. CDC International Influenza Activities and Support, FY 2011



U.S. CDC International Influenza Activities and Support, FY 2013



U.S. CDC and WHO Collaborations— Influenza

The HHS/CDC Influenza Division has maintained cooperative agreements with WHO Headquarters and the WHO Pan American Health Organization (PAHO) and the Regional Office for the Western Pacific (WPRO) for many years to address seasonal and pandemic influenza. In 2006, new cooperative agreements were put in place with the WHO Regional Office for South-East Asia (SEARO), the Regional Office for Africa (AFRO), the Regional Office for the Eastern Mediterranean (EMRO) and the Regional Office for Europe (EURO). The main purpose of the cooperative agreements is to address global and regional preparedness for influenza—both seasonal and avian—through support to enhance the WHO Global Influenza Surveillance and Response System (GISRS), and technical support to countries' influenza prevention and control programs. This effectively increases the number of countries participating in the global system and more importantly enhances the early warning capacity and communications so there is a greater chance for early identification of a pandemic.

Recently, we have expanded our focus to also support efforts to increase influenza prevention through vaccination globally. Greater use of influenza vaccines will reduce the burden of influenza every year, but also provide a greatly expanded base of timely vaccine manufacturing to be used during pandemic influenza. Towards this goal, we have supported activities that will develop the evidence for use of vaccines globally and in partner countries. Activities include supporting partners to develop estimates of influenza-associated disease and cost burden, projects to understand the effectiveness of influenza vaccines in special populations relevant to policy expansion, and supporting countries' policy making bodies. Information about the project activities for the regional offices is integrated under the specific regions. CDC's Influenza Division provided funding and technical support to WHO Headquarters annually for multiple projects related to influenza, outlined below.

Activities supported through WHO

Influenza Laboratory Surveillance

- Strengthening of global influenza laboratory surveillance through improved diagnostic capacity and enhanced shipping capacity of influenza viruses/specimens to WHO Collaborating Centers (WHO CC).
- Strengthening global coordination and communication of GISRS by conducting periodic National Influenza Center (NIC) surveys and feeding results of the analysis into a NIC meeting with all regions.
- Supporting NICs to attend the WHO vaccine composition consultations in September and February to support this goal.

Influenza Epidemiology and Surveillance

- Strengthening influenza monitoring at the global level including development of automated analysis and visual presentation tools.

- Developing a risk assessment tool.
- Supporting developing countries in risk assessment and response.
- Supporting countries in the development of influenza surveillance systems and assessment of disease burden to inform vaccine and antiviral use decisions.
- Developing estimates of influenza deaths during seasonal epidemics and pandemics.
- Developing a tool for community-level risk assessment for H5N1 infection in collaboration with OIE (World Organisation for Animal Health) and FAO (Food and Agriculture Organization of the United Nations).

Strengthening Influenza Pandemic Preparedness and Response Planning

- Review of national pandemic assessment and development of lessons learned to revise pandemic preparedness guidelines.
- Review of:
 - » measures and indicators of severity during a pandemic.
 - » the concept of pandemic phases for decision-making.
- Maintenance and improvements to the digital library.

Public Health Leadership and Global Coordination

- Provision of technical guidance and support to member states for—
 - » development of coordinated pandemic preparedness initiatives.
 - » developing future strategies aligned with WHO Headquarters and regional office guidance for global pandemic preparedness with a view toward long-term public health capacity and compliance with IHR.
- Dissemination of guidance:
 - » to minimize social and economic disruption.
 - » to other United Nations agencies and programs.

Seasonal Influenza Vaccine Introduction

- Collection and dissemination of information on influenza vaccine availability and utilization.
- Assurance of quality and safety of influenza vaccines by visiting manufacturing sites and technical reviews of production procedures.
- Support for influenza vaccination policy through the development of mathematical models to estimate potential public health impact of various vaccine introduction strategies and potential impact of vaccine introduction on mortality among children younger than 5 years old.
- Capacity development and facilitation of influenza vaccine policy in WHO Regions.
- Support of WHO's Strategic Advisory Group of Experts to update global vaccine recommendations.
- Support of WHO's Global Action Plan for Influenza Vaccines to expand the availability of influenza vaccines globally.

Influenza Reagent Resource (IRR)

The Influenza Reagent Resource (IRR) was established by the U.S. CDC to provide registered users with reagents, tools and information for studying and detection of influenza virus. The IRR acquires, authenticates, and produces reagents that scientists need to carry out basic research and develop improved diagnostic tests, vaccines, and detection methods. Public health labs also use the reagents across the globe for the surveillance of newly emerging strains of influenza, such as H1N1 and H5N1. By centralizing these functions within the IRR, access to and use of these materials in the scientific and public health community is monitored and quality control of the reagents is assured.

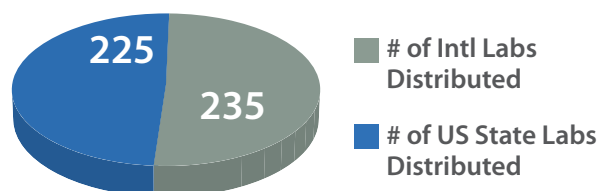
The roles of IRR in pandemic preparedness and influenza research are:

- To manufacture and distribute influenza diagnostic kits, viruses, and reagents to public health, commercial, domestic, and international research laboratories.
- To improve pandemic preparedness, enhance detection and control of seasonal influenza, and provide better access to reagents via a secure, web-based system.
- To augment CDC's international pandemic preparedness plan to provide a surge option (~\$10+ million per year) which can be exercised to distribute reagents and diagnostic kits to domestic and international public health laboratories.

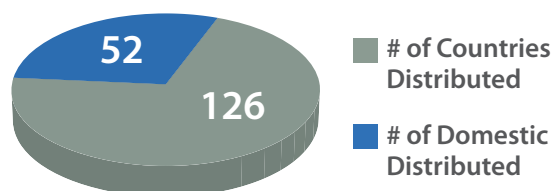
CDC and IRR responded quickly to the recent H7N9 activity and continued to provide reverse transcriptase polymerase chain reaction (RT-PCR) seasonal influenza diagnostic kits, ancillary reagents, reference viruses and other materials. In FY12–13 alone, IRR distributed to 126 countries supporting more than 230 international laboratories. These kits and reagents were also provided to more than 220 public health laboratories domestically in 50 states and territories.

Worldwide Distribution of Reagents:

Shipments to Laboratories

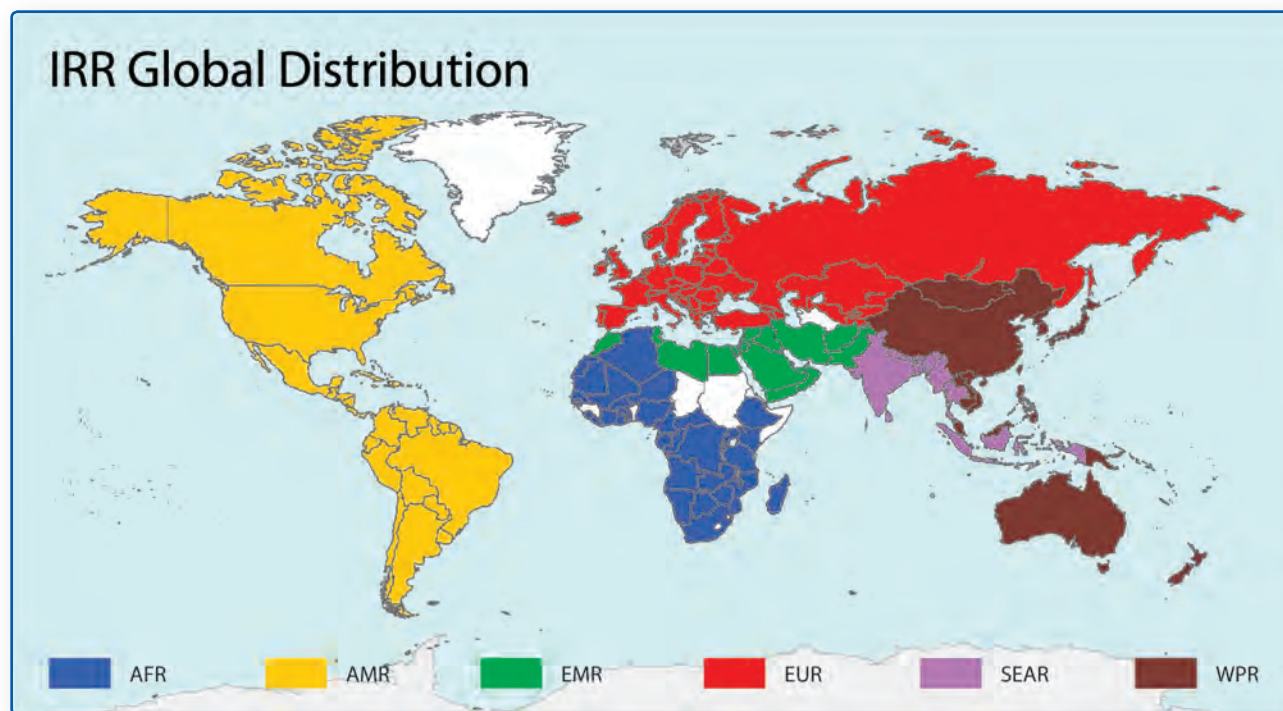


Shipments to Countries and US States



Example Product Shipment Levels:

Example Products	Total Kits International	Total Kits in U.S.	Total Kits
H7N9 RT-PCR Kit	103	76	179
Seasonal RT-PCR Kits (type, sub, H5)	546	436	982
WHO Reference Kit	225	76	301



A map of IRR's distribution of diagnostic kits and reagents to countries/regions.

The IRR website is live and displays over 700 different reagents and kits available to the public health labs globally. Fluorder@cdc.gov remains active for labs experiencing technical difficulties or special circumstances. A major registration campaign was undertaken over the past year and has led to the vast majority of orders being placed electronically on the website. Enhancements were also made to allow dual login for those researchers collaborating on special projects, making ordering and tracking reagents for the projects versus the normal surveillance activity orders easier to view and approve.

The IRR is providing better access to quality influenza-related reagents by manufacturing and distributing influenza viruses a la carte and as panels, recombinant proteins, antisera, monoclonal antibodies, ribonucleic acid (RNA) standards, non-influenza respiratory pathogens and more. Institutions that have access to these reagents are qualified domestic and international WHO NICs and public health laboratories, commercial test developers, vaccine manufacturers, and research institutions.

WHO AFRICAN REGION (AFR)

WHO African Region (AFR) Overview

Currently there are 13 bilateral cooperative agreements in the sub-Saharan region of Africa for the building of sustainable surveillance. These agreements are with ministries of health or institutions designated by a country's Ministry of Health (MOH) to work with the U.S. Centers for Disease Control and Prevention (CDC).

In addition, CDC's direct assistance also supports additional countries through our existing bilateral agreements to support neighboring countries interested in building their surveillance systems.

CDC direct country support via non-research cooperative agreements is established in the following countries:

- Angola
- Democratic Republic of Congo
- Ethiopia
- Madagascar
- Mali
- Mozambique
- Nigeria
- Republic of Côte d'Ivoire
- Rwanda
- South Africa
- Tanzania
- Uganda
- Zambia

In addition, CDC supports the World Health Organization (WHO) Regional Office for Africa (AFRO) via a cooperative agreement.

The core activities of our bilateral agreements and technical assistance are:

- To build sustainable national capacity for seasonal influenza, pandemic influenza and other emerging diseases and preparedness for implementation of International Health Regulations (2005).
- To make routine contributions of surveillance data to WHO's Global Influenza Surveillance and Response System (GISRS).
- To increase the geographic reach of WHO GISRS.
- To provide early access to critical virus isolates from humans and birds for WHO GISRS.
- To increase the quantity of shipments and influenza isolates provided by African influenza laboratories for analysis by WHO Collaborating Centers.
- To develop sustainable epidemiologic and virologic surveillance systems for severe influenza, in order to gain an understanding of the burden of disease from influenza in the WHO African Region.

In addition to our bilateral work, we also partner with:

- The U.S. Naval Medical Research Unit No. 3 (NAMRU-3) in Accra, Ghana to jointly support the following West African countries in building influenza surveillance: Burkina Faso, Mali, Mauritania, and Togo.
- Institut Pasteur in Paris, France to support activities in Cameroon, Central African Republic, and Senegal.

- World Health Organization in Geneva, Switzerland and the U.S. Agency for International Development to support activities in Burkina Faso, Malawi, Mozambique, and Republic of Congo.
- The Indian Ocean Commission in Port Louis, Mauritius to enhance surveillance in Mauritius and build capacity in the Seychelles.

CDC expanded its cooperative agreement portfolio in 2013 to include two new cooperative agreements with Kenya and Uganda to introduce or expand the use of seasonal influenza vaccines by public health programs outside the United States. Core activities of the agreement include: conducting a needs assessment to identify barriers, developing a three-year action plan to introduce vaccines, implementing the plan and introducing or expanding vaccine use to the target population through a national policy.

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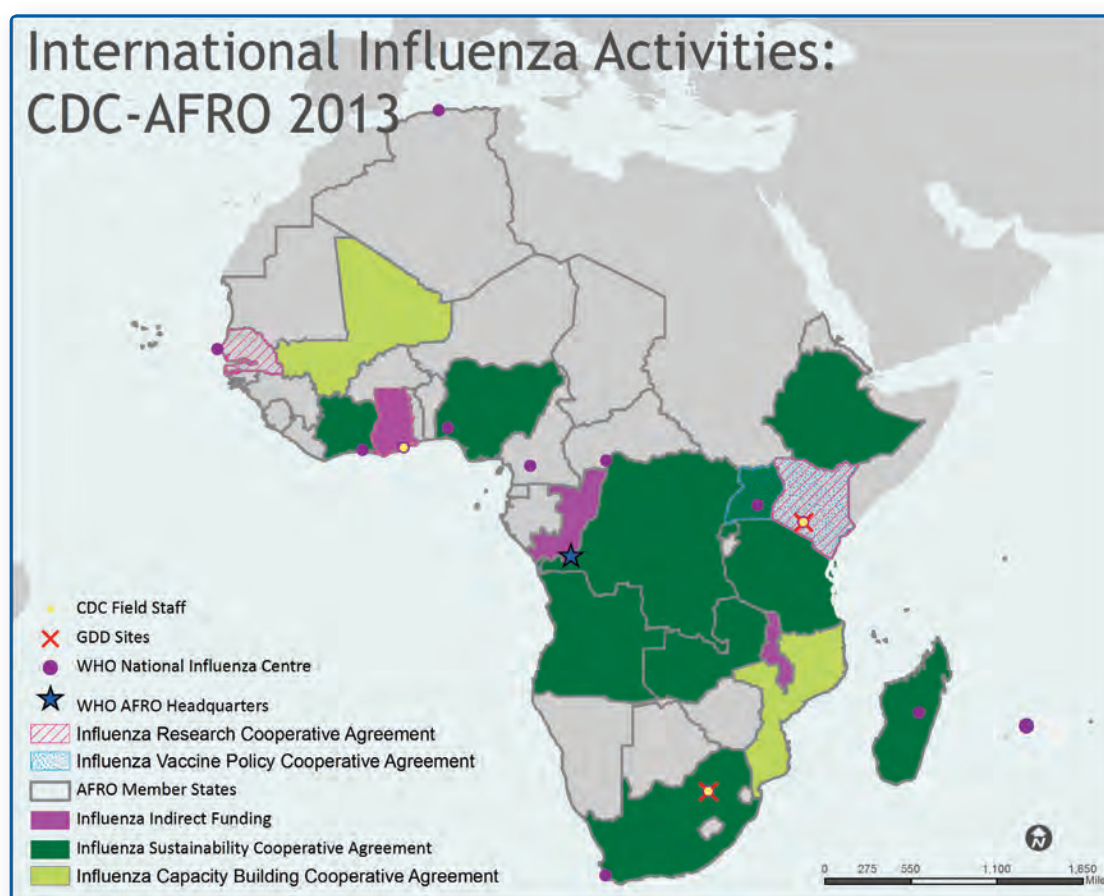
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WHO Regional Office for Africa (AFRO)



Highlights

- Supporting island countries in the Indian Ocean to adapt the sentinel surveillance protocol.
- Expanding the Influenza Laboratory Network in the WHO African Region.
- Collaborating with CDC for providing primers to the AFR Influenza Laboratory Network for detection of A(H7N9) by PCR.
- Countries supported to use the infrastructure of influenza reference laboratories for confirmation of MERS-CoV.
- Maintaining weekly data on virological surveillance of influenza in FluNet.
- Sustaining performance of the External Quality Assurance Programme (EQAP) of the AFR influenza laboratory network.

U.S. CDC Direct Support

The five-year cooperative agreement “Surveillance and Response to Seasonal and Pandemic Influenza by the World Health Organization Regional Office for Africa” began on September 30, 2011 and is in its second year of implementation. The WHO Regional Office for Africa (AFRO) is located in Brazzaville, Republic of Congo. The Office serves 47 countries of which 30 are targeted by this project. In 2013, WHO AFRO staff

provided support to countries in the Region through on-site training, review of protocols, strengthening laboratory capacity through provision of laboratory reagents and equipment and hands-on training sessions for selected laboratories.

WHO AFRO staff and consultants are providing standardized guidelines and protocols, on-site training on both epidemiological and virological surveillance of influenza.

Support has been provided in form of technical assistance to member countries to strengthen surveillance, preparedness, and response to priority diseases but with a special focus on influenza-like illnesses (ILI) and severe acute respiratory infections (SARI).

Countries within the network are regularly supplied with laboratory equipment and reagents thus enhancing and sustaining diagnostic capacity for influenza in the region.

Surveillance

The WHO/AFRO Protocol for National Influenza Sentinel Surveillance has been disseminated to Member States and was adapted by Zimbabwe for the local context. In addition, island nations of the Indian Ocean—namely Comoros, Madagascar, Mauritius, Seychelles and Reunion—were trained on the new protocol and are being supported to develop/update their protocols using the WHO generic protocol. Countries are continuing to report the epidemiologic characteristics of ILI and SARI using Integrated Disease Surveillance and Response (IDSR) as a platform.

Surveillance Activities

- Disseminated the WHO/AFRO protocol for National Influenza Sentinel Surveillance.
- Adaptation of the protocol for National Influenza Sentinel Surveillance by Zimbabwe.
- Conducted the following key activities: site visit to assess needs and necessary adjustments, support organization of national workshops for adaptation of the WHO generic guideline to the local context, on-site training at the sentinel sites using the adapted protocol and regular teleconferences to troubleshoot any identified bottlenecks.
- Continued support and guidance through teleconferences to Burundi, Malawi, Mozambique, Republic of Congo and Sierra Leone to kick-start epidemiological surveillance activities after providing onsite-visits and training on epidemiological surveillance of influenza.

Laboratory

As of August 2013, the Regional Influenza Laboratory Network is comprised of National Influenza Reference Laboratories in 30 countries. Thirteen laboratories from 12 countries are registered as National Influenza Centres (NIC)—Mauritius has been designated recently. Burundi, Malawi, Mozambique, Republic of Congo, Sierra Leone and Zimbabwe have been supported to enhance capacity for virological surveillance of influenza. The laboratory in Tanzania will soon be designated as NIC. The members of the Influenza Laboratory Network are sharing weekly data on virological surveillance of influenza (Mozambique and Republic of Congo started sharing weekly data on influenza). Between week one and week thirty-one in 2013 [AFRO weekly data updated on August 4, 2013], the networking labs tested 26,568 specimens for influenza and found that 3,756 (14%) were positive for influenza. Of the 1,100 influenza viruses detected in the Region, 65% were identified as influenza A and 35% were identified as influenza B. Of the influenza A viruses that were subtyped, the A (H1N1)pdm09 was the predominant subtype.

Laboratory Activities

- Joined the EQAP for influenza laboratories (Republic of Congo). As a result, the performance on influenza EQAP for 27 laboratories in 25 countries is being monitored.
- Supported six countries (Burundi, Malawi, Mozambique, Seychelles, Sierra Leone and Zimbabwe) in maintaining virological surveillance of influenza through provision of reagents and supplies for specimen collection and conducting PCR.
- Provided Mauritius and Seychelles with equipment (real time PCR machines) and Seychelles, in addition received a Biosafety Cabinet. Burundi received a real time PCR machine through USAID and is being supported on Biosafety Cabinet Level 2, microcentrifuge eppendorf and micropipettes. On-site training on PCR including collection and handling of specimens in selected sentinel sites was conducted in Burundi, Mozambique, Republic of Congo and Sierra Leone. Zambia is being provided with reagents for virus isolation and training will be done in close collaboration with the National Institute for Communicable Diseases (NICD) in South Africa once the reagents are received by the laboratory.

Preparedness

WHO/AFRO in collaboration with partners is finalizing the development of a framework for supporting countries to develop comprehensive epidemic and pandemic preparedness plan that will include acute infectious respiratory diseases.

Preparedness Activities

- Through the CDC project and Emerging Pandemic Threats (USAID) program, collaboration between human and animal health strengthened for joint surveillance and outbreak investigation including influenza public health risks at the human-animal interface.

Training

- Trained scientists from influenza laboratories in Burundi and Sierra Leone on conducting real-time PCR in Rwanda and Ghana respectively.
- Participated in the training on influenza organized for the Indian Ocean Island nations of Comoros, Madagascar, Mauritius, Seychelles and Reunion.
- Participated in the retraining of the Zimbabwe sentinel surveillance staff.

Published Papers

JOB AIDS for collection, storage and transport of specimens for laboratory confirmation of Middle East Respiratory Syndrome coronavirus (MERS-CoV): available in English, French and Portuguese on the WHO AFRO Website.

Kebede S, Conteh I, Steffen C et al. Establishing a national influenza sentinel surveillance system in a limited resource setting, experience of Sierra Leone. *Health Research Policy and Systems* 2013, 11:22.

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Angola



Capital: *Luanda*

Infant Mortality Rate: *81.75/1,000 live births*

Population: *18,565,269 (July 2013 est.)*



Overview

Acute respiratory disease is one of the major causes of morbidity and mortality within the Angolan population and the country is classified at high risk for infection and spread of avian influenza within the Pandemic Risk Index (PRI) scale. The Republic of Angola has been collaborating with the U.S. CDC on influenza control since 2006 through the Cooperative Agreement (CoAg) for avian influenza. The National Institute of Public Health (INSP) is the Central Reference Laboratory (CRL) of the Ministry of Health (MoH). Notably, influenza laboratory diagnosis capacity has improved since the beginning of the collaboration. The agreement has also enhanced the general level of preparedness and response capacity for influenza and other emerging diseases in Angola.

In 2011, the country was approved for a new five year CoAg. The current proposal was submitted by the National Public Health Directorate (DNSP) on behalf of the Ministry of Health to strengthen the existing influenza surveillance system, initiated during the previous cooperative agreement. Last year's performance was affected by lack of laboratory consumables due to insufficient funds.

Highlights

- Created two new sentinel sites (Municipal Hospital of Cazenga and Samba).
- Conducted regular data analysis meetings with the data manager, senior and junior epidemiologists and the virologist.
- Conducted TWG (Technical Work Group) meetings.

Surveillance

The country has been able to implement one fully operational sentinel site— Pediatric Hospital David Bernardino (HPDB) in the capital city, Luanda. During this period, two new sentinel sites (municipal hospitals of Cazenga and Samba) have been created in the province of Luanda. We updated the case definitions for influenza-like illness (ILI) and severe acute respiratory illness (SARI) in accordance with WHO guidelines. ILI and SARI were incorporated in the list of notifiable diseases. A student from the Field Epidemiology and Laboratory Training Program (FELTP) was integrated in the TWG to monitor the new sentinel sites. A database in Epi Info 7 was developed for the registration of epidemiological and laboratory data.

Surveillance Activities

- Educated laboratory focal points and emergency room hospital staff at the following sentinel sites, Hospitals Américo Boavida and Josina Machel about the importance of sample collection.
- An FELTP student conducted sensitization meetings for doctors, nurses, and laboratory technicians from Hospital Josina Machel (sentinel site) on the importance of sample collection from all suspect cases.
- Developed a check list for sentinel site supervision.
- Notified and received samples for 292 cases (142 female and 150 male) of ILI by HPDB.
- Requested sample collection and diagnosis material from WHO AFRO, through the WHO local office.

Laboratory

- Due to lack of reagents, samples from HPDB are not being tested at this time.

Training

- Trained laboratory technicians at the new sentinel sites (two for each unit).
- Participated in the CDC Grants Management Training (Principal Investigator and Finance Focal Point).
- Attended the Data Management and Basic Epidemiologic Analysis for Influenza Training Course in Johannesburg, South Africa, November 2011.
- Attended the 3rd Annual African Network for Influenza Surveillance and Epidemiology (ANISE) Meeting in Nairobi, Kenya, February 2012.

Publications

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Democratic Republic of Congo



Capital: Kinshasa

Infant Mortality Rate: 74.87/1,000 live births

Population: 75,507,308 (July 2013 est.)



Overview

CDC provides financial and technical assistance to the Ministry of Health (MoH) through the Kinshasa School of Public Health. The strategy is to develop an efficient and sustainable surveillance system which eventually will be funded and maintained by the national government of Democratic Republic of Congo (DRC). An enhanced routine surveillance system currently collects information used to estimate the national influenza burden. The system reports regular surveillance findings to the WHO Global Influenza Surveillance Network. In 2011, the surveillance system expanded to the neighboring country, Republic of Congo, and will expand to two additional provinces in DRC by the end of 2013.

Highlights

- Conducted a review of the surveillance system implemented during the previous five years project.
- Developed a sustainability plan for the national surveillance system.
- Maintained a routine influenza surveillance system that collects, analyzes and reports quality epidemiologic and virologic data.
- Disseminated surveillance findings including participating fully in the Global Influenza Surveillance and Response System (GISRS).

Surveillance

In DRC, the MoH 4th Directorate has instituted an integrated disease surveillance system, which provides routine reporting on 13 diseases that have epidemic potential, including influenza. This weekly surveillance is done in collaboration with the National Institute of Biomedical Research (INRB). Thanks to support from the CDC, the influenza sentinel surveillance system has been functional since 2006. Staff from sentinel sites identify suspect cases of influenza and take samples that are sent to INRB within 72 hours. INRB conducts analysis and writes weekly virological reports that are disseminated to all stakeholders, including sentinel site staff. The MoH 4th Directorate ensures the coordination of the sentinel surveillance activities and disseminates weekly reports.

Surveillance Activities

- Developed standard data collection tools and standard weekly reports which include virologic and epidemiologic data.
- Selected five new sentinel sites: two in Bas-Congo, two in Katanga and one in Kasai-Oriental. DRC's influenza sentinel surveillance system now has ten sentinel sites: two ILI specific sites and eight ILI and SARI sites.
- Notified and received samples for 4,437 influenza suspect cases: 3,246 ILI (73.2%) and 1,191 SARI (26.8%) from October 2011 to September 2012.
- Trained sentinel site staff in 2013 on completing notification forms, sampling techniques, packaging and shipping storage.

Laboratory

INRB, the DRC National Influenza Laboratory, is currently a Level 2 Biosafety Laboratory; with efforts underway to upgrade to Level 3 designation. During the previous five year project, the lab staff were trained in influenza diagnosis using real time RT-PCR techniques. Thus, the molecular diagnosis is conducted using real time RT-PCR of Influenza types A and B; the positive samples for influenza A are later sub-typed into seasonal H1N1 and H3N2, and avian H5N1 and pandemic H1N1. Weekly reports are produced and disseminated to share virological findings with all stakeholders. Since 2009, INRB has participated in reporting to the WHO External Quality Assessment with satisfactory results. Laboratory technicians from INRB were trained in the use of QIAcube for automatic viral extraction, this training was provided by an expert from Nairobi, Kenya. INRB is participating in WHO's Global Influenza Surveillance and Response System (GISRS) by providing data through WHO electronic systems.

Laboratory Activities

- Procured reagents, lab supplies and equipment.
- Established internet connectivity for the INRB influenza team.
- Received and analyzed 1,888 samples from October 2011 to September 2012. Among them, 1,180 were ILI cases (62.5%) and 708 were SARI cases (37.5%). After analysis, 93 samples were positive for influenza viruses (4.9%): 53 positive for influenza viruses A (57.0%) and 40 for influenza virus B (43.0%). Among the 53 samples positive for influenza virus A, 48 were sub-typed as seasonal influenza virus H3N2 (51.6%) and 5 as pandemic influenza virus (5.4%).
- Produced weekly virological reports and disseminated to sentinel sites and partners.



Poultry Market at Mbuji-Mayi near Dipumba Hospital.

Preparedness

In DRC, pandemic preparedness activities are carried out by the MoH in collaboration with all partners, notably CDC and WHO. Those activities consist of investigating influenza outbreaks, immunization planning for vulnerable groups, and simulation exercises.

Preparedness Activities

- Revised immunization plan for women and children. This plan has not yet been implemented due to fear of side effects.
- Received primers for H7N9 influenza virus from CDC.
- Investigated influenza outbreaks at Kahemba in the province of Bandundu and at Kingabwa on the border of the Congo River in Kinshasa.
- Organized a simulation exercise at Kisantu in Bas-Congo Province, September 2013.

Training

- Organized a short-term training session for 50 sentinel site staff members in each of the following provinces: Kinshasa, Bas-Congo, Katanga and Kasai-Oriental.
- Trained two physicians and three lab technicians from INRB on the use of QIAcube for automatic viral extraction.
- Attended the Data Management and Basic Epidemiological Analysis Training Course for African Countries in November 2011 (Johannesburg, South Africa).

Publications

Karhemere S, Tamfumum M, Kabamba J, Wemakoy O. Evaluation of the sentinel surveillance system, Kinshasa, DR Congo, 2009–2011 [abstract].

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Ethiopia



Capital: Addis Ababa

Infant Mortality Rate: 58.28/1,000 live births

Population: 93,877,025 (July 2013 est.)



Overview

With the support of CDC, influenza surveillance in Ethiopia was initiated in 2008. The first cooperative agreement between the Federal Ministry of Health (MOH)–Ethiopian Health and Nutrition Research Institute (EHNRI) and CDC began in August 2007.

EHNRI continues to build laboratory and epidemiologic surveillance capacity to determine seasonality and burden of influenza disease in Ethiopia. EHNRI also improved capacity of laboratories to detect influenza viruses through training for laboratorians and surveillance officers. In 2009, an emergency operating center under the emergency public health management directorate was established.

Highlights

- Entered surveillance data from sentinel sites into database and descriptive data analysis was conducted by time, place, and person.
- Submitted an abstract for a poster presentation at the Options for the Control of Influenza Conference – the abstract was accepted.
- Provided alert message to public health units on H7N9 influenza.
- Distributed influenza sentinel surveillance guidelines and communication materials to sentinel sites.
- Incorporated influenza activities in Public Health Emergency Management Annual Plan.

Surveillance

Sentinel surveillance has the potential to provide more complete data about some of the epidemiologic characteristics of severe acute respiratory infection (SARI) and influenza-like illness (ILI). Ethiopia has selected 20 priority diseases with mandatory reporting. Among those required to be reported immediately are avian-human influenza, pandemic influenza, and severe acute respiratory syndrome (SARS). In Ethiopia, currently eight sentinel sites (five SARI sites and three ILI sites) are actively working. All sites have received training, laboratory supplies and budget to run influenza surveillance related operations.

Surveillance Activities

- Compiled and entered surveillance data into database using Epi-info statistical software.
- Monitored the quality of surveillance data based on gaps identified and provided feedback to the reporting sentinel sites.
- Developed weekly public health emergency management bulletin and shared with partners and government organizations.
- Conducted Influenza Technical Working Group meetings.
- Hosted a CDC Atlanta expert who visited the national surveillance unit located at the Public Health Emergency Management Center (PHEMC), national influenza laboratory, and sentinel sites to provide technical assistance and feedback.

Laboratory

The National Influenza Laboratory (NIL) at EHNRI is the only laboratory capable of influenza diagnostic testing in the country. The laboratory became functional in June 2009. The NIL has worked closely with CDC to establish a state-of-the-art laboratory. Routine testing of respiratory samples collected through the SARI/ILI sites commenced in 2009. Collaboration between human and animal health laboratory staff is also being supported.

Laboratory Activities

- Provided laboratory supplies and cost estimates for the newly selected SARI sentinel sites in four regions.
- Provided onsite technical assistance to most sentinel sites weekly.
- Received throat swab specimens from sentinel sites each week.
- Collected a total of 1,006 specimens, of which 999 were tested at NIL by PCR, with 284 testing positive for Influenza; 93 for Flu B, 63 A/seasonal H3, and 128 were influenza A (H1N1) pdm 2009.
- Reported laboratory results to WHO AFRO weekly.

Preparedness

An overhaul of the entire health sector was carried out in 2009, during which new organizational structures were set up, including PHEMC. This center is responsible for preparedness, early warning and response to any public health emergencies including avian and human influenza (AHI) and pandemic influenza. The newly established body is now situated at EHNRI in order to spearhead epidemiological surveillance of diseases and events with the EHNRI laboratory providing technical support.

Preparedness Activities

- Incorporated influenza sentinel surveillance activities in 2013/2014 Public Health Emergency Management Annual Plan.
- Conducted a training workshop in September 2013 to review annual activities and provide training on influenza surveillance to medical directors, focal persons, and surveillance and laboratory experts from different levels.
- Developed sustainability plan for influenza surveillance system.
- Printed and distributed 300 Influenza Sentinel Surveillance Guidelines to the sentinel sites.
- Printed and distributed 2,000 SARI (in English) and 4,000 ILI brochures (2,000 in Amharic and 2,000 in English) for health workers at the sentinel sites.

Training

- Provided on-site orientation to all new SARI sites on specimen collection, storage and transportation, how to report using both case-based and weekly aggregated report formats.
- Provided orientation on H7N9 for department heads and experts from regional Public Health Emergency Management Centers, Regional Public Laboratories, Disease Prevention and Health Promotion Directorates during PHEM Annual Review Meeting (April 2013).
- Provided a two day training for 40 health workers from former and newly identified influenza surveillance sentinel sites, regional laboratories and PHEM Centers (September 2013).
- Conducted technical review meeting in October 2012 to strengthen sentinel of surveillance activities.



Ambulatory patients waiting for clinical services at one of the influenza sentinel surveillance sites in Addis Ababa, Ethiopia.

Ghana



Capital: Accra

Infant Mortality Rate: 39.7/1,000 live births

Population: 25,199,609 (July 2013 est.)



Overview

Influenza surveillance in Ghana is carried out through collaboration between the U.S. Centers for Disease Control and Prevention (CDC), the U.S. Naval Medical Research Unit No. 3 (NAMRU-3) based in Egypt, the Ghana Health Service (GHS), and the Noguchi Memorial Institute for Medical Research (NMIMR). This partnership has been in place since 2007. Influenza surveillance in Ghana is conducted through sentinel sites located in all regions of the country. In addition, Ghana serves as a platform to assist regional neighbors in developing influenza surveillance systems. Countries benefiting from this partnership are Togo, Burkina Faso, Mali, Angola, Mauritania and Sierra Leone.

Highlights

- Prepared five manuscripts on Influenza in Ghana for publication with two posters accepted for the Options for the Control of Influenza VIII Conference.
- Established a health facility-based surveillance platform for influenza and other respiratory illnesses in the Greater Accra region of Ghana.
- Prepared a new protocol on the incidence of influenza among HIV-infected and HIV-uninfected residents of Shai-Osudoku and Ningo-Prampram Districts.
- Provided technical and logistical support for the National Influenza Laboratory in Sierra Leone.
- Enhanced national surveillance of influenza and other respiratory viruses through review meetings and refresher trainings of Ghana Health Service staff.

Surveillance

Ghana has surveillance programs in all of its ten regions, with 24 influenza-like illness (ILI) and four severe acute respiratory illness (SARI) sites. Sites provided updates for distribution in the Ghana Health Service weekly epidemiological situation bulletin, thus providing a profile of influenza virus activity in Ghana throughout the year. A population-based study is also being used to document ILI in the out-patient setting and SARI in hospitalized patients to determine the proportion attributable to influenza infection in Ghana. This surveillance platform has been established in the nine target health facilities. Bi-weekly reports are generated showing total attendance, demographic details and clinical histories. Epidemiological data on respiratory illness and the total number of outpatient consultations are also collected bi-weekly from the remaining eight public health facilities in the two districts.

The Ghana National Influenza Center (NIC) provided technical assistance for Sierra Leone by receiving and testing respiratory samples enabling influenza surveillance and reporting to WHO by Sierra Leone.

Surveillance Activities

- Conducted an evaluation of the influenza surveillance system in Ghana.
- Provided weekly updates to WHO FluNet and the WHO African Regional Office.
- Surveyed health facility utilization practices by district residents with respiratory infections.

Laboratory

Seasonal influenza surveillance continued in the 10 regions of Ghana. Between October 1, 2012, and September 30, 2013, Ghana's National Influenza Center (NIC) at the NMIMR, processed 2,322 influenza specimens and 313 were found positive for the influenza virus. Samples were collected from a total of 33 sites (civilian and military) across the country. No cases of the novel influenza A/H7N9 have been found. Representative Ghanaian influenza virus isolates were shared with the WHO Collaborating Centre (CC) in London for a contribution to the global antigenic analysis of circulating influenza viruses. The Ghana NIC also tested 241 respiratory samples (nine influenza A(H3N2) viruses were detected) on behalf of the Central Public Health Laboratory (CPHL), Sierra Leone.

Laboratory Activities

- Tested a total of 2,322 influenza specimens with 313 positive for influenza virus.
- Submitted a total of 37 positive samples to the WHO CC London as part of WHO GISRS.
- Conducted ten supervisory visits and provided logistical support to 33 sites in the national influenza surveillance network.

Preparedness

The collaborative agreement between the NMIMR and CDC has strengthened influenza surveillance activities in Ghana. Key agencies involved in implementation are the Ghana Health Service, NMIMR and CDC. Capacity building has occurred through various meetings and refresher trainings of Ghana Health Service staff to enhance national surveillance of influenza and other respiratory viruses (December 2012 through August 2013). The GHS influenza focal point attended a Regional Training Workshop on Influenza Data Management and Scientific Writing in Côte d'Ivoire in May 2013 and shared his experiences with colleagues upon return to help improve data analysis. An Influenza Surveillance Review Meeting was held for regional surveillance officers and sentinel site teams to strengthen ILI surveillance as well as to enhance the preparedness and response to the emergence of Influenza A(H7N9) and the MERS coronavirus.

Preparedness Activities

- Trained Ghana Health Service staff members from select district and regional hospitals with the Integrated Management of Adolescent and Adult Illnesses Guidelines to improve health care capacity for severe acute respiratory illnesses.
- Conducted a one day meeting of Deputy Directors of Public Health of the Ghana Health Service including the NIC Head and discussed national preparedness and response to the emergence of Influenza A (H7N9) and the Novel Coronavirus.
- Updated Regional and District Surveillance/Disease Control Officers from three regions in Ghana on surveillance, outbreak investigations and implementation of the IHR 2005 with special emphasis on respiratory infections such as pandemic influenza.

Training

- Trained a member from CPHL, Sierra Leone, who visited the NIC, Ghana for training on laboratory diagnosis of influenza viruses in April 2013.
- Conducted a technical support visit to CPHL, Sierra Leone to provide technical assistance troubleshooting molecular diagnosis for influenza viruses in July 2013.
- Initiated molecular testing of respiratory specimens for influenza viruses by the polymerase chain reaction method at CPHL, Sierra Leone with technical support via email and telephone from the NIC at NMIMR.

Publications

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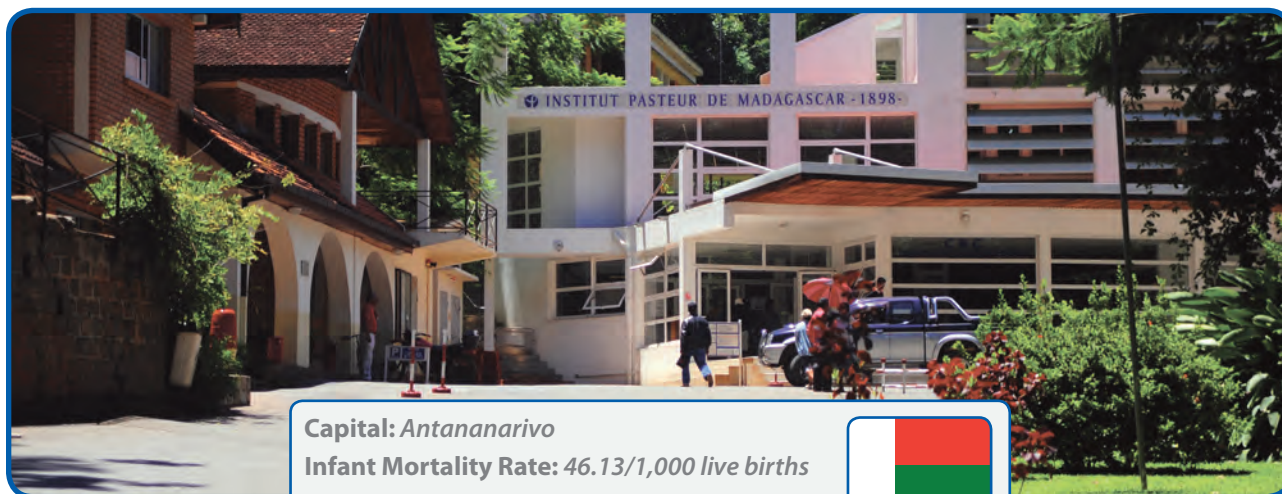
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Special Project

Surveillance Platform for Health facility-based Surveillance for Influenza and Other Respiratory Illnesses in Residents of Shai-Osudoku and Ningo-Prampram Districts, Ghana

Among African children influenza has been shown to cause 22% and 10% of out-patient and in-patient respiratory illnesses respectively, and in Ghana, 30% of outpatient visits for respiratory disease during rainy seasons from 2008 through 2010 were positive for influenza. Few data exist in West Africa, on the rate of mild and severe disease in different groups and what specific risk factors may be important for severe disease. This study seeks to collect comprehensive data to determine seasonal baseline rates of ILI and hospitalization due to SARI in a population of approximately 130,000 persons within an existing health and demographic surveillance system in Ghana.

Madagascar



Capital: Antananarivo

Infant Mortality Rate: 46.13/1,000 live births

Population: 22,599,098 (July 2013 est.)



Overview

CDC provided support to substantially sustain the capacity of the National Influenza Center (NIC) and Health Authorities for surveillance and diagnosis of influenza-like illness (ILI) and severe acute respiratory infection (SARI) [including Highly Pathogenic Avian Influenza (HPAI) in humans] in Madagascar. The cooperative agreement (CoAg) also increases the capacity of the Central, Regional and District Health Authorities to provide a rapid public health intervention in response to a pandemic outbreak and to implement appropriate disease containment measures.

This CoAg is aimed at supporting the national efforts to address a possible second wave of pandemic A/H1N1 or of A/H5N1 from a disease prevention and control standpoint. In addition, the project intends to address preparedness for possible other emerging SARI so as to monitor the emergence of pandemic viruses; reduce morbidity and mortality due to possible emerging respiratory infectious diseases, both through rapid detection and containment; and consequently reduce economic effects and social upheaval/unrest due to a pandemic. Efforts to better understand the epidemiology of influenza in Madagascar and estimate incidence and burden of disease are also supported by the CoAg.

Highlights

- Conducted training based on techniques for the diagnosis of influenza with two technicians from the National Public Health Laboratory in Brazzaville (Congo) in April 2013.
- Opened two regional laboratories in Toamasina and Mahajanga.

Surveillance

To date, the ILI sentinel surveillance system encompasses 34 sites. All sites send daily epidemiological information regarding influenza to WHO's FluNet. On a weekly basis, twelve of them send respiratory specimens to the NIC for analysis.

A sentinel network for SARI surveillance is functional and encompasses 17 hospitals. Two hospitals (Antananarivo and Moramanga) recruit all SARI cases for virological surveillance of hospitalized cases. The two newly opened regional laboratories at Toamasina and Mahajanga have the capacity for influenza detection using CDC real-time RT-PCR kits and participate in ILI surveillance.

Surveillance Activities

- Continued ILI and SARI surveillance activities, including sampling and analysis.
- Supported all hospitalization costs including treatment in the context of SARI surveillance.
- Trained staff from the SARI sentinel site located in Fenoarivo on SARI surveillance and specimen collection.
- Shared weekly data with the Malagasy Ministry of Health (MoH), World Health Organization (WHO) and other partners.
- Developed a quarterly bulletin in collaboration with the NIC and the Epidemiological Department at the MoH. It is distributed electronically to partners and stakeholders.

Laboratory

Before the CoAg with CDC, the NIC in Madagascar already had the capacity for performing diagnostic tests, but there was room to improve diagnostic capacity and additional ways to prepare for a surge in testing during future pandemics. The CoAg supported laboratories in Madagascar, Mauritius and Seychelles, through the acquisition of new equipment and sampling material, allowing for an increase in the number of specimens that can be processed.

In order to implement diagnostic capacity, two regional laboratories for influenza detection were set up in 2012. The CoAg supported the creation of these laboratories.

Facing the threat of potential pandemics due to two new respiratory viruses infecting humans (influenza A/H7N9 and new coronavirus MERS-CoV), the Malagasy NIC implemented the assays for the detection of these new viruses and also implemented the techniques in both regional laboratories.

Laboratory Activities

- Tested 1,759 influenza specimens.
- Tested 596 SARI cases at the NIC using an in-house panel system for the detection of 14 respiratory viruses.
- Tested all SARI cases received since April 2013 (107) for influenza A/H7N9 and MERS-CoV viruses.
- Submitted a total of 65 positive isolates and 25 positive swabs to the WHO Collaborating Center in London as part of the WHO Global Influenza Program.
- Participated in the WHO External Quality Assessment Project (EQAP) and scored 100% for quality assurance.

Preparedness

CDC support has allowed the NIC to establish and strengthen both ILI and SARI surveillance systems. In the actual context of potential pandemics, the NIC implemented techniques of detection for influenza virus A/H7N9 and MERS coronavirus in both regional laboratories (Mahajanga and Toamasina) on July 2013.

Preparedness Activities

- Trained technicians from both regional laboratories in Mahajanga and Toamasina on techniques for detection of A/H7N9 and MERS-CoV viruses.
- Trained sentinel site leaders to strengthen and improve SARI surveillance systems in September 2013.

Training

- Trained ILI sentinel site physicians on respiratory specimen sampling for influenza diagnosis (October 2012).
- Co-hosted a training in Mauritius with the purpose of establishing influenza surveillance in the Indian Ocean island countries (January 2013). Participants were from Mauritius, Madagascar, Reunion and Seychelles. It was funded jointly by CDC and the Association of Public Health Laboratories (APHL). The project has supported national efforts to implement laboratory capacities in Mauritius and Seychelles.
- Conducted a workshop for 14 participants at Institut Pasteur— Madagascar (IPM) focused on the revision of the national capabilities in preparedness and response to pandemic influenza (March 2013).
- Trained staff members from the reference hospital in Fenoarivo on influenza and virological surveillance (March 2013).
- Trained two technicians from the National Public Health Laboratory in Brazzaville (Congo) on techniques for diagnosis of influenza by NIC staff (April 2013).

Publications

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Research Projects

- Viral Etiology of SARI in Madagascar
- Seasonality of influenza in Antananarivo, Madagascar, from 2002 to 2012

**see Research Section for additional information*

Mali

Capital: Bamako

Infant Mortality Rate:

106.49/1,000 live births

Population:

15,968,882 (July 2013 est.)



Overview

In 2009, the Center for Vaccine Development (CVD)/Centre National d'Appui à la lutte contre la Maladie (CNAM)-Mali (CVD/CNAM)-Mali was designated as a National Influenza Centre by the Ministry of Health. Since that time, CVD/CNAM-Mali has embarked on influenza surveillance as part of a series of research studies. While this surveillance has been informative (trends, seasonality) and the laboratory has gained a great deal of competence (contributing data to FluNet and the WHO/AFRO Weekly Report), it has not comprised a formal surveillance system as it has only involved Bamako, the capital city, and is still working on meeting global standards.

Mali was awarded a capacity building cooperative agreement, Surveillance and Response to Avian and Pandemic Influenza by National Health Authorities outside the United States in September 2013. The agreement aims to establish a formal influenza surveillance system in Mali, strengthen ongoing activities, and enhance the level of preparedness and response to annual influenza epidemics and future pandemics.

Highlights

- Awarded Capacity Building Cooperative Agreement.
- Participated in the WHO External Quality Assessment Project (EQAP) and completed two with a score of 100%.
- Collected samples and provided results to FluNet and WHO/AFRO.
- Procured reagents from CDC.

Mozambique

Capital: Maputo

Infant Mortality Rate:

74.63/1,000 live births

Population:

24,096,669 (July 2013 est.)



Overview

Mozambique is located in Southern Africa and has a population of around 22 million inhabitants. The country is administratively divided into 11 provinces and 148 districts. The capital of the country is Maputo. Health care in Mozambique is mainly delivered through a tiered public health system that is managed by the Ministry of Health (MOH). The coverage of the National Health Network in Mozambique is low (approximately 40%) because health facilities in rural areas are sparse and frequently people have to walk long distances to the closest health unit. The only alternative for many of those living in rural areas is traditional medicine. Traditional medicine plays an important role in the National Health System, as a considerable proportion of population resorts to it when ill. In common episodes of respiratory illness, people tend to treat themselves using traditional medicine.

Mozambique was awarded a capacity building cooperative agreement, Surveillance and Response to Avian and Pandemic Influenza by National Health Authorities outside the United States in September 2013. The agreement aims to build and strengthen public sector laboratory and surveillance capacity for acute respiratory infection (ARI) and influenza-like illness (ILI).

Highlights

- Awarded Capacity Building Cooperative Agreement.
- Implemented an electronic system for data management in all districts.
- Participated in WHO's EQAP Panel and scored 100%.
- Experienced in virus isolation and cell culture techniques.

Nigeria



Capital: Abuja
Infant Mortality Rate: 72.97/1000 live births
Population: 174,507,539 (July 2013 est.)



Overview

The Nigerian Federal Ministry of Health (FMOH) has been collaborating with CDC on influenza control since 2006. This support has enabled Nigeria to establish a system for early detection and effective response to avian and pandemic influenza. To improve integration, coordination and sustainability, the project has been relocated to the National Epidemiology Division (under the Nigeria Center for Disease Control). Currently there are four sentinel sites, located in four tertiary health institutions in four of the six geopolitical zones of the country. Each of these sites has an influenza-like illness (ILI) component in the outpatient clinic and a severe acute respiratory infection (SARI) component in the inpatient unit.

Highlights

- Acquired H7N9 primers from the Influenza Reagent Resource (IRR).
- Hosted a meeting of stakeholders on Influenza Surveillance Sustainability Planning (August 2013).
- Increased population awareness for the program via meetings, workshops, presentations and publications in local and international journals.
- Drafted an influenza sustainability plan.

Surveillance

All demographic data including oropharyngeal and nasopharyngeal samples of ILI and SARI cases collected are sent to the national influenza reference laboratory (NIRL) where diagnosis and analysis is carried out. The NIRL also received samples from suspected cases of avian flu (H7N9) from the University College Hospital, Ibadan (outside the surveillance network) and Aminu Kano Teaching Hospital (within the surveillance network) with all results to date being negative. The total samples received for ILI and SARI between October 2012 and August 2013 were 2,014 while those processed were 1,515. During the period, the project was awarded a supplementary grant by CDC to expand SARI surveillance to one urban site in each of the two remaining geopolitical zones not currently covered by the initial grant.

Surveillance Activities

- Developed indicators to evaluate site performance efforts.
- Conducted the 2011/2012 annual review meeting with the sites, trained NISS staff on sample collection, storage and transportation.
- Prepared a manuscript for publication on influenza surveillance.
- Created awareness among departmental staff and Nigeria Field Epidemiology and Laboratory Training Programme (NFELTP) residents on H7N9 with the Nigeria Centre for Disease Control (NCDC).

Laboratory

The laboratory ran smoothly without any experience of out of stock reagents. Samples collected were speedily investigated using RT-PCR with a relatively short turn-around-time. Equipment (stratagene) was installed to provide additional back-up to the two current RT-PCR machines in the laboratory. Training and retraining of staff occurred while laboratory activity documentation improved. Although equipment for carrying out cell culture was installed, it has yet to be validated. Validation of BSL-2 equipment for PCR was completed. The laboratory registered with IRR and has been benefitting from the available supplies of influenza primers (including H7N9) and other reagents necessary for molecular diagnosis of Influenza. The laboratory received a team of NFELTP residents from Namibia.

Laboratory Activities

- Received 2,014 nasopharyngeal and oropharyngeal samples consisting of 1,638 ILI and 376 SARI samples and processing 1,239 ILI and 277 SARI samples as of August 2013.
- Submitted 33 positive samples to WHO CC, Atlanta where samples were further characterized.
- Participated in a workshop on BioRisk Management organized by Sandia Laboratories (USA) in Lagos, April 2013.
- Updated laboratory standard operating procedures (SOP).
- Received consumables for the laboratory from NCDC.

Preparedness

A new unit has been carved out by the Epidemiology Branch of the NCDC which is overseeing the pandemic preparedness. This unit has started active collaboration with the NISS Project to update the pandemic preparedness plan developed some years back (2006). The plan has been included for support in the current Federal Ministry of Health's budget plan. Improvement of laboratory detection of influenza and other respiratory viruses was key in the plan as was expansion of the number of laboratories with capacity for molecular diagnosis. Lastly, NISS is collaborating with the "Early Warning and Alert Response Network" (EWARN) established by the Federal Ministry of Health, and domiciled under NCDC, in response to previous flood disaster, to fortify the network for quick response to epidemics. NISS is also working with the FMOH's Integrated Disease Surveillance and Response (IDSR) network to actualize preparedness.

Preparedness Activities

- Collaborated with the pandemic preparedness unit within the Epidemiology Unit of NCDC (NISS belongs to this branch).
- Conducted a preparedness plan update meeting with the pandemic preparedness unit of the Epidemiology Branch.
- Conducted a meeting with NCDC management, EWARN and other stakeholders on pandemic preparedness.
- Participated in the Ministry's pandemic preparedness exercise towards H7N9.
- Reviewed Nigeria's performance rating with Pandemic Preparedness Unit on the 12 core capabilities carried out by CDC and FMOH in August 2012.

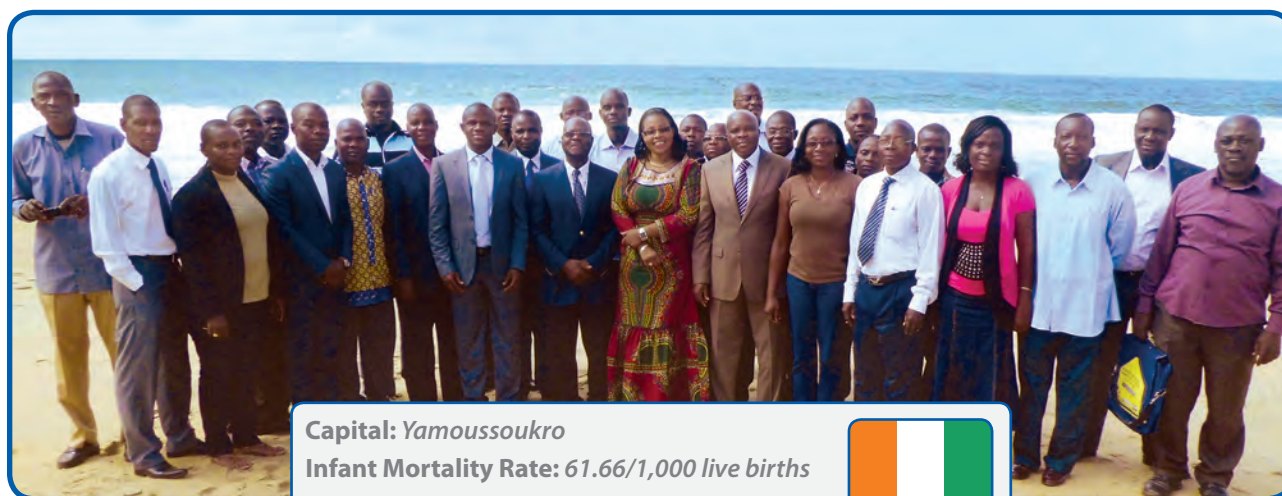
Training

- Participated in BioRisk Management Training, organized by Sandia Laboratories (USA) in Lagos, Nigeria (April 2013).
- Attended the Data Management and Scientific Writing Workshop for Influenza, Côte d'Ivoire (May 2013).
- Conducted the Annual Influenza Review and Capacity Building Meeting in Kuchikau, Nassarawa State, Nigeria (June 2013).

Publications

Five-year Review of the National Influenza Sentinel Surveillance (NISS), Nigeria Bulletin of Epidemiology, ISSN:2006-6082 Special Edition, December 2012.

Republic of Côte d'Ivoire



Capital: Yamoussoukro

Infant Mortality Rate: 61.66/1,000 live births

Population: 22,400,835 (July 2013 est.)



Overview

Since 2006, CDC's Influenza Program has supported the national sentinel surveillance network in Côte d'Ivoire in collaboration with the Ministère de la Santé et de la Lutte contre le Sida (MSLS)/ Ministry of Health, the National Institute for Public Hygiene (INHP) and the Institut Pasteur of Côte d'Ivoire (IPCI). In order to harness the gains of the prior cooperative agreement and continue to maintain the quality of the influenza surveillance and control system in Côte d'Ivoire, a second five-year funding agreement was received in 2011.

This agreement provides supplementary support to the Ivorian Government in order to ensure the sustainability of the influenza surveillance system over time. Among other objectives, this funding will enable an estimation of the burden that influenza has caused in Côte d'Ivoire in terms of morbidity and mortality. Moreover, it will facilitate the development of an influenza vaccine policy based on surveillance data, as well as improved detection and control of influenza and other severe respiratory illnesses.

Highlights

- Developed a new protocol for influenza surveillance and implemented a reconfiguration of sentinel sites in order to make the network more efficient.
- Increased laboratory diagnostic capacity by acquiring technical equipment for molecular biology and antiviral susceptibility testing [Institut Pasteur of Côte d'Ivoire (IPCI) and the National Influenza Center (NIC)].

Surveillance

During this period, the sentinel network developed new objectives including determination of disease burden and severity factors for influenza. A new configuration of the sentinel sites was implemented based on new criteria (geographical distribution, improved site management, etc.). Using the new criteria, the surveillance sites have been reduced to nine, including four in Abidjan and five outside Abidjan. The surveillance sites notify the national epidemiological office of new cases on a weekly basis. Of these sites, eight are severe acute respiratory illness (SARI) and influenza-like illness (ILI) (3 in Abidjan and 5 outside). The remaining site is an ILI only site (Attecoubé Hospital in Abidjan).

With the distribution of reporting tools, the new influenza surveillance protocol and policies to sentinel sites have become routine and effective. To ensure timely information and availability of laboratory results, all sentinel sites were provided with internet connection. In addition to internet access, INHP, the NIC located at IPCI and three sentinel sites (Man, Yopougon Attie, San Pedro) received information technology equipment resulting in improved communication.

Surveillance Activities

- Conducted an annual review of surveillance activities and the influenza surveillance network in Bouaké, February 2013.
- Reconfigured the influenza surveillance network by implementing a sustainability plan with a workshop in October 2012.

Laboratory

In order to fulfill its role as a NIC and reinforce operational capacity, the influenza laboratory was provided with reagents, consumables and equipment such as QIAcube, conventional PCR machines through the cooperative agreement. The laboratory analyzed 517 influenza samples targeting influenza AH1N1, (AH1N1)pdm09, AH3N2, AH5N1 and B viruses in 2010. In 2012, 1,186 samples were analyzed. During the period from January to August 2013, 1,128 samples were routinely tested for influenza viruses and other respiratory viruses.

Preparedness

An awareness and communication tour was held for the general public on high-risk behavior and influenza prevention. Two campaigns were conducted in February 2013: (i) in the towns of Abengourou, Bondoukou, Bouna and Nassian (ii) in Korhogo, Ferke, Tengrela and Boundiali. Four hundred (400) persons at the community level, as well as political, administrative, traditional, and religious, and civil society participants and authorities were invited to the meetings.



Influenza Surveillance Network Annual Review Meeting in Bouake, February 2013.



Regional Training Workshop on Influenza Data Management and Scientific Writing, Abidjan, May 2013.

Training

- Trained an INHP epidemiologist on descriptive epidemiologic techniques, epidemiologic tools (assessment and biostatistics) in Ouagadougou, Burkina Faso, November 2012 and April 2013.
- Trained 50 laboratory technicians and doctors stationed at surveillance sites on lab management, influenza diagnostics and biosecurity.
- Trained 50 laboratory technicians and doctors at sites on sample collection, packaging, storage and transportation, as well as sample analysis (i.e., PCR), and cell culture.
- Trained nine focal points on Epi-Info in Yamoussoukro.
- Reviewed records at each sentinel site in Abidjan in August 2012 to estimate the burden of influenza. From January 2007 to December 2011, twenty six thousand fifteen (26,015) suspected cases of influenza were detected along with 650 deaths.
- Hosted the Regional Training Workshop on Influenza Data Management and Scientific Writing in Abidjan, May 2013. Participants from 10 West African countries and facilitators from CDC and CSTE were present at this workshop.
- Conducted a review of all sentinel sites in June 2013, to evaluate and address the daily constraints (high workload, time-consuming registration of flu cases) and communication challenges (internet connection issues) health care providers are facing.

Publications

Coulibaly D, Nzussouo NT, Kadjo HA, Traoré Y, Ekra DK, Chérif D, Kouassi PD, N'gattia AK, Dagnan SN. Pandemic Influenza A(H1N1) in Côte d'Ivoire: health-care providers' knowledge of influenza and attitudes towards vaccination. *J Infect Dev Ctries* 2013; 7(7):499–506. doi:10.3855/jidc.2771.

Nzussouo NT, Kadjo HA, Coulibaly D, Ekaza E, Kouakou B, N'Golo DC, Tempia S, Davis R, Dosso M, Thompson M. Comparing influenza positivity rates by Real-Time RT-PCR, Elisa and viral culture methods in Côte d'Ivoire, West Africa, in 2009. *Afr. J. Infect. Dis.* 2013. 7(2): 31–35.

Rwanda



Capital: Kigali

Infant Mortality Rate: 61.03/1,000 live births

Population: 12,012,589 (July 2013 est.)



Overview

Influenza activities are carried out through a CDC cooperative agreement with the Center for Treatment and Research on AIDS, Malaria, Tuberculosis and Other Epidemics (TRACPlus) within the Rwanda MOH. CDC supports TRACPlus in preparedness and communication, surveillance and disease detection, and response and containment to improve Rwanda's capacity to identify and manage outbreaks of avian and pandemic influenza. The influenza surveillance network in Rwanda is currently composed of six (6) sentinel surveillance sites (i.e. 2 referral hospitals and 4 district hospitals), the Rwanda Biomedical Center/National Reference Laboratory Division (RBC/NRL) as the National Influenza Testing Centre and the Rwanda Biomedical Center/Epidemic Infectious Diseases Division (RBC/EID) as the support coordination institution.

Highlights

- Revised Influenza Surveillance Standard Operations Procedures (SOP) to include new WHO case definitions for severe acute respiratory illness (SARI) and influenza-like illness (ILI), enhanced SARI surveillance data collection form and performance indicators.
- Launched an enhanced SARI surveillance data collection tool at each sentinel site to include risk factors and outcomes of severe disease.
- Conducted a laboratory assessment in August 2013.
- Developed an Influenza National Sustainability Plan to phase out CDC funding by July 2016.

Surveillance

In July 2008, the Ministry of Health (MoH) has established influenza sentinel surveillance (ISS) network to describe the epidemiology and seasonality of influenza in the country. The network is currently composed of six (6) sentinel surveillance sites (i.e. 2 referral hospitals and 4 district hospitals), the National Reference Laboratory (NRL) as the national influenza testing center and the Rwanda Biomedical Center/Other Epidemic and Infectious Diseases Division (RBC/EID) as the support/coordination center. Each site has a full time surveillance officer who conducts most of the influenza work at the site. The surveillance officer is assisted by a clinician. The clinician provides oversight and helps engage other clinicians and nurses in the hospital to identify cases with symptoms that fit the Standard WHO case definitions for ILI and SARI. Each sentinel site has inpatient pediatric, adult, maternity, and emergency wards and an outpatient department that participate in the ISS.

Surveillance Activities

- Developed and validated influenza surveillance performance indicators.
- Collected a total of 1,207 questionnaires and entered into the central database.
- Developed a protocol for evaluation of the attributes of influenza surveillance system.
- Resumed weekly reporting to WHO FluID after more than six months of discontinuation.

Laboratory

The National Reference Laboratory (NRL) is the National Influenza Testing Centre since 2008. It is a Biosafety Level II (BSL-2) with some enhanced BSL-3 procedures. It has supported the ISS network with PCR assays for detection of seasonal human (A/H1, A/H3, A/H1N1pdm09, B), avian (A/H5N1; A/H7N9) and pandemic influenza (A/H1N1pdm09) strains and subtypes using CDC primers/probes and protocols. Over 1,139 respiratory specimens have been tested and the positivity rate of 14.0% (160/1,139) detected. The laboratory has successfully participated on the WHO External Quality Assessment Project (EQAP) for influenza PCR assays since 2009 to date. Currently, there is no virus culture performed by the NRL due to lack of adequate space. There is ongoing plan to procure a BSL-2 Containment Virology Laboratory to accommodate viral isolation on cell culture. The identification of viral isolates will help the NRL to acquire capabilities for WHO accreditation as National Influenza Center (NIC).

Laboratory Activities

- Tested a total of 1,207 respiratory samples with positivity rate of 12.8% (154/1,207).
- Tested 40 respiratory samples negative to Influenza by RT PCR using Multiplex PCR to validate protocol.
- Conducted four supervisory site visits and provided logistical support to sentinel sites.
- Registered to CDC's Influenza Reagents Resource (IRR).

Preparedness

Since the notification of human infection with avian influenza A(H7N9) virus by the Chinese Government to the World Health Organization on March 31, 2013, the Government of Rwanda has closely monitored the situation by implementing preparedness and response activities and information sharing.

Preparedness Activities

- Hosted regular meetings in the last two years between Ministry of Health and Ministry of Agriculture to discuss the collaboration regarding information sharing, public awareness, surveillance, and rapid response team readiness.
- Produced and disseminated TV/Radio spots on avian influenza A(H7N9) to raise public awareness.
- Updated health care providers on key facts regarding avian influenza A(H7N9).
- Alerted influenza surveillance sentinel sites and other health facilities to report any unusual clusters of pneumonia occurring within 7 to 10 days of each other with family or social connections.
- Forecasted needs regarding specimen collection kits, personal protective equipment (PPE), and antivirals.

Training

- Conducted refresher trainings on influenza epidemiology, data and specimen collection as well as new trainings on enhanced SARI data collection.
- Attended the Data Management and Basic Epidemiologic Analysis for Influenza Training Course in Johannesburg, South Africa, November 2011.
- Attended the 3rd Annual African Network for Influenza Surveillance and Epidemiology (ANISE) Meeting in Nairobi, Kenya, February 2012.



Didactic training on how to conduct influenza sentinel surveillance at Gihundwe District Hospital.

South Africa



Capital: Pretoria

Infant Mortality Rate: 42.15/1,000 live births

Population: 48,601,098 (July 2013 est.)



Overview

CDC collaborates with the National Institute for Communicable Diseases (NICD)/National Health Laboratory Service (NHLS) to strengthen laboratory and epidemiologic capacity of national health authorities for the detection, surveillance, and response to seasonal, pandemic, and zoonotic influenza in South Africa and countries of the Southern Africa Development Community. CDC sponsored a data management training course for influenza surveillance data managers and epidemiologists. Surveillance for influenza has provided a platform to explore the role of other viral respiratory pathogens in causing pneumonia in South Africa. Robust estimates of influenza burden in specific populations (e.g. HIV-infected) have provided evidence for policy improvements on the use of the influenza vaccine in targeted groups. Strengthening pandemic preparedness and response capacity at the local level provides a platform for improved preparedness and response for other communicable diseases.

Highlights

- Developed a draft of the national influenza policy with National Department of Health and the Biovac Institute.
- Developed a sustainability plan for the influenza programme including plans to integrate into an established national infectious disease surveillance programme (GERMS).
- Established laboratory assays for MERS-CoV and avian influenza H7N9 following emergence of these pathogens.

Surveillance

The severe acute respiratory illness (SARI) and the influenza-like illness (ILI) programmes continue at hospitals and outpatient clinics across the country. The SARI programme routinely tests for RSV, influenza A and B, adenovirus, human metapneumovirus, parainfluenza 1, 2, 3, rhinovirus and enterovirus. An additional ILI routine surveillance site was established last year. The ILI surveillance programme enrolls patients by a standard case definition of ILI. It provides a platform for the influenza shedding study and allows for a better description of the risk factors for ILI and SARI in a high HIV prevalence setting. Additional protocols are included to allow for identification of *Pneumocystis jirovecii*, *M. tuberculosis*, *Streptococcus pneumoniae*, *Bordetella pertussis*, *Haemophilus influenzae* type B, atypical bacterial causes of pneumonia (*Legionella* species, *Chlamydophila pneumoniae* and *Mycoplasma pneumoniae*), coronaviruses and bocavirus. Describing these pathogens will allow for a full description of the causes of pneumonia in our setting. Taqman array card testing for additional respiratory pathogens has been established.

Surveillance Activities

- The National Influenza Center (NIC) was the first reference laboratory in Africa to initiate testing for MERS-CoV; the NIC is now accredited by both the South African National Accreditation System (SANAS) and the Department of Agriculture Forest and Fisheries (DAFF) for human and zoonotic influenza strain identification.
- Established surveillance to investigate human-animal interface in areas where avian influenza outbreaks have been recorded.

Laboratory

Since A(H1N1) pdm09 predominated in 2013, most virus isolates were made from clinical specimens positive for this strain including 41/46 cell culture and 18/36 egg isolates. Hemagglutination inhibition assays characterized 98% (40/41) of A(H1N1)pdm09 isolates with normal reactivity to the A/California/7/2009 reference. Three A(H3N2) isolates reacted with ≥ 2 fold lower titer to the reference antiserum, A/Perth/16/2009. Influenza B virus isolates showed normal reactivity to B/Wisconsin/1/2010 (Yamagata lineage) antisera. H3N2 hemagglutinin (HA) genes from 2013 are in genetic group 3 and specifically 3C. For 70 A(H1N1) pdm09 positive samples sequenced 99% (69/70) are in lineage 3C. Seven influenza B strains belong to clade 2 of the B/Yamagata lineage. Influenza A(H1N1)pdm09 positive samples (n=203) tested for the H275Y oseltamivir resistance mutation were wild type. For influenza virus isolates [A(H1N1)pdm09: n=16, A(H3N2): n=1, influenza B: n=7] tested for phenotypic resistance to oseltamivir and zanamivir 1 A(H1N1)pdm09 were resistant and one showed reduced sensitivity.

Laboratory Activities

- Expanded surveillance for ILI in ostrich farming areas to detect transmission of influenza A at the animal-human interface allowed testing of respiratory samples from farm owners and workers, animal handlers, abattoir workers and veterinary personnel.
- Collaborated with DAFF to do surveillance for influenza A in pigs.
- Supported South African Development Community countries by testing specimens for suspected avian influenza and performing inter-laboratory quality assurance testing.

Preparedness

Assays to test for the MERS coronavirus by real time reverse transcription PCR of the E and orf-1b genes are established. The assay for the E protein gene target (UpE) is considered highly sensitive, and has been implemented at the Centre for Respiratory Diseases and Meningitis (CRDM). A second confirmatory PCR on the open reading frame 1b (ORF1b) and a pan-coronavirus PCR can run on UpE positive specimens. For A(H7N9) preparedness we established the real time RT-PCR assays to test for the H7 and N9 genes as well as other avian H5, H6; H7 and H9 influenza strains.

Serum hemagglutination inhibition assays have been established for serological surveillance for human exposure to the following avian influenza virus strains: inactivated A(H5N2), A(H6N2), A(H6N8); A(H7N1), A(H7N7). The virology laboratory was accredited by SANAS in May 2011 as well as DAFF to support diagnostic testing of avian influenza A/H5 in ostriches during the H5N2 avian influenza outbreak using the CDC real-time RT-PCR assay. In-house RT-PCR assays for avian influenza A/H5, A/H7 and A/H9 have been established which enhance our capacity to provide reference laboratory support for avian influenza virus diagnosis. We have also established the H7N9 typing RT-PCR for detecting cases of the emerging strain from China.

Preparedness Activities

- Contributed to WHO working groups on novel coronavirus.
- Conducted meetings to discuss pandemic preparedness and the National Influenza Centre's role in detecting imported cases.
- Supported the National Department of Health (NDOH) on vaccine and clinical treatment guidelines for 2013 influenza season.
- Established surveillance in humans on farms where newly positive Avian Influenza cases were detected in ostriches.
- Established surveillance for influenza in pigs for the first time in South Africa.
- Established real-time PCRs for MERS-CoV, as well as a pancoronavirus PCR.

Training

- Presented three papers on respiratory syncytial virus (RSV) at the 8th Annual International RSV Symposium, Sante Fe, New Mexico (US).
- Hosted the 9th Influenza Symposium in March 2013 in Johannesburg, South Africa.
- Hosted the African Influenza and Emerging Respiratory Virus Preparedness Meeting in Cape Town, South Africa (September 2013).
- Attended the Influenza in Africa Workshop: Afriflu 2012.
- Attended the Data for Action: Research Methods and Data Analysis Course (Epi Info) facilitated through the Centre for Statistical Analysis and Research at Cedar Park Hotel, Johannesburg (May 2013).

Publications

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Tanzania



Capital: Dar es Salaam
Infant Mortality Rate: 45.1/1,000 live births
Population: 48,261,942 (July 2013 est.)



Overview

The Ministry of Health and Social Welfare (MOHSW), Preventive Services Department through its Epidemiology and Diseases Control section collaborates with CDC to sustain influenza surveillance networks and respond to seasonal and pandemic influenza in Tanzania. Influenza epidemiologic surveillance is done in six sentinel surveillance sites [five severe acute respiratory infection (SARI) and influenza-like illness (ILI) sites and one ILI site]. The influenza virologic surveillance is being done through the National Influenza Laboratory (NIL) which is responsible for the implementation of laboratory aspects including setting up adequate standard operating procedures for sample collection, storing, shipping and testing of samples collected from the sentinel surveillance sites.

Highlights

- Increased collaboration between public and private health facilities.
- Increased the capacity to detect, diagnose, and manage other emerging and re-emerging diseases.
- Contributed to the country's timely response to Rift Valley fever in 2007, the 2009 H1N1 influenza pandemic and the dengue fever outbreak in 2010 and 2013.
- Established linkages between human and animal surveillance through the sharing of influenza surveillance reports, technical committee meetings, joint trainings and public awareness sessions on regular basis.
- Provided SARI reports to MOHSW through IDSR from the sentinel sites.

Surveillance

Influenza surveillance activities are conducted at the six sentinel sites and a total of 3,444 samples were sent to the NIL. Two biannual meetings were hosted with various stakeholders to evaluate achievements and challenges of influenza surveillance and identify steps to address these challenges. The result of these meetings is improvement for the sentinel sites increasing the target of specimen collection by 70%.

During the biannual meeting, performance indicators were developed and shared with the flu team. Upon developing indicators, two underperforming sites were dropped. Two supportive supervisory visits to the existing six sentinel sites were conducted on a quarterly basis. The supervisory visits resulted in a review of surveillance implementation activities, mentoring and on the job training.

Surveillance Activities

- Reviewed surveillance implementation activities, provided feedback to site authorities and began discussions on sustainability issues during supervisory site visits.
- Drafted a sustainability plan which indicates how the Government will sustain the program after the CDC funding ends.
- Shared surveillance data with other agencies and the Prime Minister's office.

Laboratory

The capacity of the MOHSW for diagnosis and surveillance of avian influenza and human influenza together with other diseases like Dengue fever, Novel Influenza A H7N9, MERS Coronavirus, Chikungunya, Yellow Fever, and Rift Valley Fever was increased. The NIL conducted PCR testing at the NIL in which a total of 3,444 specimens for influenza type A and B and subtypes A (H1), A (H3), and A (H1pandemic) using real-time RT-PCR with positivity rate of 8.6%.

The NIL participated in the yearly External Quality Assessment Project (EQAP) conducted by WHO panels 6–12 since 2008–2013 with 100% scores. The NIL has also started the process to obtain NIC certification with the initial assessment already completed and application pending review by WHO.

The National Laboratory Quality Assurance and Training Centre were audited by SADCAS with ISO15189 standard with only one nonconformance observed, and were recommended for accreditation.

Laboratory Activities

- Submitted a total of 120 virus isolates to the WHO Collaborating Center in Atlanta.
- Initiated the process to obtain NIC certification; an initial assessment has been completed and the application has been sent to WHO.
- Serviced laboratory equipment and procured reagents.
- Tested a total of 3,444 specimens giving results for influenza type A and B and subtypes A (H1), A (H3), and A (H1pandemic) using real-time RT-PCR with positivity rate of 8.6%.

Preparedness

Tanzania's MOHSW continued to work with CDC, the United Nations, and other stakeholders in the implementation of the preparedness and response plan for avian and pandemic influenza and other emerging infectious diseases.

The preparedness activities were carried out at a minimal pace as limited funding was available to implement the plan except for the MOHSW-CDC CoAg which concentrated on surveillance component.

The MOHSW received a total of 15,000 sets of personal protective equipment (PPE) from CDC for preparedness against emerging and re-emerging infectious diseases

Following the outbreaks of influenza H7N9 in China, coronavirus in the Middle East and dengue fever in our country, the MOHSW in collaboration with other stakeholders have been working closely in activating the emergence preparedness and response plan.

Preparedness Activities

- Produced and distributed standard case definitions (SCD), notification letters and case management protocol to Regional Health Management Teams regarding the threat of both MERS Coronavirus and H7N9 outbreaks.
- Strengthened the surveillance at the point of entry.
- Prepared leaflets for community awareness about H7N9.
- Developed sustainability plan and elaborated strategies on how the influenza surveillance system can continue without the USG financial support.
- Distributed PPEs to the regions, districts and health facilities in the country at large.

Training

- Trained and activated 36 district rapid response teams for timely response of influenza.
- Trained 27 sentinel site staff (surveillance officers, clinicians and laboratory experts) on surveillance and response to the emerging and re-emerging infectious diseases including H7N9.
- Provided refresher and on-the-job training to sentinel surveillance staff during supervisory visits.
- Conducted training on data management to 18 sentinel site staff members.
- Trained 24 Regional and Council Health Management team members on disease surveillance and outbreak response.
- Provided cell culture training to two laboratory technicians in South Africa.

Uganda



Capital: *Kampala*

Infant Mortality Rate: 62.47/1,000 live births

Population: 34,758,809 (July 2013 est.)



Overview

Influenza surveillance activities in Uganda began in the 1960's, but work stopped in the late 1990's due to lack of funding. Financial and technical assistance to the Ministry of Health (MOH) through the Uganda Virus Research Institute (UVRI) was initiated in 2006 to help support the national avian flu preparedness plan and to establish a sustainable influenza surveillance network. The program established a sentinel-site surveillance system in four geographically distinct regions among clinic and hospital outpatients. The sentinel-site system includes: 10 sentinel sites (four outpatient clinics where influenza-like illness (ILI) is assessed and five hospitals where severe acute respiratory infection (SARI) is assessed and one hospital where both ILI and SARI are assessed). All sentinel clinics and hospitals are public facilities. In 2006, UVRI was recognized as a National Influenza Center (NIC) by the World Health Organization (WHO), and began collecting national surveillance for influenza. Standardized data collection instruments and case definitions are consistent with global standards. Data for burden of disease estimates is now routinely collected.

Highlights

- Awarded Vaccine Policy Cooperative Agreement.
- Commenced the expansion of the influenza laboratories and work is on course to be completed in December.
- Trained NIC staff, sentinel site staff and health workers on Seasonal Influenza Vaccination in March 2013.
- Initiated SARI surveillance activity in three hospitals in the capital city, Kampala.

Surveillance

In our sentinel system, surveillance for SARI is now the priority. Presently Arua Regional Referral Hospital, Mbarara Regional Referral Hospital, Tororo District Referral Hospital, and Fort Portal Regional Referral Hospital, all do SARI Surveillance alone. Kawaala Health Centre IV, Kitebi and Kisenyi Health Center III do ILI surveillance alone. Entebbe General Hospital does both ILI and SARI Surveillance for comparison of data. The capacity for a better routine influenza surveillance system in Uganda that collects, analyzes, and reports quality SARI and/or ILI virological and epidemiologic data on both children and adults is continually being enhanced. We standardized protocols for SARI and ILI surveillance. Training on use of these new forms was carried out in each sentinel site and use of these forms is now implemented at each sentinel site. We have continued to monitor the use of the new forms to ensure their completeness and timely reporting.

Surveillance Activities

- Collected samples more regularly and posted data to the MOH Weekly Epidemiology Newsletter, FluNet and WHO AFRO's system weekly.
- Upgraded the epidemiology and virology database.
- Reviewed and upgraded the surveillance system based on recommendations so that the system can be sustained by the MOH and Ugandan government.
- Continued SARI surveillance in regional referral hospitals.
- Continued data collection and data analysis for burden of disease studies.

Laboratory

The laboratory received good quality samples from the various ILI and SARI sentinel sites. 2,387 samples were received. Of these 2,347 samples were tested and only 40 were discarded due to failure to meet our testing criteria. 1,432 were ILI samples and 955 were SARI samples. All samples were diagnosed by PCR and were subtyped. A total of 357 samples were positive for influenza. Of the SARI samples, 91 were positive [Influenza A(H3N2) = 64; A(H1N1)2009 = 5; influenza B = 22]. Of the ILI samples, 266 were positive [Influenza A(H3N2) = 151; A(H1N1)2009 = 34; influenza B = 81]. Virus isolation was carried out on the positive samples. The laboratory sent two shipments of positive samples and isolates to the WHO Collaborating Centre (CC) in Atlanta. Training on sample collection was conducted for new sentinel site staff. The laboratory participated in the WHO External Quality Assessment Project (EQAP) 13 and improved the laboratory database.

Laboratory Activities

- Tested all samples from sentinel sites for influenza.
- Maintained and cleaned data in the virological laboratory database.
- Shipped isolates to WHO CC— 114 PCR +ve specimens and 24 virus isolates shipped.
- Participated in the WHO EQAP with 100% positive score for the 13th time.
- Continued to respond to outbreaks in communities. NIC staff responded to two outbreaks in a school and orphanage this year.
- Maintained cold chain in sentinel sites which have limited electricity supply (was achieved by supplying LN2 to the sites on a regular basis).
- Automated nucleic acid extractions; this enables staff to attend to other urgent tasks within the lab.
- Reduced the number of rejected specimens.

Preparedness

The NIC is part of the National Task Force for Pandemic Preparedness in the country. We report our data to the Surveillance and Response Committee of the National Task Force. The committee meets quarterly and the National Task Force meets twice a year.

The National Influenza Center laboratory was assessed by a WHO Regional Team for emergency preparedness.

We were requested by the Minister of Health to prepare a document summarizing seasonal influenza in Uganda, and capacities for diagnosis and information on the different Influenza outbreaks in the world (H5N1, H1N1 pandemic, and H7N9 also including MERS-CoV). The document was to be used as part of support for preparedness activities.

Preparedness Activities

- Presented influenza surveillance data to National Task Force on Pandemic Preparedness.
- Participated in quarterly and semi-annual meetings of the National Task Force.
- Completed an emergency preparedness assessment (National Influenza Center Laboratories, MOH) by a WHO AFRO Regional Team.
- Prepared a document on influenza in Uganda and the different influenza outbreaks in the world for the Minister of Health.
- Responded to two clusters of influenza disease in schools.

Training

- Attended the Data Management and Basic Epidemiologic Analysis for Influenza Training Course in Johannesburg, South Africa, November 2011.
- Attended the 3rd Annual African Network for Influenza Surveillance and Epidemiology (ANISE) Meeting in Nairobi, Kenya, February 2012.

Publications

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Zambia



Capital: *Lusaka*

Infant Mortality Rate: *68.58/1,000 live births*

Population: *14,222,233 (July 2013 est.)*



Overview

The overall goal of Zambia's influenza program is to strengthen influenza surveillance and the surveillance of other communicable diseases by bolstering the public sector laboratory and surveillance capacity for influenza-like illness (ILI) and severe acute respiratory infection (SARI). The cooperative agreement was implemented by the University Teaching Hospital (UTH) and the Lusaka District Health Office on behalf of the Ministry of Health (MOH) and in close collaboration with CDC-Zambia, CDC-South Africa, and the National Institutes for Communicable Diseases (NICD, South Africa), and the World Health Organization (WHO). The cooperative agreement enables Zambia to strengthen its developing surveillance system and the surveillance of emerging pandemic viruses. Currently, Zambia has four influenza-like illness (ILI) sites and four severe acute respiratory infection (SARI) surveillance sites in Lusaka and Ndola.

Highlights

- Established additional surveillance and testing sites in the Copperbelt Province— two SARI sites and two ILI sites.
- Conducted refresher trainings for surveillance officers in the clinics and a refresher training for laboratory personnel.
- Started reporting influenza isolates on FluNet.
- Identified suspect H1N1 09 from Mumbwa and Serenje districts in the Central Province and sent samples to NICD who confirmed our results.

Surveillance

Zambia has a surveillance system which is supported by MOH. During the outbreak of H1N1 09 in the Serenje and Mumbwa districts, the local ministry of health team gave regular updates to the public on prevention and spread of influenza. During this period, experts from CDC and NICD visited Zambia to strengthen the influenza surveillance activities.

Local teams also made supervisory visits to the newly opened sites in Ndola. Currently, the Ndola site submits data to the reference laboratory at UTH which is shared on FluNet.

Surveillance Activities

- Conducted supervisory visits (experts from NICD) to Lusaka as well as the newly opened influenza sentinel sites in the Copperbelt Province.
- Provided regular updates and health tips to the public during the outbreak of H1N1 09 in Serenje and Mumbai districts.
- Conducted supervisory visits to other influenza sentinel sites in the Copperbelt Province.

Laboratory

The Zambia influenza surveillance program has for the first time managed to commission another influenza testing site. The scientists at the new laboratory were trained by experienced staff from NICD and then by the local influenza team on typing, subtyping and real-time PCR techniques. Notable progress in laboratory surveillance capacity has been achieved over the past four years. Our influenza surveillance network now includes eight sentinel sites which are comprised of four SARI and four ILI sites. In addition, Zambia now has two laboratories in Lusaka and Ndola. Notable progress is being made towards becoming a NIC. The program is now able to send data on influenza isolates to FluNet. Furthermore, training has been organized on virus isolation techniques to enhance the process of becoming a NIC.

Laboratory Activities

- Prepared and sent influenza isolates to WHO Collaborating Center in the United Kingdom.
- Tested a total of 1,030 influenza specimens (980 from sentinel hospitals; 50 from 2009 H1N1 outbreak sites).
- Conducted two supervisory visits and provided logistical support to laboratories within the network.
- Submitted a total of 35 samples to NICD as part of the Quality Assurance Program.
- Participated in the WHO EQAP and scored a 100%.
- Completed testing of influenza negative results for other respiratory viruses.

Preparedness Activities

- The Ministry of Health held four quarterly surveillance trainings that brought together surveillance officers from all 10 provinces.
- The Ministry of Health adapted the WHO Integrated Disease Surveillance and Response Manual as the national standard for disease surveillance, which includes influenza surveillance.
- The Ministry of Health held provincial surveillance trainings in IDSR that included outbreak investigations. These trainings were conducted in all 10 provinces and brought together surveillance officers from all districts in the each province.

Training

The Zambia influenza team continues to provide technical assistance and training to ensure the functioning of the sentinel surveillance system, quality of the surveillance data, prompt data analysis, and integration of the information into preparedness and response activities. The following trainings were organized in Zambia.

- Trained influenza sentinel surveillance officers on specimen collection, safety, packaging and handling.
- Conducted training for typing, subtyping and RT PCR techniques for four laboratory staff from Ndola.



The Zambian Influenza Surveillance Team: Hope Nkamba, Costa Malama, Paul Simusika (back) and Idah Ndumba, Mwaka Monze, Mazyanga Liwewe (front).

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WHO EASTERN MEDITERRANEAN REGION (EMR)

WHO Eastern Mediterranean Region (EMR) Overview

Currently there are five bilateral influenza cooperative agreements in the Eastern Mediterranean Region of WHO. These agreements are with ministries of health or institutions designated by the Ministry of Health (MOH) to work with CDC to build capacity to routinely identify, diagnose and respond to seasonal and pandemic influenza across the Eastern Mediterranean Region.

CDC direct country support via cooperative agreements is established in the following countries:

- Afghanistan
- Morocco
- Tunisia
- Egypt
- Pakistan

Two additional cooperative agreements were awarded for FY13, with work beginning in FY14. One additional capacity building was awarded to Tunisia. Morocco was awarded a cooperative agreement for the development of influenza vaccine policy.

In addition, CDC supports the WHO Regional Office for the Eastern Mediterranean (EMRO) via a cooperative agreement.

The core activities of cooperative agreements and technical assistance between WHO/EMRO and CDC are:

- To enhance the quality, sensitivity and effectiveness of surveillance system for influenza and severe acute respiratory infections (SARI) as well as sustaining and further enhancing the laboratory capacities of National Influenza Centers for timely detection of novel influenza virus;
- To develop the capacities of the countries to use routinely collected surveillance data to improve their understanding on influenza epidemiology so as to better inform the national health authorities on appropriate preventive and control strategies for influenza; and
- To support the development of appropriate public-health policies that will promote introduction and increased use of seasonal influenza vaccines in at-risk population groups in the region.

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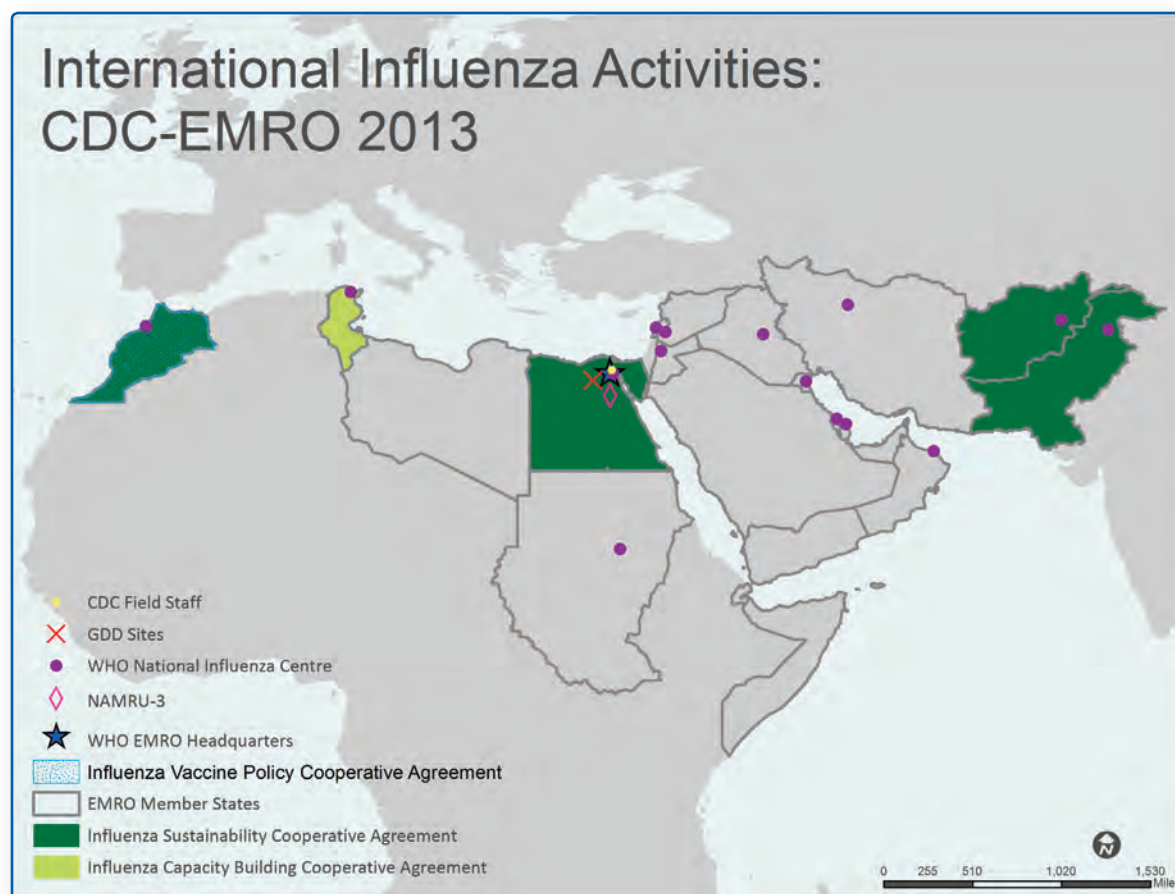
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WHO Regional Office for the Eastern Mediterranean (EMRO)



Highlights

- Developed concrete road maps for establishing sentinel surveillance system for SARI/ILI in Djibouti, Lebanon, South Sudan and Yemen.
- The Regional Office made visible progress in designating the Central Public Health Laboratories in Libya and Yemen to become National Influenza Centres (NIC).
- Five countries in the region have acquired the skills and knowledge for estimating the disease burden associated with influenza in general populations using SARI sentinel surveillance data.
- The Regional Office is regularly publishing a weekly epidemiological monitor to inform the Member States of the influenza situation in the Region, as well as of other public health emergencies of potential concern in the region.
- Eight out of the sixteen NICs in the region are regularly sharing seasonal influenza viral isolates to the Global Influenza Surveillance and Response System (GISRS); eleven out of these sixteen NICs are also participating in the WHO External Quality Assessment Project (EQAP) with notable proficiency test results.

U.S. CDC Direct Support

This current five year project (2011–2016) on strengthening surveillance and response to seasonal and pandemic influenza by the Regional Offices of the World Health Organization is built on a previous cooperative agreement (2006–2010) between the Regional Office of the Eastern Mediterranean (EMRO) of WHO and the U.S. Centers for Disease Control and Prevention (CDC) on a project titled Strengthening Surveillance and Response to Avian and Pandemic Influenza in the Eastern Mediterranean Region that was launched in October 2006.

The current project draws on existing partnerships and collaborative arrangements in the Eastern Mediterranean Region of WHO between WHO/EMRO, FAO, UNICEF, IOM, GDDRP, NAMRU-3 and WHO Headquarters on strengthening, consolidating and sustaining regional preparedness for human pandemic influenza.

The unit of Pandemic and Epidemic Diseases (PED) under the Division of Communicable Disease of WHO/EMRO is the lead technical unit responsible for implementation of this current cooperative agreement.

The overarching objective of this current cooperative agreement is to improve the epidemic and pandemic preparedness for influenza in the Eastern Mediterranean Region of WHO through implementation of three major projects. These include (i) enhancing the quality, sensitivity and effectiveness of surveillance system for influenza and severe acute respiratory infections (SARI) as well as sustaining and further enhancing the laboratory capacities of National Influenza Centers for timely detection of novel influenza virus; (ii) developing the capacities of the countries to use routinely collected surveillance data to improve their understanding on influenza epidemiology so as to better inform the national health authorities on appropriate preventive and control strategies for influenza; and (iii) supporting the development of appropriate public-health policies that will promote introduction and increased use of seasonal influenza vaccines in at-risk population groups in the region.

Surveillance

The Regional Office has continued to provide technical and operational support to the countries in the Region for enhancing the quality, sensitivity and effectiveness of surveillance systems for influenza and SARI in the Eastern Mediterranean Region.

As a result of this ongoing support, 14 out of 23 countries in the Region are currently implementing sentinel surveillance systems for SARI and influenza-like illness (ILI).

In addition, 12 out of 23 countries in the Region are currently participating in the virological surveillance for seasonal influenza as part of the Global Influenza Surveillance and Response System (GISRS).

Surveillance Activities

- Conducted technical missions to Yemen, South Sudan and Djibouti during October–November 2012, to assist in planning sentinel surveillance systems for influenza and SARI in collaboration with the respective national Ministries of Health. The objective of the mission was to assess the readiness and training needs of the country for establishing sentinel surveillance system for influenza and SARI. Following these missions, a concrete road map was elaborated which would be followed up for implementation in the coming project period of September 30, 2013 to September 29, 2014.

- Conducted a sub-regional workshop in collaboration with the Ministry of Health, Jordan, in Amman, Jordan, November 11–15, 2012 to design an appropriate surveillance system for influenza in refugees and displaced population settings. Countries hosting large number of internally displaced populations attended this workshop. As an outcome of this workshop, draft guidance on establishing appropriate surveillance system for influenza in refugees and displaced population was developed with the focus on early detecting any suspected cluster of influenza or any other acute respiratory infections of potential public health concern in these settings.
- Organized the second meeting of the Eastern Mediterranean Region Acute Respiratory Infection Surveillance (EMARIS) network in partnership with GDDRP of NAMRU-3. This meeting was held in Sharm El-Sheikh, Cairo, Egypt on December 12–13, 2012. The theme of this year's EMARIS network meeting was "Data for Action" which led to endorsing a resolution in the meeting by the participating countries on strengthening data collection for surveillance of influenza and SARI and using the surveillance data to generate evidence for informed public health decisions for prevention and control of influenza in the countries.
- Conducted a technical mission in Lebanon from December 3–12, 2012 in order to assess the sentinel sites proposed by the Ministry of Public Health (MOPH) for establishing surveillance for ILI and SARI. The mission led to detailing a road map for establishing a SARI surveillance system in the country which will be followed up for implementation during the project period of September 30, 2013 to September 29, 2014.

Laboratory

Sixteen NICs are currently functional in the Region, owing to the technical and financial support provided to the countries through the cooperative agreement. Eight out of the sixteen NICs are regularly sharing seasonal influenza viral isolates to the GISRS; eleven out of these sixteen NICs are also participating in the WHO EQAP with notable proficiency test results.

Laboratory Activities

- Conducted a technical mission in Lebanon from December 3–12, 2012 to discuss ways to revitalize the functions of the National Influenza Centre currently hosted at the Rafik Hariri University Hospital (RHUH) and assess the existing capacity of laboratory to support virological surveillance for ILI and SARI, particularly for isolation and detection of influenza virus by molecular techniques. The mission team members also conducted a short training session on influenza specimen collection, storage, shipment and diagnosis of influenza virus infection using PCR techniques.
- Provided technical support to Iraq, Jordan, Palestine and Tunisia in view of unexpectedly high and severe transmission of influenza in these countries during the last winter (December–February 2013). Laboratory tests performed in the NICs of these countries confirmed that the transmission was caused by influenza A(H1N1) pdm2009. Support was extended to these countries in order to share the influenza viral isolates with a WHO Collaborating Centre for characterization and to understand the changing virulence, if any.
- Conducted a technical mission for assessment of influenza laboratory and specimen collecting sites in Libya, in collaboration with Ministry of Health (MOH) from March 3–7, 2013. The mission assessed the competence and existing capacity of the Public Health Laboratory in Libya to conduct virological surveillance for seasonal influenza and be designated as a NIC.

- Provided logistics and operational support to seven NICs in the Region in terms of providing laboratory reagents, primers, collection kits, etc. to further improve their capacities for isolation and sequencing of seasonal influenza virus including any novel influenza virus.

Preparedness

The national preparedness plan for human pandemic influenza continues to be reviewed and updated in all the 23 countries in the Region following the experiences gained and lessons learned during the pandemic (H1N1) 2009. Technical support was provided in the areas of assessment and risk management during the current period.

Preparedness Activities

- Participated in a technical mission, upon an invitation from the Kingdom of Saudi Arabia, from October 23–31, 2012 to observe and review the public health preparedness measures for influenza and other respiratory viruses undertaken by the Kingdom for the Hajj 1433/2012. The technical mission advised the Ministry of Health of Kingdom of Saudi Arabia on implementing appropriate surveillance strategies and public health measures for prevention and control of influenza and other respiratory infections amongst the Hajj pilgrims and also identified a number of important issues for consideration of the Kingdom for maintaining an effective surveillance and response system for influenza and other respiratory infections in the Kingdom.
- Organized a regional consultation on risk communication for pandemic influenza in Hammamet, Tunisia from October 18–20, 2012. Forty-six participants representing Ministries of Health, crisis management centres, academic institutions and WHO staff from country offices, regional office and WHO Headquarters attended this consultation. The objective of this consultation was to improve the effectiveness of risk communicating before, during and after pandemic influenza through a systematic and structured application of appropriate communication strategies and health messages targeted for different audiences.
- Conducted a meeting on Influenza at the human-animal interface in Cairo, Egypt from March 19–21, 2013. The main objective of this consultative meeting was to develop a strategic framework for risk assessment for influenza and other viral zoonotic diseases at the human-animal interface and to identify the areas of collaboration between the animal and human health sector for prevention, detection and response to influenza caused by any novel virus. The meeting was attended by a total of 30 participants representing the Ministries of Health and Ministries of Agriculture and Animal Resources from Egypt, Iran, Jordan, Pakistan and Sudan; and experts from FAO, OIE, NAMRU-3, CDC and WHO. Following the consultative meeting, an agreement was reached for strengthening collaborations between the human and animal sectors and strengthening joint surveillance and response activities at the human-animal interface to provide early warning for emergence of novel influenza and other respiratory viruses of pandemic zoonosis in the Eastern Mediterranean Region.
- Organized a sub-regional workshop on improving public health preparedness for epidemic influenza in Amman, Jordan on August 20–22, 2013. The objective of the meeting was to improve the preparedness for seasonal outbreaks of influenza in the Eastern Mediterranean Region drawing on lessons from the severe and high transmission of influenza in some countries of the region as observed during the last winter (2012–2013). The Head of Disease Surveillance

Departments and the Head of Public Health Laboratories of Iraq, Jordan, Libya, Morocco, Palestine, Tunisia and Yemen attended this meeting along with representatives from NAMRU-3, WHO Collaborating Centre for Reference and Research on Influenza, Division of Virology, National Institute for Medical Research, Mill Hill, London, UK as well as staff members from WHO/HQ, WHO/EURO.

Training

WHO EMRO conducted a number of training activities to improve surveillance and response capacities of the countries in the areas of pandemic and seasonal influenza.

- Conducted a sub-regional training workshop on early recognition, detection and response to respiratory outbreaks in Cairo, Egypt from October 14–17, 2012. A total of 22 participants from Djibouti, Jordan, Lebanon, Oman, Morocco, Palestine, Somalia and South Sudan attended this sub-regional training workshop.
- Conducted a training course on data management for surveillance of influenza and SARI in Cairo, Egypt from April 21–25, 2013. The purpose of the course was to orient the participants to understand the basic concepts of epidemiological data analysis, the application and hands-on practice of data management techniques in analysis of influenza and SARI surveillance data. A total of 23 participants from Afghanistan, Iraq, Jordan, Lebanon, Morocco, Oman, Pakistan, Palestine, Somalia, Tunisia and Yemen attended this course.
- Conducted a sub-regional training workshop, on estimating the burden associated with influenza in general population using sentinel surveillance data, in Sharm El-Sheikh, Egypt from December 9–11, 2012. The workshop was attended by five participants from Egypt and Morocco, four participants from Jordan and Pakistan and two participants from Oman. It was facilitated by WHO Temporary Advisers who were drawn from the Field Epidemiology and Laboratory Training Programme of Pakistan, MRC Centre for Outbreak Analysis and Modeling, Imperial College, UK and the Centre for Population Health Sciences, the University of Edinburgh in UK. During the workshop, the participants were trained on calculating the disease burden estimation for influenza using the WHO manual and the electronic tools adapted by the Regional Office. Using the acquired knowledge and skills in the workshop, the participants from the attending countries calculated a national level disease burden estimation for influenza in the general population using its own SARI surveillance data.

Special Influenza Project

The Regional Office, along with the GDDRP and NAMRU-3, is extending technical support to the national health authorities of all the 23 countries in the Region to strengthen the Eastern Mediterranean Region Influenza Surveillance Network (EMRISN) to improve both epidemiological and virological surveillance for SARI and ILI in the region. The Regional Office is encouraging the participating countries in the network to enhance the quality, sensitivity and effectiveness of surveillance system for SARI and ILI and to use routinely collected surveillance data to improve their understanding on influenza epidemiology so as to better inform the national health authorities on appropriate preventive and control strategies for influenza.

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Afghanistan



Capital: *Kabul*

Infant Mortality Rate: *119.41/1,000 live births*

Population: *31,108,077 (July 2013 est.)*



Overview

The Islamic Republic of Afghanistan's Ministry of Public Health (MOPH) received funding from CDC in 2006 through the cooperative agreement "Surveillance and Response to Avian and Pandemic Influenza." Those funds were targeted for activities related to capacity building. Those funds supported the Afghan Public Health Institute (APHI), a division of the MOPH, in a number of activities including: planning and conducting pandemic preparedness and response activities, establishing surveillance for influenza-like illness (ILI) and severe acute respiratory illness (SARI), building laboratory capacity for the testing of influenza specimens, health education, and training activities. After successful completion of the first cooperative agreement, the second cooperative agreement "Sustainable Influenza Surveillance Network and Response to Seasonal and Pandemic Influenza by National Health Authorities outside the United States" was awarded in September 2011.

Highlights

- Conducted a simulation exercise for various stakeholders, including related ministries.
- Supplied National Influenza Centre (NIC) with required influenza reagents.
- Conducted financial audit of the influenza capacity building cooperative agreement.
- Conducted training on communicable disease surveillance and response, epidemiology, influenza and other priority health problems in Afghanistan.

Surveillance

The primary disease surveillance system in Afghanistan is the Disease Early Warning System (DEWS), established in 2006, with technical support from WHO and financial support of USAID. DEWS is a sentinel site based surveillance system for weekly reporting of infectious disease morbidity and mortality, operating in public and private health facilities. DEWS collects data for 15 reportable diseases, including influenza. DEWS has 330 sentinel sites in all 34 provinces of the country.

Surveillance Activities

- Routinely collected ILI and SARI surveillance data at ten sentinel sites located in eight regions of Afghanistan.
- Responded to and investigated one suspected avian influenza case.
- Investigated ten acute respiratory illness (ARI) outbreaks in Afghanistan.
- Investigated two SARI outbreaks, with specimens collected from patients both inside and outside the country.
- Reported 2,494,455 ARI cough-and-cold cases and 498,583 ARI pneumonia cases.

Laboratory

The Central Public Health Laboratory (CPHL), NIC, supports the DEWS program in laboratory confirmation of influenza specimens collected both during routine surveillance and from nationwide outbreaks. In 2012, the laboratory performed a total of 4,940 tests on specimens received from all of the DEWS coverage regions. The NIC worked closely with DEWS/MOPH to establish state-of-the-art laboratories for influenza testing. With the support of our international partners, including WHO and NAMRU-3, NIC staff have been trained extensively on typing and subtyping viruses, PCR and real-time PCR detection, and other diagnostic testing techniques. Notable progress in laboratory surveillance capacity has been achieved over the past five years.

Laboratory Activities

The National Influenza Center performed the following tests on specimens received from 10 influenza sentinel sites.

- Performed 434 tests for ILI cases.
- Performed 221 tests for SARI cases.
- Tested samples from two SARI outbreaks.

Preparedness

Afghanistan has detected and responded to 457 disease outbreaks detected by DEWS, including several outbreaks of ARI cough-and-cold and ARI pneumonia. MOPH has also established more sentinel surveillance sites across the country. Through a Codan radio network communication system, daily morbidity and mortality reports for ARI, diarrhea, and injury are collected from all 34 provinces.

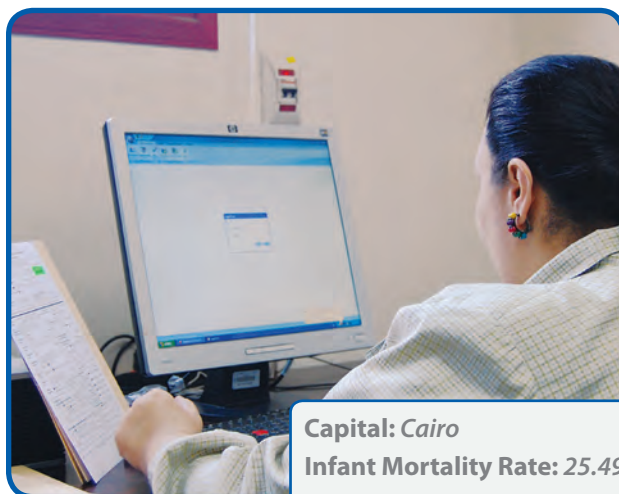
Preparedness Activities

- Conducted six DEWS coordination meetings, the aims of which were to enhance surveillance activities and improve action on outbreak detection and responses.
- Trained two people as International Health Regulations (IHR) focal points.
- Conducted outbreak investigation and response refresher training for DEWS provincial officers and CDC officers.
- Procured laboratory reagents for the NIC.

Training

- Conducted a simulation exercise in Kabul for various stakeholders, including other related ministries. The training focused on the importance of pandemic influenza.
- Supported two MOPH staff members who attended the Influenza Data Management Regional Training in Cairo, Egypt.
- Supported 12 DEWS staff members who completed an MPH course in Jodhpur, India.

Arab Republic of Egypt



Capital: *Cairo*

Infant Mortality Rate: 25.49/1,000 live births

Population: 32,649,130 (July 2013 est.)



Overview

The influenza program in Egypt was established more than 10 years ago through an interagency agreement between CDC and NAMRU-3. A cooperative agreement with the MOH provides support to conduct epidemiologic and laboratory surveillance for influenza and to build capacity in Egypt's National Influenza Center (NIC) to detect and isolate seasonal and novel influenza viruses. An influenza cooperative agreement with the Regional Office of the Eastern Mediterranean (EMRO) of WHO provides international support to countries in this region for pandemic influenza preparedness and response, infection control, International Health Regulations, health communications, and outbreak response. CDC's efforts currently support 13 eastern Mediterranean NICs, an ARI surveillance network, and influenza surveillance in West Africa. The program also conducts population based studies of the burden of influenza and effectiveness of prevention measures.

Highlights

- All influenza-related activities are coordinated by an influenza surveillance group at the Ministry of Health and Population (MOHP). Included in these activities are the nationwide hospital-based surveillance for avian and pandemic influenza, and the ILI and SARI sentinel surveillance programs.
- MOPH launched a web-based reporting system in 2011 in eight of 16 sentinel sites.
- Established the National Egyptian Disease Surveillance System (NEDSS) for communicable diseases in 2002.

Surveillance

Influenza surveillance was established in Egypt in 1999 and has expanded throughout the period of CDC funding that began in 2009. Laboratory capacity has been enhanced and the number of sites has increased. These improvements have led to an increase in the level of preparedness and response in the country. The MOHP collaborates with NAMRU-3 in Cairo, and the regional WHO office to enhance on-going surveillance activities, and also participates in the Eastern Mediterranean Acute Respiratory Infection Surveillance (EMARIS) Network.

Surveillance Activities

- Provided refresher training for sentinel site staff to ensure knowledge and responsibilities are clear.
- Employed data entry personnel in 21 governorates.
- Published weekly and monthly surveillance reports, integrating data from all sentinel sites.
- Published scientific articles on epidemiology, influenza and IHR were distributed during training and supervisory field visits to surveillance staff.
- Shared a weekly report including merged Central Public Health Laboratory (CPHL) and NAMRU-3 laboratory data with stakeholders.
- Influenza surveillance activities successfully detected early changes in influenza activity in 2012.
- Distributed surveillance bulletins to communicate surveillance results to remote audiences.

Laboratory

We have eight sentinel laboratory sites conducting influenza PCR testing in seven governorates. These laboratories are visited regularly to evaluate their performance as part of a continuous improvement process.

Junior staff who work in the PCR laboratories are regularly sent to NAMRU-3 for refresher training on real-time PCR.

WHO EMRO has done a basic assessment for our CPHL PCR unit, including a gap analysis with the goal to achieve International Organization for Standardization (ISO) 15189/2007 accreditation.

Laboratory Activities

- Tested 2,570 samples for influenza by PCR; 310 tested influenza A-positive (223 H3N2, 82 H1N1pdm09, five H5N1) and 120 tested positive for influenza B.
- Conducted seven two-week PCR lab training courses at government labs.
- Improved laboratory capacity through routine laboratory visits in collaboration with NAMRU-3.
- Participated in meetings and discussions as part of the Four-way Linking Project, which involves improving collaboration and communication between laboratory and epidemiology groups of human sectors (MOHP) and the laboratory and epidemiology groups of veterinary services sector. These meetings have been very successful and are a great benefit to both sectors.
- All influenza data has been reported to WHO's Flu-Net.
- A strategic plan for pandemic preparedness has been developed. The plan includes all phases (pre-pandemic, alert and pandemic phases).

Preparedness

The MOHP, as the representative of the preventive medicine sector, has reviewed and updated Egypt's national pandemic preparedness plan. Several workshops were coordinated by the MOHP – Epidemiology and Surveillance Unit (ESU) and were attended by the vaccination unit, communicable disease control, infection control and quarantine departments to discuss their roles and cooperation in preparedness and response to pandemic threats. There was also collaboration with veterinary services in risk assessment and joint response activities. Several training workshops were conducted on the pandemic preparedness framework including rapid response, risk communication, and humanitarian principles and standards. The extension of SARI sentinel sites to enhance influenza surveillance and early detection of MERS-CoV was established in five high-risk governorates.

Preparedness Activities

- Task force meetings were held by the preventive sector at the national level to review and update Egypt's national pandemic preparedness plan.
- The central epidemiology and virology laboratory teams in the MOHP and veterinary sector continue their collaboration in risk assessment and joint response activities at the national level.
- Extension of SARI sentinel sites to enhance influenza surveillance and early detection of MERS-CoV was established in five high-risk governorates including, Cairo, Alexandria, and the most populous governorates from Upper and Lower Egypt.
- Regional pandemic and outbreak response training workshops were held by the epidemiology and surveillance unit to enhance influenza surveillance.
- Risk communication training workshops were held by CDC for MOHP staff at the national and sub-national levels.
- Humanitarian principles and standards (SPHERE training) workshops were held by CDC for MOHP staff at the national and sub-national level.
- Regional risk communication training workshops were held by the epidemiology and surveillance unit in the pandemic preparedness framework.

Training

The MOHP conducted the following trainings in FY 2012:

- Seven training workshops were implemented on enhancing human influenza surveillance, emerging infectious diseases and IHR for 280 participants from 17 governorates.
- Nineteen training workshops were implemented on application of NEDSS Online for 527 participants from 20 governorates.
- Eight training courses were implemented in collaboration with CPHL on enhancing epidemiologic and laboratory surveillance for 112 participants from 26 governorates.
- Four hundred twenty field visits were made for follow up of ILI, SARI, communicable disease surveillance, infection control, and NEDSS Online system procedures in all 27 governorates of Egypt.

Morocco



Capital: *Rabat*

Infant Mortality Rate: *25.49/1,000 live births*

Population: *32,649,130 (July 2013 est.)*



Overview

The Kingdom of Morocco's National Institute of Hygiene (NIH) is both a National Influenza Center (NIC) and the recipient of a U.S. Centers for Disease Control and Prevention (CDC) cooperative agreement Strengthening Influenza Surveillance Networks in Morocco. The NIH was initially funded in 2006 to strengthen laboratory and epidemiology capacity for influenza surveillance.

The NIH has developed a web-based database to collect both epidemiologic and laboratory information related to influenza-like illness (ILI) and severe acute respiratory infection (SARI). The NIH collaborates on influenza surveillance activities in the 16 administrative regions of Morocco with the epidemiological disease and surveillance units in the country's Ministry of Health (MOH).

Highlights

- Awarded Vaccine Policy Cooperative Agreement.
- Received ILI samples from both a private physicians' network and from a health unit network; received SARI samples from SARI sites in regional hospitals.
- Processed 862 samples, of which 245 were positive for influenza.
- Performed testing for other respiratory pathogens, including RSV, adenovirus, and parainfluenza.

Surveillance

Morocco's MOH uses multiple surveillance systems to characterize the epidemiology of influenza, both for the observation of seasonal influenza trends, and to be prepared in the event of a pandemic. SARI is tracked through a network of 16 regional hospitals where syndromic and virologic data are collected. ILI is tracked through a network of 380 health units and a network of 110 private physicians. Sixteen of the 380 health units collect both syndromic and virologic data.

The internet database developed by the NIH provides instant notification of influenza activity. Influenza data are entered into the database by the sentinel sites and the NIC.

Surveillance Activities

- Continued to test influenza specimens, despite challenges accessing funds.
- Tested 862 specimens during the 2011–2012 season. Seventy-four percent (638) of specimens were collected by the ILI surveillance system, at sites in both the private physician network and the health unit network. The remaining 224 specimens were obtained from SARI surveillance sites in regional hospitals.
- Twenty-eight percent of specimens were positive for influenza, including 231 A(H3N2), 13 B viruses, and one A(H1N1)pdm09 virus. Specimens were also tested for RSV, adenovirus, and parainfluenza.

Laboratory

Morocco's surveillance network includes one NIC and 16 regional laboratories. The NIC has the capacity to conduct real-time PCR testing, virus culturing, HAI testing, DFA testing, sequencing and phenotypic analysis of drug susceptibility. Four regional laboratories are equipped with PCR machines.

Laboratory Activities

- Procured laboratory consumables and standard reagents, such as immunofluorescence assay (IFA) kits, PCR reagents, and bacterial tests.

Training

- Attended the Data Management and Basic Epidemiologic Analysis for Influenza Training Course in Johannesburg, South Africa, November 2011.
- Attended the 3rd Annual African Network for Influenza Surveillance and Epidemiology (ANISE) Meeting in Nairobi, Kenya, February 2012.
- Attended the WHO/CDC Influenza Data Management Training in Cairo, Egypt, April 2013.

Publications

Barakat A, Ihazmad H, El Falaki F, Tempia S, Cherkaoui I, El Aouad R. 2009 Pandemic influenza A virus subtype H1N1 in Morocco, 2009–2010: epidemiology, transmissibility, and factors associated with fatal cases. *J Infect Dis.* 2012 Dec 15;206 Suppl 1:S94–100. doi: 10.1093/infdis/jis547.

Radin JM, Katz MA, Tempia S et al. Influenza surveillance in 15 countries in Africa, 2006–2010. *J Infect Dis.* 2012 Dec 15;206 Suppl 1:S14–21. doi: 10.1093/infdis/jis606.

Pakistan



Capital: Islamabad

Infant Mortality Rate: 59.35/1,000 live births

Population: 193,238,868 (July 2013 est.)



Overview

Pakistan has had a cooperative agreement with CDC since 2006 which supports development of state-of-the-art laboratories at designated sentinel sites in Pakistan for rapid confirmation of human and novel influenza cases. The funds also support activities aimed at pandemic influenza preparedness through improved national influenza surveillance, as well as the development of a national vaccine policy. Significant progress has been made in light of continuing social and political challenges. A total of eight sentinel sites are located in outpatient departments of major provincial tertiary care hospitals, as well as one in the federal capital, Islamabad. Sites were selected on the basis of representative geographic distribution, high population density, and patient turnover rate.

Highlights

- Pathologists, laboratorians, scientists and physicians attended a scientific seminar discussing global epidemiology of influenza, risk factors and management.
- Key surveillance staff of the Balochistan Health Department attended rapid response training.
- Hosted awareness seminars on epidemiology and prevention strategies at medical schools across the country in 2012 and 2013.
- Hosted Consultation on Enhanced SARI Surveillance for Avian Influenza H7N9 and MERS-CoV to obtain feedback on the induction of additional SARI sites.

Surveillance

There was no sentinel site lab-based influenza surveillance prior to the cooperative agreement. Currently, eight sentinel sites are reporting influenza-like illness (ILI)/severe acute respiratory infection (SARI) cases to the National Influenza Center (NIC) at the National Institute of Health (NIH).

Surveillance Activities

- Activated laboratory-based surveillance for ILI/SARI cases at three new sentinel sites at Multan, Muzaffarabad and Gilgit this year.
- Conducted sentinel site physician orientation and rapid response trainings in the three newly established sentinel sites.
- Trained and activated rapid response teams for timely response.
- Modified and periodically reviewed case definitions and standard operating procedures for sampling, storage and sample transportation based on emerging H7N9 and MERS-CoV situations.
- Dispatched viral transport media (VTM) to provincial health departments and high-risk districts on a regular basis to ensure safe transport of specimens.
- Procured and administered seasonal influenza vaccine to personnel engaged in influenza surveillance.
- Strengthened online submission of epidemiological data on ILI and SARI cases on FluID.

Laboratory

The second cooperative agreement envisaged strengthening of the laboratory network for lab-based influenza surveillance using virus isolation and molecular diagnosis of influenza. The existing sentinel site laboratories routinely process specimens and send aliquots to NIH Pakistan for confirmation and virus isolation. Three additional influenza labs have been established in the new sentinel surveillance sites. Influenza surveillance has been strengthened through the network of the existing laboratories where PCR is done by trained lab personnel.

Laboratory Activities

- Processed and reported 6,068 samples from eight sites in 2011–2013; 1,112 of those were positive.
- Provided logistic and technical support to all sentinel influenza laboratories.
- Shared virologic data regularly via WHO FluNet.
- Initiated indigenous sequencing of influenza viruses with technical support from CDC.
- Authorized NIH as the testing laboratory for Influenza A/H7N9 and MERS-CoV since it is the designated national laboratory for viral diagnostics.
- Influenza virus samples are regularly submitted through the Global Influenza Surveillance and Response System (GISRS) to CDC to be included for consideration in annual Northern Hemisphere vaccine recommendations.
- Developed a manual on influenza diagnostic protocols that will be distributed to all laboratories.

Preparedness

Based upon the National Preparedness Plan for Prevention and Control of Avian and Pandemic Influenza, a national program was implemented in 2006 by the Ministry of Health. Provincial health departments in Pakistan are responsible for implementing major components including emergency response, provision of appropriate health services, procurement of antivirals/vaccine, disease containment and communication.

Training

- Organized two short courses on epidemiology and biostatistics for the surveillance, epidemiology, and public health officers in June 2011 and July 2012.
- Hosted five, three-day courses on bio-safety and bio-security for laboratorians, pathologists, scientific officers, technologists and technicians during which over 100 laboratory-related personnel were trained.
- Conducted four, two-day rapid response trainings which were attended by 126 staff in Multan, Lahore, Karachi and Quetta.
- Provided sentinel site physician training to twenty doctors at Nishtar Medical College, Multan.
- Organized three awareness seminars for the medical students and faculty of the medical schools in Peshawar, Lahore and Rawalpindi.
- Conducted PCR training for 14 laboratory staff from the Quetta, Gilgit, and Muzaffarabad sentinel sites.
- Organized the first ever laboratory quality management training in collaboration with FELTP Pakistan. It was attended by laboratorians, pathologists, scientific officers, technologists and technicians; over 40 personnel were trained.
- Organized a laboratory quality management course for provincial sentinel site staff, laboratorians, Disease Early Warning System (DEWS) and FELTP officers in July 2013.

Publications

Badar N, Bashir Aamir U, Mehmood MR et al. Influenza Virus Surveillance in Pakistan during 2008–2011. *PLoS One*. 2013 Nov 8;8(11):e79959. doi: 10.1371/journal.pone.0079959. eCollection 2013.

Bashir Aamir U, Badar N, Mehmood MR et al. Molecular Epidemiology of Influenza A(H1N1)pdm09 Viruses from Pakistan in 2009–2010. *PLoS One*. 2012;7(8):e41866. doi: 10.1371/journal.pone.0041866. Epub 2012 Aug 20.

Nisar N, Bashir Aamir U, Badar N et al. Prediction of clinical factors associated with pandemic Influenza A (H1N1) 2009 in Pakistan. (In Press).

Tunisia

Capital: *Tunis*

Infant Mortality Rate:

24.07/1,000 live births

Population:

10,835,873 (July 2013 est.)



Overview

Influenza surveillance was implemented in Tunisia as national preventive program in 1980. It involves many stakeholders at the national level: the Directorate of Care and Primary Healthcare Direction (DSSB) and National Influenza Center (NIC) in addition to the Ministry of Agriculture for wildlife monitoring and the National Observatory of New and Emerging Diseases (ONMNE) for annual data analysis and dissemination.

The primary surveillance program for estimating influenza-like illness (ILI) at the national level was established by DSSB all over the country with the participation of 268 sentinel sites selected by the regions and representing about 10% of the total health sites and more than 3% of the whole population. These sites are located within the 24 governorates of Tunisia. The program is conducted seasonally during the period from the beginning of October until the end of April each year.

In September 2013, Tunisia was awarded a capacity building cooperative agreement, Surveillance and Response to Avian and Pandemic Influenza by National Health Authorities outside the United States. The overarching goal of the project is to mitigate the effects of a future influenza pandemic by enhancing preparedness and response capacity in the country. With cooperative agreement funds, Tunisia aims to improve the current influenza surveillance system by strengthening ongoing activities and enhance the level of preparedness and response to annual influenza epidemics and future pandemics.

Highlights

- Awarded Capacity Building Cooperative Agreement.
- Established surveillance sites within the 24 governorates of Tunisia.

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WHO EUROPEAN REGION (EUR)

WHO European Region (EUR) Overview

Currently, there are seven bilateral influenza cooperative agreements that support influenza activity in the European Region. These cooperative agreements are with ministries of health or other institutions that work with the U.S. Centers for Disease Control and Prevention (CDC) to build capacity in order to routinely identify, diagnose and respond to seasonal and pandemic influenza.

CDC supports the following countries and/or entities via cooperative agreements:

- Armenia
- Georgia
- Kyrgyzstan
- Moldova
- Russian Federation
- The Southeast European Center for Surveillance and Control of Infectious Diseases— SECID (Priority countries— Albania, Bosnia and Herzegovina, Macedonia, and Montenegro)
- Ukraine

In addition, CDC supports WHO EURO via a cooperative agreement to provide technical and coordination support to Member States. This cooperative agreement also supports influenza activities in Romania.

The core activities of these bilateral agreements are:

- To build sustainable national capacity for the detection, identification and response to seasonal, avian and novel influenza.
- To develop interagency pandemic preparedness plans.
- To strengthen capacity for integrated laboratory and epidemiologic surveillance for influenza-like illness (ILI) and severe acute respiratory infections (SARI), which includes making routine contributions to WHO's Global Influenza Surveillance and Response System (GISRS) and implementing International Health Regulations 2005 (IHR).
- To develop and train local rapid response and containment teams.

Influenza Division Contacts

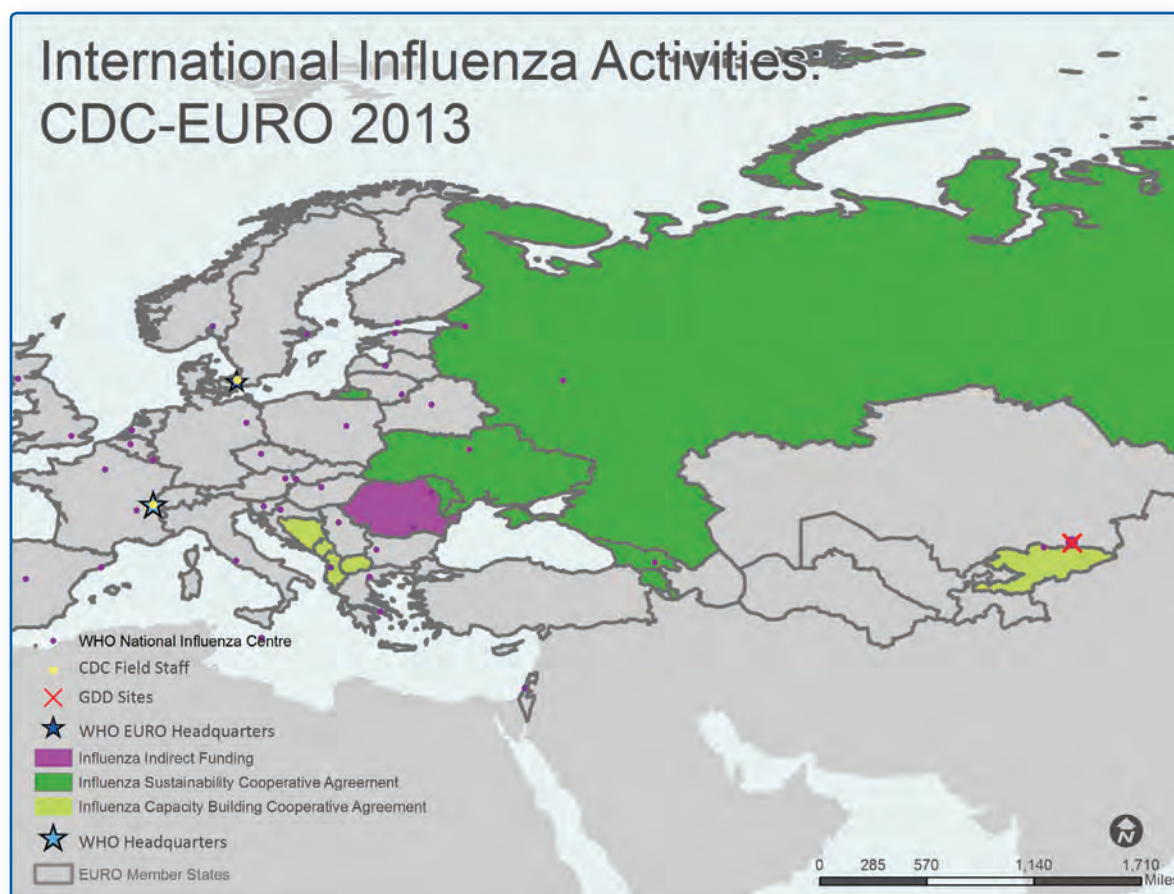
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WHO Regional Office for Europe (EURO)



Highlights

- Published 32 weekly EuroFlu influenza surveillance bulletins; three issues of Flu Focus; seasonal influenza vaccination recommendations; regular Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and avian influenza A(H7N9) summaries; four peer-reviewed articles and one textbook chapter.
- Conducted the first WHO/Europe Flu Awareness Day; one subregional and one regional (jointly with ECDC) influenza surveillance meeting; missions to nine countries to strengthen surveillance, vaccine uptake and conduct burden studies; a multi-country severe acute respiratory infection (SARI) risk factor study and training in data management; facilitation of pandemic workshops in six countries to strengthen response to avian influenza A(H7N9).
- Recognized the National Influenza Centre, Republic of Moldova.
- Participated/presented at 15 international and WHO meetings.

U.S. CDC Direct Support

The second five-year cooperative agreement Surveillance and Response to Pandemic and Avian Influenza by Regional Offices of the World Health Organization began in September 2011 and entered its second year in 2012.

The WHO Regional Office for Europe (WHO/Europe) in Copenhagen, Denmark, serves 53 Member States (MS) with a population exceeding 900,000 million. Influenza activities are conducted by the Influenza & Other Respiratory Pathogens programme (IRP). In 2012/13, IRP ran the Regional surveillance platform, EuroFlu; organized the European Region influenza surveillance network Annual Meeting with the European Centre for Disease Prevention and Control (ECDC); provided training and technical assistance to Member States to strengthen influenza (outpatient and SARI) surveillance, as well as conducted studies to determine risk factors for severe disease due to influenza and burden of disease; supported the sharing of influenza viruses within GISRS; implemented the second survey on vaccine policies and uptake in the Region and piloted a tool to increase influenza vaccine uptake in health care workers; supported pandemic plan revisions; and developed and disseminated technical guidance related to the outbreaks of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and avian influenza A(H7N9).

In 2013/2014, IRP will continue the above activities and, in addition, will conduct a series of workshops and trainings in clinical management, outbreak response and laboratory detection to prepare countries to respond to cases of avian influenza A(H7N9) or other forms of severe influenza. At least one National Influenza Centre (NIC) will be assessed for recognition by WHO and external quality control for virus isolation: and antiviral susceptibility testing, coupled with follow-up training for participating laboratories, will be conducted. Further improvements to data analysis and presentation in the EuroFlu bulletin will be made. The joint WHO/Europe-ECDC pandemic guidance will be finalized, in-line with the revised WHO global pandemic guidance.

Surveillance

WHO/Europe publishes the EuroFlu bulletin in English and Russian (www.euroflu.org) weekly during the influenza season (weeks 40 to 20) and biweekly outside of the season. Surveillance is coordinated with ECDC. The timing and duration of the 2012/2013 season were similar to previous seasons in the European Region, although influenza activity and morbidity rates (outpatient and SARI) were higher than in the previous season. All three seasonal influenza viruses co-circulated, 63% were influenza A and 37% influenza B; and of the sub-typed influenza A viruses, about two-thirds were A(H1N1)pdm09 and one third A(H3N2). Excess all-cause mortality in up to 18 countries that participate in the EuroMoMo project was only observed in those above age 64 and was comparable with the previous season. Circulating viruses matched with those recommended by WHO for inclusion in the 2012/2013 Northern Hemisphere seasonal influenza vaccine and there was no indication of increased resistance to neuraminidase inhibitors.

Surveillance Activities

- Summarized and published the EuroFlu bulletin with data from, on average, 47/53 MS, including sentinel SARI data from 12 MS.
- Published a report describing key features of the 2012/2013 influenza season.
- Conducted the third joint WHO/Europe and ECDC annual influenza meeting for MS and a sub-regional surveillance network meeting for newly independent states.

- Piloted the quantification of the qualitative indicator for influenza activity on the EuroFlu platform to aid interpretation of data and comparison across seasons.
- Performed a multi-country study to identify risk factors for severe outcomes in SARI cases from sentinel SARI surveillance.
- Published WHO/Europe recommendations for seasonal influenza vaccination, including a summary of WHO recommendations on influenza vaccine composition and target groups for vaccination.
- Collaborated with the Vaccine European New Integrated Collaboration Effort (VENICE) and ECDC on the second regional survey on influenza vaccine policy and uptake.
- Developed and piloted a tool to aid MS in targeting health care workers for influenza vaccination in one country.
- Conducted the first Flu Awareness Day to promote vaccination in the Region and answer any questions about influenza prevention and treatment, through web-articles, a twitter chat and a video “The 5 things everyone needs to know about flu”.

Laboratory

In the European Region, 41 of 50 MS with influenza surveillance now have NICs recognized by WHO. Through the CDC cooperative agreement, NICs in the European Region receive training in influenza laboratory techniques, support to improve laboratory quality, assistance with shipment of viruses to WHO Collaborating Centres for Reference and Research on Influenza (WHO CC), and reagents for influenza testing.

Laboratory Activities

- The NIC in Republic of Moldova was formally recognized by WHO, bringing the number of countries in the Region with a WHO-recognized NIC to 41.
- A total of 26 countries sent 29 shipments of viruses to the WHO CC before the WHO Consultation on the Composition of Influenza Virus Vaccines for the Northern Hemisphere 2013/2014. The global WHO shipment fund was used to ship 17 of those shipments from 15 countries. A WHO training on shipping infectious substances was provided to 24 specialists from national, regional and sub-regional levels and reference laboratories in Kazakhstan.
- Sixty-one influenza laboratories in 47 MS participated in the WHO EQAP and 78% achieved correct results (10 out of 10)— compared with 67% in 2012.
- Staff from two NICs received training at the WHO CC, National Institute for Medical Research, London, United Kingdom.

Preparedness

In response to lessons learned from the 2009 pandemic, WHO/Europe and ECDC developed joint pandemic preparedness guidance for the Region, to be published in 2014. IRP also provided assistance in the development of WHO pandemic guidance and implementation of the Preparedness Framework. Assistance was provided to countries in developing their pandemic plan.

In response to the MERS-CoV and avian influenza A(H7N9) outbreaks, WHO/Europe provided support to countries, mainly by disseminating key information in regular, timely summaries and posting WHO recommendations and guidance on the WHO/Europe website in English and Russian. Assistance was provided to NICs for development of PCR capacity for the detection of these emerging viruses. Trainings in clinical management of severe influenza were conducted in Azerbaijan and Uzbekistan.

Preparedness Activities

- A workshop on pandemic preparedness held for 23 countries of the South-eastern Europe Health Network, the newly independent states, Israel, Switzerland and Turkey.
- Finland revised and published its national pandemic plan.
- In collaboration with GIZ (Deutsche Gesellschaft für Internationale Zusammenarbeit), support was provided to Tajikistan in revising and implementing its national pandemic plan.
- The WHO/Europe influenza website was upgraded to include information on emerging respiratory viruses, including avian influenza A(H7N9) and MERS-CoV.
- IRP staff co-authored Chapter Nine (Pandemic Preparedness) of the 2nd edition of Pandemic Influenza textbook.
- Approximately 80 clinicians were trained in the clinical management of severe influenza cases in Azerbaijan and Uzbekistan in September 2013.

Training

WHO/Europe, in conjunction with selected Member States, hosted the following regional and inter-country trainings in 2012/2013:

- Staff from the NICs in Russia and Serbia received training at the WHO CC, National Institute for Medical Research, London, UK.
- WHO training on shipping infectious substances was provided to 24 specialists from national, regional and sub-regional levels and reference laboratories in Kazakhstan.
- Training in data analysis and management for seven countries conducting sentinel SARI surveillance and participating in the multi-country study on risk factors for severe disease was conducted in collaboration with CDC and the University of Nijmegen Medical Centre, the Netherlands.
- Training on sentinel surveillance was held for approximately 200 sentinel network clinicians and laboratory specialists in Romania.
- A training in the clinical management of severe acute respiratory infections focused on the current A(H7N9) outbreak was provided in Azerbaijan and Uzbekistan.

Published Papers

The IRP team regularly contributes to peer-reviewed articles for medical journals, with the intention of disseminating information about the work done in collaboration with Member States to a wider audience. The following articles were co-authored by IRP members during 2012–2013:

Palm D, Pereyaslov D, Vaz J, Broberg E, Zeller H, Gross D, et al. "Laboratory capability for molecular detection and confirmation of novel coronavirus in Europe, November 2012", *Euro Surveill.* 2012;17(49).

Brown C and Hegermann-Lindencrone M. "Pandemic preparedness" in Van-Tam J and Sellwood C (eds) (2012) *Pandemic Influenza*, 2nd Edition. CABI, Wallingford, United Kingdom.

Brown C. "The role of the WHO Regional Office for Europe in response to seasonal, avian and pandemic influenza." *Bundesgesundheitsblatt, Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz*, January 2013, Volume 56, Issue 1, pp 47–55. Abstract.

Jorgensen P, Wasley A, Mereckiene J, Cotter S, Weber JT, Brown C, "Unequal access to vaccines in the WHO European Region during the A(H1N1) influenza pandemic in 2009." *Vaccine*; 31 (38) 2013, 4060–62.

Thompson CI, Lackenby A, Daniels RS, McCauley JW, Pereyaslov D, Broberg EK, et al. "Evaluation of influenza virus antiviral susceptibility testing in Europe: results from the first external quality assessment exercise." *J Clin Virol.* 2013;56(3):212–8.

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Armenia



Capital: Yerevan

Infant Mortality Rate: 17.59/1,000 live births

Population: 2,974,184 (July 2013 est.)



Overview

In 2006, the State Hygiene and Anti-Epidemic Inspectorate (SHAEI) of the Ministry of Health (MOH) in Armenia began a cooperative agreement with CDC to develop and enhance influenza surveillance and laboratory capacity. Since 2010, Armenia has conducted both influenza-like illness (ILI) and severe acute respiratory infection (SARI) surveillance in the cities of Yerevan, Kapan (Syunik marz) and Vanadzor (Lori marz) and the sentinel surveillance system now includes a fully functioning PCR laboratory in each city. With a direct focus on avian and human influenza, Armenia's epidemiological surveillance capacity has been enhanced since the beginning of the partnership with the CDC.

Highlights

- Conducted a laboratory assessment of National Reference Virology Laboratory in CDC/Yerevan with CDC experts during CDC/WHO joint mission to Armenia.
- Shipped positive samples to the WHO Collaborative Centre in London, Mill Hill.
- Launched an additional PCR laboratory in Syunik marz in 2012, with 112 samples tested in the first year.

Surveillance

The sentinel system in Armenia is integrated into the general epidemiological surveillance system of infectious diseases. ILI sentinel surveillance includes four polyclinics: two in Yerevan, one in Vanadzor, and one in Kapan. SARI sentinel surveillance includes nine hospitals: seven in Yerevan, one in Vanadzor, and one in Kapan. Each hospital has doctors in key departments designated as surveillance doctors. The sentinel sites include one pediatric (Yerevan), one maternity (Yerevan), two adult (Yerevan) and five general (Yerevan, Vanadzor and Kapan) hospitals.

The surveillance system provides a good representation of age groups, gender, ethnicity, socio-economic status and risk factors/medical conditions. Protocols, ILI and SARI forms, specimen collection supplies, and training were provided by the MOH/SHAEI staff to all sites. Influenza surveillance national standards, including sentinel surveillance guidelines, were updated based on new WHO and CDC recommendations and requirements.

Funding was received to enhance SARI surveillance for H7N9 in Armenia in FY 2013. Plans to enhance the system include: increasing the number of SARI specimens collected so that specimens are collected from 100% of patients meeting the SARI case definition; addition of a SARI site near the border crossing site in Tavush marz; and addition of a SARI site at or near major poultry trade centers in Kotayq/Yerevan.

Surveillance Activities

- Identified two new sentinel sites –Tavush marz (border crossing point) and Kotayq marz (major poultry trade center).
- Updated the influenza surveillance national standards, including sentinel surveillance guidelines, to include new WHO and CDC recommendations and requirements for H7N9 and Coronavirus.

Laboratory

A laboratory assessment was conducted in the National Reference Virology Laboratory at CDC/Yerevan in collaboration with CDC experts. Positive samples were shipped to the WHO Collaborating Centre in London, Mill Hill. Laboratory supplies and accessories needed for maintenance and implementation of the influenza sentinel surveillance were procured, including the QIAamp Viral RNA and Superscript III Platinum One step qRT-PCR system (Invitrogen) kits, masks, and gloves. Overall, the CDC/Yerevan, Lori marz and Syunik marz PCR laboratories have tested 700 samples taken from sentinel sites in Yerevan, Vanadzor (Lori marz) and Kapan (Syunik marz). Data are uploaded to the EuroFlu site regularly. Plans were made to enhance laboratory capacity to conduct testing for potential cases of H7N9 by providing all PCR laboratories with the necessary supplies and equipment.

Preparedness

A monitoring and evaluation exercise was conducted by the Project Team Leader, an expert/consultant, and Armenian WHO focal points on influenza epidemiology and virology, and other responsible persons.

Training

- Developed training modules on SARI, H7N9 and coronavirus (including case definitions, management, sampling and testing). The trainings were based on revised influenza sentinel surveillance guidance and WHO and CDC recommendations. Training modules were designed for sentinel doctors and nurses and included pre-and post-test surveys.
- Conducted training on the influenza electronic data management system for sentinel site doctors and nurses, epidemiologists and supervisors. Personnel from new sentinel sites that need to be trained were identified.

Kyrgyzstan

Capital: Bishkek

Infant Mortality Rate:

29.73/1,000 live births

Population:

5,548,042 (July 2013 est.)



Overview

Kyrgyzstan is located in Central Asia and gained its independence from the Soviet Union in 1991. During Soviet times, Kyrgyzstan conducted routine influenza surveillance as part of a universal syndromic disease surveillance system with mandatory registration of all acute respiratory viral illness (ARVI) cases without laboratory confirmation. After the collapse of the Soviet Union, this system was interrupted due to lack of logistical support and trained personnel. Currently, universal surveillance for influenza and ARVI is ongoing, but the system continues to face serious challenges.

Since 2008, Kyrgyzstan has conducted sentinel surveillance for ILI and SARI at two sites, the cities of Bishkek and Osh. Data from the sentinel system is reported to EuroFlu on a weekly basis during the flu season. Also in 2008, the Virology Laboratory at the Department of the State Sanitary and Epidemiological Surveillance (Republican SES) in Bishkek was recognized as a National Influenza Center by WHO.

In September 2013, Kyrgyzstan was awarded a capacity building cooperative agreement, *Surveillance and Response to Avian and Pandemic Influenza by National Health Authorities outside the United States*. The overarching goal of the project is to mitigate the effects of a future influenza pandemic by enhancing preparedness and response capacity in the country. With cooperative agreement funds, Kyrgyzstan aims to improve laboratory capacity, strengthen surveillance for seasonal influenza in clinics and hospitals, revise the national pandemic preparedness plan, and enhance capacity for early warning and rapid response.

Highlights

- Awarded Capacity Building Cooperative Agreement.
- Shared seasonal influenza viruses with WHO Collaborating Centers.
- Submitted weekly virologic data to EuroFlu and FluNet during the influenza season.
- Participated in the WHO External Quality Assessment Project.

The Southeast European Center for Surveillance and Control of Infectious Diseases (SECID)

Bosnia and Herzegovina

Capital: Sarajevo

Population: 3,875,723

Montenegro

Capital: Podgorica

Population: 653,474

Macedonia

Capital: Skopje

Population: 2,087,171

Albania

Capital: Tirana

Population: 3,011,405

Overview

The countries of South East Europe (Albania, Bulgaria, Bosnia and Herzegovina, Croatia, Macedonia, Moldova, Montenegro, Romania and Serbia) have been collaborating in the field of communicable disease surveillance since the Dubrovnik Pledge in 2001, within the framework of the South-eastern Europe Health Network (SEEHN). Following upon this collaboration, the South East European Center for Surveillance and Control of Infectious Diseases (SECID) was established in 2013 near the Institute of Public Health in Tirana, Albania to support the countries of South East Europe (SEE) in the field of surveillance and control of infectious diseases, including influenza and International Health Regulations (IHR) implementation.

In September 2013, SECID was awarded a capacity building cooperative agreement, *Surveillance and Response to Avian and Pandemic Influenza by National Health Authorities outside the United States*. The project aims to strengthen influenza surveillance and response and pandemic preparedness in SEE countries. Revision of pandemic preparedness plans, IHR core capacity development, and support to ensure NICs in the region are fully functioning are the main goals of the five year agreement. The project will focus on the priority countries of Bosnia and Herzegovina, Montenegro, Macedonia and Albania, with support for other countries in the region to address specific problems and further enhance collaboration in the region as a whole.

Highlights

- Awarded Capacity Building Cooperative Agreement.
- WHO recognized NICs in Albania, Bulgaria, Croatia, Moldova, Romania and Serbia.
- Collaborated with WHO Regional Office for Europe and European Center for Disease Control (ECDC) on laboratory trainings and pandemic preparedness activities.

Republic of Georgia



Capital: *Tbilisi*

Infant Mortality Rate: *14.21/1,000 live births*

Population: *4,555,911 (July 2013 est.)*



Overview

CDC has supported the development of influenza surveillance in the Republic of Georgia through a cooperative agreement with the National Center for Disease Control and Public Health of Georgia (NCDC Georgia) since 2006. Since the beginning of the cooperative agreement, both epidemiology and laboratory components of the influenza surveillance system have been greatly strengthened. Quality assurance measures have been developed and implemented in the laboratory and at the surveillance sites. The influenza surveillance system has been enhanced by conducting annual rounds of surveillance system monitoring and trainings of epidemiologists and clinicians in influenza epidemiology and surveillance. A national preparedness plan was developed in 2006 and approved by the MOH in 2009. Some parts of the plan have since been updated and a new version should be approved soon. The National Influenza Lab (NIL) at NCDC Georgia was recognized by the World Health Organization (WHO) as a National Influenza Center (NIC) in 2007.

Highlights

- Established an influenza sentinel surveillance system throughout the country.
- Developed and implemented quality assurance measures in laboratories and at surveillance sites.
- Enhanced the influenza surveillance system by conducting a number of annual rounds of surveillance system monitoring and trainings of epidemiologists and clinicians in influenza epidemiology and surveillance.

Surveillance

Since 2012, when influenza and ARI were excluded from the list of notifiable diseases of the national surveillance system, the ILI/SARI sentinel system became the only source of data for influenza surveillance. However, during the previous year, data received from sentinel sites and the national routine surveillance system was monitored by the Project Management Unit, and the acquired results showed that the sentinel surveillance system precisely reflected trends reported by the national routine surveillance system.

Surveillance Activities

- Continued regular monitoring of health care facilities throughout the country to reveal gaps and challenges in the influenza surveillance system.
- Provided sentinel and non-sentinel sites with all necessary equipment and supplies, including liquid nitrogen for adequate storage and transportation of collected specimens.
- Submitted virological and epidemiological data electronically to the European Influenza Surveillance Platform (www.euroflu.org) on a weekly basis.
- Updated and uploaded data to the NCDC Georgia website (www.ncdc.ge) regularly throughout the year.
- Prepared and disseminated surveillance reports among health care professionals and stakeholders throughout Georgia.

Laboratory

The NIL was established at NCDC Georgia in 2006 and was recognized as a NIC by WHO in 2007. Over the past 7 years, laboratory capacity was strengthened as a result of staff training on RT-PCR testing, virus isolation, and hemagglutination inhibition, as well as the procurement of essential equipment and supplies.

In FY 2013, Georgia received emergency supplemental funding to enhance SARI surveillance for H7N9. Funding will be used to establish three additional SARI sentinel sites and to ensure specimens are collected from and laboratory testing is conducted on all SARI and pneumonia cases. Previously, SARI specimens have only been collected on days specified by protocols and were not collected from all cases.

Laboratory Activities

- Procured reagents and supplies for the NIC.
- Confirmed and reported 29 lethal cases due to A/H1p during the 2012–2013 season. The age of fatal cases ranged from 2 to 75 years; 23 fatal cases (79.3%) were in the 30–64 year age group.
- Tested a total of 1,509 specimens for influenza at NIL from October 2012 to September 2013. Of the samples tested, 332 were found to be positive for influenza A/H1p, and 111 were positive for Influenza B.
- Collected 30 samples from the specimens taken during the 2012–2013 influenza season and sent them to the WHO CC London for virus isolation, sequencing and resistance screening.

Preparedness

A draft of a national preparedness plan was developed in 2006, and approved by the MOH in 2009. This plan was activated during the pandemic with great success. Two lead specialists of NCDC Georgia participated in a workshop focused on updating National Preparedness Plans organized by WHO in Copenhagen, Denmark in December 2012.

Training

- Conducted trainings for health care providers, including clinicians and sentinel site personnel, on influenza surveillance, prevention and infection control.
- During visits to monitor sentinel surveillance sites, conducted on-site surveillance training for epidemiologists responsible for patient registration and reporting in order to improve their skills and to strengthen the system.

Republic of Moldova



Capital: Chisinau

Infant Mortality Rate: 13.28/1,000 live births

Population: 3,619,925 (July 2013 est.)



Overview

Prior to working with CDC, Moldova implemented hospital-based surveillance in nine sentinel sites, where data was collected on acute respiratory infection (ARI), influenza-like illness (ILI), and severe acute respiratory infection (SARI). In 2009, the Moldovan Ministry of Health (MOH)/National Centre of Public Health (NCPH) was awarded a cooperative agreement from CDC to strengthen human and infrastructure capacities for pandemic preparedness, influenza surveillance, monitoring and early response, communication and infection control. The MOH started laboratory-based surveillance at five sites in 2011. Each sentinel site reports data to the National Viral Laboratory (NVL), which publishes regular surveillance reports regarding epidemiologic and laboratory data and reports weekly through WHO's EuroFlu network. Seminars and trainings have been held to improve biosafety sample collection and shipment, information collection for ARI, ILI, and SARI based on a standard case definition, and reporting. In addition to the partnership with CDC, Moldova also collaborates with the World Health Organization (WHO) Regional and Country Offices, as well as other international partners.

Highlights

- Improved the influenza surveillance system by strengthening the existing hospital-based surveillance and establishing laboratory-based surveillance.
- Collected SARI data from nine hospital-based surveillance sentinel-sites.
- Trained laboratory scientists and technicians on sample collection and screening diagnostics methods.

Surveillance

During the reporting period two laboratory-based sentinel sites were established. Five laboratory-based sentinel sites collected samples and sent them to the NVL. About 50 samples are sent weekly, including samples from patients with SARI. During the last two years, the nine hospital-based surveillance sentinel-sites started to collect data for SARI. Software for influenza surveillance data collection from the nine hospital-based surveillance sentinel sites was established and implemented and medical staff were trained to use the software. The software analyzes data and sends information weekly to the WHO EuroFlu Network. A working group updated the national definitions and main indicators for the 2012/2013 influenza season to be input into the EuroFlu website (for geographical spread, intensity, impact, trend and the dominant type/subtype).

Surveillance Activities

- Three specialists from the NCPH attended the working meeting "Influenza, ARI & SARI Surveillance", hosted by Cantacuzino Institute, Bucharest, Romania (October 2012).
- Three specialists from the NCPH attended the ESCAIDE Conference, Edinburgh, Scotland, UK (October 2012).
- Trained sixty participants on multiple surveillance, outbreak investigation and response, and disease-control activities.

Laboratory

All specimens collected from five laboratory-based sentinel-sites are tested weekly in the NVL. A well-functioning system with a well-maintained cold chain is in place to transport specimens to the NVL in a timely manner. Specimens are all collected at the beginning of the week to ensure they arrive at the National Laboratory by Thursday for testing and are not refrigerated for more than three days. About 50 samples are sent weekly. To improve specimen transportation, a car was purchased with financial support from the CDC grant. The newly renovated NVL provides real-time PCR testing for influenza including detection, typing and subtyping. The NVL fulfilled the terms of reference of a National Influenza Center (NIC) and was designated by WHO as a NIC in 2013.

Laboratory Activities

- Collected and tested specimens from five laboratory-based sentinel-sites weekly in the National Viral Laboratory (NVL).
- Collected and sent more than 100 clinical samples for confirmation and quality control assurance of laboratory testing to the WHO CC in London.
- Participated in external quality control programs at WHO CC London, WHO CC Hong Kong and WHO CC Atlanta while keeping internal quality control procedures in place at NVL.
- Strengthened laboratory capacity by having three specialists from the NVL attend the 3rd International Influenza Meeting in Muenster, Germany, September 2012. Expenses were covered by the CDC grant.
- Procured consumables and reagents for laboratory diagnosis of influenza.
- Purchased hardware for reporting results from the influenza laboratory network at the national level to WHO, CDC and other international partners.

Preparedness

A joint WHO/CDC mission was conducted in December 2012. During the visit, the team worked with Moldova influenza staff to assess the national core capabilities for pandemic influenza preparedness and response. Recommendations from the mission included: to ensure the decision making structure incorporates information from a multi-sectoral group and WHO; to work towards standard operational procedures for decision making; to prioritize the funding allocated to the plan for the highest priority issues; and to work towards sustainable funding. Because the world has entered an era in which the numbers of new and re-emerging global health threats (infections such H1N1 influenza, H5N1 influenza, SARS, drug-resistant pneumonia; natural disasters, and other public health emergencies) argue for a longer-term, more strategic, and more coherent approach to global health preparedness, the Republic of Moldova is in the process of revising the National Pandemic Plan

as a part of the National Preparedness and Response to Public Health Emergencies Plan in accordance with the International Health Regulation (2005).

Preparedness Activities

- Conducted the national intersectoral workshop "Evaluation of the progress of implementation of the International Health Regulation and the National Pandemic Plan for Influenza" in September 2012.
- Conducted interdepartmental working group meetings monthly to discuss proposals for improvement of the National Pandemic Plan.
- Hired a local consultant to review and re-write the National Pandemic Plan and facilitate the activities of the Interdepartmental working group.
- Started to re-write the National Pandemic Plan utilizing concrete practical "guidelines" with a focus on identification of key individuals and institutions, ways of proceeding, reporting, behaving, equipment and consumables to be used, methodology, etc.
- Attended the "Workshop on Pandemic Preparedness guiding principles for revision of pandemic preparedness plans", in Copenhagen, Denmark (December 2012).
- Assessed the preparedness for public health emergencies at the national and territorial levels.

Training

- Conducted the national intersectoral workshop "Evaluation of the progress of implementation of the International Health Regulation and the National Pandemic Plan for Influenza" in September 2012.
- Attended the Laboratory Management Training Course in Bangkok, Thailand (2 attendees).
- Attended the Updating Protocols for Influenza, SARI, ARI Surveillance and Laboratory Diagnostic Workshop in Bucharest, Romania.

Publications

Cojocar R, Spînu C, Gheorghita S et al. Improvement of the influenza, ARI and SARI surveillance system in Republic of Moldova. European Scientific Conference on Applied Infectious Disease Epidemiology, 24–26 October 2012, Edinburgh, Scotland, UK. ESCAIDE reference number: 2012953, pp.99.

Spînu C, Cojocar R, Spînu I et al. Clinical— epidemiological and virological recovery of influenza, IRVA and SARI surveillance system. 23rd Annual Meeting of the Society for Virology, 6–9 March 2013, Kiel, Germany. pp.72.

Spînu C, Scoferța P, Cojocar R et al. The significance of the influenza, ARI and SARI surveillance system in Republic of Moldova. Third International Influenza Meeting, 2–4 September, 2012, Muenster, Germany. pp.133.

Russian Federation



Capital: *Moscow*

Infant Mortality Rate: *7.19/1,000 live births*

Population: *142,500,482 (July 2013 est.)*



Overview

CDC and the Russian Federation began their partnership to enhance the level of preparedness and response to annual influenza epidemics and future pandemics in 2011. The Research Institute of Influenza (RII) in St. Petersburg and the D.I. Ivanovsky Research Institute of Virology (IIV) in Moscow are recognized by the World Health Organization (WHO) as a National Influenza Centers (NIC). The NIC at RII continues to provide technical assistance and training to ensure the functionality of the sentinel surveillance system in Russia and Commonwealth of Independent States (CIS) countries. Revisions to the state pandemic plan and regional pandemic plans are currently underway.

Highlights

- Improved infrastructure of routine surveillance for influenza-like illness (ILI) and acute respiratory infection (ARI) for rapid recognition of influenza epidemics.
- Strengthened capacity of the sentinel surveillance system for determination of virus pathogenicity and groups risk for severe acute respiratory infection (SARI).
- Procured reagents and protocols for identification of potentially pandemic H2, H5, and H7 viruses.
- Prepared a draft of the Rospotrebnadzor Order for sustainability planning in Russia.
- Established an internet connection between the NICs and 59 collaborating regional base laboratories (cRBL) at the local Federal Centers for Hygiene and Epidemiology.

Surveillance

Influenza activity at RII and IIV is based on collaboration with 59 regional base laboratories (RBL). The RBLs send weekly data to the NICs on acute respiratory infections (ARI) and influenza-like illness (ILI) morbidity, hospitalization and death cases as well as laboratory data on virus isolation, immunofluorescence assay (IFA) and RT-PCR data. Russia has implemented real-time RT-PCR in 55 RBLs for influenza surveillance. The majority of isolates are forwarded to the NICs for antigenic and genetic investigation. In addition, sentinel surveillance for SARI is established in 17 hospitals. Influenza surveillance data were used to determine the impact of influenza and ARI for the 2012–2013 influenza season in St. Petersburg, which was used as a model to develop an index for the country as a whole. Risk factors for SARI and death cases were determined through analysis of data obtained from the traditional and sentinel surveillance systems.

In FY 2013, Russia received emergency supplemental funding to enhance SARI surveillance for H7N9. Funding will be used to introduce a new SARI case definition, based on the WHO EURO definition, at each of the nine regional SARI sites. Utilization of the new definition will increase the number of SARI cases investigated, as the previous definition was based on more narrow criteria. Funding will also be used to establish an additional SARI sentinel site in both Moscow and Stavropol.

Surveillance Activities

- Conducted supervisory visits jointly with CDC to sentinel sites and cRBLs in St. Petersburg and Vladimir (December 2011).
- Issued MDCK cells for all cRBLs for virus isolation during the 2012–2013 and the 2013–2014 seasons.

- Presented at the “Diagnostics and Prophylaxis of Infectious Diseases” Conference in Novosibirsk.
- Two scientists participated in a WHO/Euro Conference in May 2013.

Laboratory

The Russian NIC at RII has worked closely with CDC to establish state-of-the-art laboratories. Notable progress in laboratory surveillance capacity has been achieved over the past years, and the success of this partnership has led to significant enhancements benefiting both Russia and the GISRS. The Russian traditional influenza surveillance network now includes 59 laboratories throughout Russia which are working in collaboration with two NICs in St. Petersburg and Moscow. The sentinel influenza surveillance network now includes eight laboratories throughout Russia which work together with 17 hospitals and 12 ambulances and in close collaboration with the St. Petersburg NIC to conduct SARI and ILI/ARI surveillance.

Laboratory Activities

- Conducted training for laboratory workers from seven CIS countries on rRT-PCR analysis and virus sequencing on the RII base during May–June 2013 with WHO EURO support.
- Increased the percent of virus isolation by introducing rRT-PCR in cRBLs.
- Tested 9,228 specimens during the 2012–2013 season and 1,338 influenza viruses were isolated (NICs at RII and IIV and 37 collaborating RBLs).
- Tested 61,713 specimens and 11,961 of them were positive for influenza during the 2012–2013 season (two NICs at RII and IIV and 55 collaborating RBLs).
- Submitted 96 influenza viruses in a lyophilized condition during the 2012–2013 season to WHO CCs in Atlanta and London.
- Provided consultative support and material backing (stocks of MDCK cells, mediums, plastics and PCR kits) to collaborating laboratories in SARI surveillance.
- Deposited 517 new viruses in the virus collection of RII in 2013.

Preparedness

Through support from CDC and WHO, Russia has considerably updated and improved its pandemic influenza preparedness plan, which could be used as a model for updating pandemic plans in other countries after adjusting for specific country resources and situations. An analysis of the usefulness of the previous pandemic plan during the pandemic was conducted at RII and the first draft of an updated influenza preparedness pandemic plan was developed at RII.

Preparedness Activities

Issued a series of Federal and Regional documents by the Federal Service on Customers Rights Protection and Human Well-being Surveillance:

- Guidelines #3.1.2.004–10 criteria for the calculation of the available stock of medicines and reagents, equipment and individual means of defense and disinfections for the period of an influenza pandemic (Moscow, Rospotrebnadzor, 2010).
- Regional Influenza Pandemic Preparedness Plan and the use of prophylactic measures for the period 2012–2015 was approved by governors of the Russian Federation regions.
- Regional plans for countermeasures against an influenza pandemic caused by a highly pathogenic virus were approved by governors of the Russian Federation regions.
- Annual Decree of the Chief Sanitary Inspector G.G. Onischenko “Measures of prophylactics of Influenza and ARI” (6 August 2012 #43) was issued.
- New reagents for the detection of influenza A(H7N9) virus and instructions for their application, for virus identification were prepared by RII in 2013.

Training

- Attended the Options for the Control of Influenza VIII Conference and provided poster presentations (four scientists from RII and two from IIV) in Cape Town, South Africa.
- Trained two specialists from the NIC at RII on virus isolation, identification and antigenic analysis including antigenic cartography method and susceptibility to antivirals at the WHO CC London.

Publications

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Lobova T.G., Prokopets A.V., Komissarov A.B., Danilenko D.M., Pyankova A.A., Sukhovetskaya V.F., Gudkova T.M., Grigorieva B.A., Grudin M.P., Eropkin M.Yu. Evolutionary Variability of Influenza B Viruses in Russian Federation in 2005–2012. *Voprosy virusologii* (Problems of Virology), 2012, vol.57, #6 p.22–26 (RU).

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Ukraine



Capital: Kyiv (Kiev)

Infant Mortality Rate: 8.24/1,000 live births

Population: 44,573,205 (July 2013 est.)



Overview

Ukraine has had a routine surveillance system since 1968. Beginning in 2006, CDC provided funding to the Program for Appropriate Technology in Health (PATH) to help the Ukraine Ministry of Health (MOH) in its efforts to strengthen influenza and pandemic preparedness. PATH facilitated the National Influenza Center's (NIC) efforts to develop national guidelines for health services in Ukraine to plan and organize measures to combat pandemic influenza. Technical support provided by PATH has since been phased out and the Government of Ukraine and the L.V. Gromashevsky Institute of Epidemiology and Infectious Diseases National Academy of Medical Science— in partnership with CDC— have assumed responsibility for the continued operation of the system. The sentinel surveillance network includes 18 hospitals and polyclinics. Funding from CDC continues to support the NIC in Kiev and four regional virologic laboratories in the sentinel sites with equipment, reagents, consumables and other items to maintain optimal functionality of the labs. These laboratories can perform PCR and virus isolation on cell culture. Samples from Ukraine are routinely submitted to the WHO CC Atlanta and the WHO CC London.

Highlights

- Prepared a draft sustainability plan.
- Received Certificate of Conformity for participating in WHO's External Quality Assessment Project.
- Published joint bulletin with State Sanitary Epidemiological Service of Ukraine.

Surveillance

A fully functioning sentinel influenza surveillance system has been established in Kiev, Odessa, Dnepropetrovsk and Khmelnytsky. Epidemiological, clinical and virological data are reported regularly to the website, which provides analysis and presentation of the information. Data findings from the 2012–2013 season for influenza-like illness (ILI) are as follows: 491 ILI cases tested (10% of the total number that met the case definition of ILI); 44 (9%) confirmed influenza viruses with 27 A viruses and 17 B viruses (related B/Ymagata lineage). Data findings for severe acute respiratory infection (SARI) are as follows: 1,099 SARI cases tested (29% of the total number that met the SARI case definition); 245 (22%) confirmed influenza viruses with 176 A viruses and 69 B viruses (related B/Ymagata lineage). All subtyped A viruses were determined as A(H3N2). Both A(H1N1–64%) and A(H3N2–36%) viruses circulated in this season. Epidemiological and virological data are submitted to EuroFlu on a weekly basis.

In FY 2013, Ukraine received emergency supplemental funding from CDC to enhance SARI surveillance for H7N9. Funding will be used to establish two new SARI sentinel sites in Simferopol and Kharkiv, two cities which have large migration flows and are not currently represented in the sentinel system. Funding will also be used to increase the number of specimens collected from patients meeting the SARI case definition and to improve capacity of the virological laboratories to conduct testing for potential cases of H7N9.

Surveillance Activities

- Improved reporting timeliness and data quality at all sites.
- Prepared a new influenza decree which is under consideration by the Ministry of Health.
- Conducted supervisory visits to influenza sentinel sites in three cities (Dnepropetrovsk, Odessa and Khmelnytsky).
- Improved web site www.ukrinfluenza.com.ua, which provides cumulative weekly reports online for submission to EuroFlu.

Laboratory

Funding from CDC continued to support the NIC in Kiev and four regional virologic laboratories in the sentinel sites with equipment, reagents, consumables and other items to maintain optimal functionality of the labs. These laboratories can perform PCR and virus isolation on cell culture. Samples from Ukraine are routinely submitted to the WHO CC Atlanta and the WHO CC London. International experts from WHO and CDC carried out an assessment of the existing influenza surveillance system and an assessment of pandemic preparedness in August 2012. In line with recommendations from the assessments, the NIC improved laboratory documentation and procured necessary reagents and supplies.

Laboratory Activities

- Trained sentinel site virologists in influenza virus isolation and identification, and real-time PCR investigation.
- Tested 2,135 SARI and ILI cases in the sentinel sites during the 2012–2013 season: 16% were influenza positive: 102 (31%) tested positive for influenza B, 229 (69%) tested positive for influenza A, 60 of them (26%) related to A(H3N2), 95 (42%) related to A(H1N1) pdm and in 74 cases (32%) influenza virus subtype was not identified.
- Confirmed that all influenza B viruses were genetically related to B/Yamagata lineage.
- Continued supporting labs with equipment and consumables.
- Continued participation in the WHO GISRS.

Preparedness

Improvements were made to the national guidelines for health services of Ukraine, which outlines planning and organization measures to combat pandemic influenza. Together with international experts from CDC and WHO, Ukraine carried out an assessment of core capabilities for pandemic preparedness in Ukraine.

Preparedness Activities

- Established new relationships and links with Sanitary-Epidemiological Service (SES), in accordance with the altered structure.
- Improved the material and technical equipment of virologic laboratories (equipment and test-systems) and trained personnel, contributing to overall improved pandemic preparedness.
- Performed high quality SARI surveillance, as illustrated by the total correlation between the number of hospitalized SARI cases and the level of influenza positive samples. The abovementioned provides an opportunity to respond to changes in the epidemiological situation in a timely manner.
- Prepared a draft order aimed at surveillance improvement, which is currently under consideration by the Ministry of Health.

Training

The NIC continued providing technical assistance and training to ensure optimal functioning of the sentinel surveillance system, quality of the surveillance data, prompt data analysis, and integration of the information into preparedness and response activities.

In 2011–2012, the following trainings were organized in Ukraine:

- Conducted a training workshop for 50 health staff involved in sentinel surveillance working at all four sites.
- Conducted training for six regional Sanitary Epidemiological Service virologists in influenza virus isolation and identification at the NIC.
- Participated in the Data Management and Analysis Training Course held in Nijmegen, Netherlands (May 2013).
- Participated in the Annual WHO Regional Office for Europe Sub-regional Influenza Surveillance Meeting in Istanbul, Turkey.
- Participated in the International Symposium “Options for the Control of Influenza VIII” in Cape Town, South Africa and presented two posters (September 2013).

Publications

Leibenko LV, Polischuk VP, Radchenko LV, Mironenko AP. Phylogenetic analysis of human influenza viruses A (H3N2), isolated in Ukraine during 2011–2012 season. Microbiology and biotechnology. 2013. #1.

Mironenko AP, Holubka OS, Onushchenko OV et al. Monitoring results influenza viruses sensitivity, which circulate in Ukraine to antiviral drugs. Ukrainian Medical Journal, 2013. 1(93): 85–86.

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WHO REGION OF THE AMERICAS (AMR)

WHO Region of the Americas (AMR) Overview

As of FY 2013, there are four bilateral influenza cooperative agreements in the Region of the Americas. These agreements with ministries of health (MOH) or institutions designated by the MOHs work with the Pan American Health Organization (PAHO)/the World Health Organization (WHO) and the U.S. Centers for Disease Control and Prevention (CDC) to build capacity to routinely identify and respond to seasonal and novel influenza strains across the Americas.

CDC direct country support via cooperative agreements is established in the following countries:

- Brazil
- Mexico
- Paraguay
- Peru

In addition, CDC supports PAHO via a cooperative agreement. CDC also supports activities with the Center for Central America and Panama (CDC-CAP) at the CDC, Global Disease Detection (GDD) site in Guatemala. These activities support programs in eight Central American/Caribbean countries including Belize, Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica, Panama, and the Dominican Republic.

The core activities of our bilateral agreements and technical assistance are:

- To build sustainable national capacity to identify and respond to seasonal influenza, pandemic influenza and other emerging diseases in accordance with International Health Regulations 2005 (IHR).
- To make routine contributions of surveillance and virology data to WHO's Global Influenza Surveillance and Response System (GISRS).
- To increase the geographic reach of WHO GISRS.
- To provide earlier access to critical virus isolates from humans and birds for WHO GISRS.
- To increase the numbers of shipments and influenza isolates provided by local influenza labs for analysis by WHO Collaborating Centers (CC).
- To develop sustainable epidemiologic and virologic surveillance systems for severe influenza in order to gain understanding of the disease and economic burden caused by influenza and other respiratory viruses.
- To develop and sustain interagency national preparedness plans.
- To develop and train local rapid response and containment teams.
- To sustain and leverage quality sentinel surveillance and study cohorts to explore the potential cost-effectiveness of expanding vaccination and incorporating new delivery mechanisms, formulations, and novel influenza vaccines in the PAHO Region.

In addition to our bilateral work, we also partner with the U.S. Naval Medical Research Unit No. 6 (NAMRU-6) in Lima, Peru to jointly support South American countries that are starting influenza surveillance.

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WHO Pan American Health Office (PAHO)



Highlights

Enhancing SARI surveillance

- Technical support to 13 countries in Latin America and the Caribbean (LAC) for the implementation of SARI surveillance (Barbados, Bolivia, Chile, Colombia, Costa Rica, Dominica, Ecuador, Honduras, Jamaica, Paraguay, St. Vincents and the Grenadines, Suriname, and Trinidad and Tobago).
- Thirteen countries (62 hospitals) in LAC provide PAHO weekly SARI surveillance data (laboratory and clinical data).
 - » Locations of hospitals (number of hospitals): Barbados (1), Bolivia (8), Chile (6), Colombia (7), Costa Rica (7), Dominica (1), Ecuador (16), Honduras (3), Jamaica (6), Paraguay (5), St Vincents and the Grenadines (1), Suriname (1), and Trinidad and Tobago (1).
- Developed an information system, PAHOFlu in Spanish, which integrates SARI laboratory and epidemiologic data and is being used in two LAC countries.
 - » System will be translated into English this project-year.
 - » Countries using the information system (number of labs/hospitals): Bolivia (8) and Chile (6).

- Weekly virologic data compiled, analyzed, and disseminated from 27 NICs and national laboratories in the Americas (available at http://ais.paho.org/hip/viz/ed_flu.asp).
- Trained 135 health care workers (HCW) from five LAC countries (Bolivia, Colombia, Costa Rica, Guyana, Honduras) in SARI surveillance; have plans to train an additional 250 HCW from 7 countries (Barbados, Chile, Colombia, Ecuador, Guyana, Paraguay, St Vincent's and the Grenadines).
- Conducted a meeting bringing together epidemiologists and laboratorians to discuss surveillance for other respiratory virus (ORV) using current influenza platforms.
- PAHO National Influenza Center (NIC) meeting of epidemiologists and laboratorians from LAC will be held.

Strengthening laboratory capacity to detect influenza and other respiratory viruses

- Supported LAC NICs shipment of samples to WHO-CC for characterization.
- Purchased equipment, reagents and supplies for real-time RT-PCR and IFA for 17 NICs and labs.
- Provided training for laboratorians from multiple countries.
- Hosted PAHO NIC meeting of epidemiologists and laboratorians from LAC (September 2013).
- Thirty-two LAC NICs and labs participated in 2012 WHO EQAP.
- IATA-based WHO training for laboratorians from all LACs NICs (planned).

Developing influenza and ORV disease burden estimates

- Ten-year trend analysis of respiratory disease mortality in LAC submitted for publication.
- Influenza-associated mortality in LAC analysis.

U.S. CDC Direct Support

The five-year cooperative agreement Surveillance and Response to Seasonal and Pandemic Influenza by Regional Offices of the World Health Organization (WHO) began in September 2011 and is in its second year of a five-year cooperative agreement.

The WHO Regional Office for the Americas (AMRO/PAHO) is located in Washington DC, United States. The Office serves 35 countries; together their population exceeds 953.6 million people. Member countries include Anguilla, Antigua and Barbuda, Argentina, Aruba, Bahamas, Barbados, Belize, Bermuda, Bolivarian Republic of Venezuela, Bolivia, Brazil, British Virgin Islands, Cayman Islands, Chile, Colombia, Costa Rica, Cuba, Dominica, Dominican Republic, Ecuador, El Salvador, French Guiana, Grenada, Guadeloupe, Guatemala, Guyana, Haiti, Honduras, Jamaica, Martinique, Mexico, Montserrat, Netherlands Antilles, Nicaragua, Panama, Paraguay, Peru, Puerto Rico, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago, Turks and Caicos, United States, and Uruguay.

In 2012–2013, PAHO provided training and technical assistance to member countries to support routine influenza SARI surveillance and build capacity to strengthen preparedness, surveillance and response and laboratory capacity. PAHO focused on updating the regional influenza surveillance guidelines based on the new WHO standards, enhancing the capacity to monitor respiratory disease activity (SARI surveillance), promoting lab participation in Global Influenza Surveillance Network (GISN) and implementing national surveillance systems for unusual SARI cases (e.g. MERS-CoV and H7N9).

Surveillance

To address the Region's need for improved SARI and unusual event surveillance, PAHO drafted the Protocol for Nationwide Enhanced SARI Surveillance. It was implemented in selected Caribbean countries and Uruguay, and is ongoing in Chile, Honduras, and Paraguay; Colombia, Ecuador, and Peru have developed work plans to establish this surveillance and several other countries are also considering implementation. Complimentary to this, PAHO is developing an information system for data entry, hospital-laboratory data linkage, and data output automation; it was implemented in Uruguay and is being modified for use in other countries. Finally, for long-term sustainability, the strategy was adopted to integrate SARI surveillance into systems being developed for health-care associated infections and mandatory reportable disease surveillance. PAHO is working with partners in the Region to develop a five-day training course to sensitize stakeholders and train health-care workers on principals of surveillance, response, outbreak investigation, and structuring hospital departments of epidemiology.

Surveillance Activities

- Technical support to 13 countries in Latin America and the Caribbean (LAC) to support SARI surveillance implementation.
- Thirteen countries (62 hospitals) in LAC providing weekly data about SARI surveillance (laboratory and clinical data) to PAHO.
 - » Locations of hospitals (number of hospitals): Barbados (1), Bolivia (8), Chile (6), Colombia (7), Costa Rica (7), Dominica (1), Ecuador (16), Honduras (3), Jamaica (6), Paraguay (5), St. Vincents and the Grenadines (1), Suriname (1), and Trinidad and Tobago (1).
- Developed an information system, PAHOFlu in Spanish, which integrates SARI laboratory and epidemiologic data and is being used in two LAC countries.
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- Trained 135 health care workers (HCW) from five LAC countries in SARI surveillance with plans to train an additional 250 HCW from seven countries.
- Conducted a meeting bringing together epidemiologists and laboratorians to discuss using influenza platforms for surveillance of other respiratory viruses.
- PAHO National Influenza Center (NIC) meeting will be conducted involving both epidemiologists and laboratorians from LAC.

Laboratory

To address challenges identified during the 2009 influenza pandemic, PAHO directed resources to increase laboratory capacity in the Region for influenza and other respiratory viruses through the purchase of automated extractors and vacuum extractors for processing specimens by real-time RT-PCR, limited decentralization of real-time RT-PCR, providing refresher courses for real-time RT-PCR and immunofluorescence, and participating in the WHO External Quality Assessment Project (EQAP). Through a PAHO-CDC collaboration, selected countries (Chile, Panama, Colombia, Caribbean) have piloted diagnostics for ORV. Additionally, to develop laboratorians capacity to analyze and disseminate their data, PAHO collaborated with the University of North Carolina at Chapel Hill to develop a 2.5-day training course on the epidemiologic analyses of influenza laboratory data. More than 45 representatives from PAHO region were trained, and the course is available online in English and Spanish. Through these contributions, the LAC regional laboratory network now consists of 23 National Influenza Centers.

Laboratory Activities

- Supported LAC NIC's shipment of samples to WHO CC for characterization.
- Purchased equipment, reagents and supplies for real-time RT-PCR and IFA for 17 NICs and labs (Bolivia, Chile, Colombia, Costa Rica, Dominican Republic, Ecuador, El Salvador, Honduras, Guatemala, Jamaica, Nicaragua, Panama, Paraguay, Peru, Suriname, Uruguay, Venezuela, CARPHA).
- Planned training of laboratorians from
 - » Colombia and Dominican Republic in molecular diagnosis of influenza at the national laboratory in Chile (one-week).
 - » Bolivia and Ecuador in viral isolation for influenza at Gorgas Institute in Panama (two weeks).
 - » Brazil and Chile in serologic methodologies at CDC (two-weeks).
 - » Argentina, Brazil, Chile, and Mexico in molecular diagnosis of ORV at Adolfo Lutz Institute in Brazil (CDC-PAHO one week course, completed).
- IATA-based WHO training for laboratorians from all LACs NICs.
- PAHO NIC meeting (September 2013) involving epidemiologists and laboratorians from LAC.
- Twenty-seven countries (Argentina, Bolivia, CARPHA (Anguilla, Barbados, Belize, Bermuda, Cayman Islands, Dominica, St. Lucia, St. Vincent & the Grenadines, Suriname, Trinidad & Tobago), Chile, Colombia, Costa Rica, Cuba, Dominican Republic, Ecuador, El Salvador, Guatemala, Honduras, Jamaica, Mexico, Nicaragua, Panama, Paraguay and Peru) routine share their influenza and ORV virologic data with PAHO.

Preparedness

PAHO has been working with countries, in this current WHO Pandemic Alert phase for Avian Influenza, to review their Surveillance for Severe Acute Respiratory Illnesses. A particular area of focus is strengthening the role of the laboratory in the reporting and feedback of the SARI surveillance system.

In light of current health risks of viruses with pandemic potential (e.g. MERS-CoV and H7N9), PAHO conducted a meeting with subject matter experts from CDC, WHO, country influenza coordinators to update a regional guidance and refine unusual SARI event surveillance guidelines. Recommendations of this meeting were incorporated into the development of an unusual SARI event surveillance training

course and pilot. These are being incorporated into a guidance document and subsequent trainings will be provided to the Member Countries.

Preparedness Activities

- **Belize**— The Ministry of Health (MOH) reviewed its SARI surveillance system (July 2013) to identify areas for strengthening. In response to the WHO declaration of alert for pandemic influenza following reports of avian influenza in Asia, reporting sites were asked to increase sampling of SARI cases from 1/5 to all cases. Laboratory management issues regarding quality and reporting of influenza have been identified and are being followed up with PAHO and CARPHA support.
- **Barbados**— The MOH conducted an assessment of its SARI surveillance system (August 2013), focusing on the laboratory component. The MOH also conducted a two-hour update for staff at the Queen Elizabeth Hospital on pandemic influenza plans, avian influenza and novel coronavirus, SARI surveillance in Barbados, and a skills-building training on nasopharyngeal sampling. PAHO will follow up with training on PCR techniques and quality assurance methods for the public health laboratory.
- **Guyana**— The MOH requested PAHO support to review its national influenza pandemic plan following the issuance of the new WHO pandemic influenza guidance.
- **Suriname**— The MOH requested PAHO support to expand its SARI surveillance sites to include two hospitals in the capital, Paramaribo and to review its national laboratory system for respiratory virus testing.

Training

- Completed four country missions; 12 more are planned. Visits include monitoring and evaluating the SARI surveillance sites and laboratories, conducting SARI surveillance trainings, and developing work plans.
- Trained 135 local level health care workers from five countries in SARI surveillance. Additional training for 250 health care workers from seven countries is planned.
- Participated in laboratory training to strengthen capacity to diagnose influenza and ORV.
- Participated in the 2012 WHO EQAP for influenza (22 countries from LAC).
- Conducted a viral isolation training course with two countries in Panama (May 2013).
- Participated in a joint PAHO-CDC training in Brazil for strengthening laboratory capacity and epidemiologic data integration in ORV surveillance. These countries evaluated PCR kits using a CDC proficiency panel and a retrospective analysis re-testing SARI cases from 2012 using ORV PCR to assess IFA concordance and epidemiologic features of different viruses.

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Brazil



Capital: Brasilia

Infant Mortality Rate: 19.83/1,000 live births

Population: 201,009,62 (July 2013 est.)



Overview

Since 2011, Ministry of Health (MS) has been developing activities to strengthen influenza surveillance in order get to know the epidemiological behavior of circulating viruses, based on the decree No. 2,693, published on November 17, 2011 and republished on April 26, 2012. Currently sentinel surveillance is under expansion, with 215 sentinel units: 134 for influenza-like illness (ILI) surveillance and 81 for SARS. The cooperative agreement established with CDC in 2011 reinforced the actions of influenza surveillance in Brazil, especially in order to support the expansion and strengthening process of the surveillance network, through training, technical supervision visits, documents review, among other actions, which so far has demonstrated a better preparedness and response to the seasonality in the country.

Highlights

- Updated treatment protocol.
- Integrated epidemiological surveillance, the laboratory network and health care activities.
- Expanded deployed sentinel units.
- Updated the influenza sentinel information system (SIVEP_Flu).
- Decentralized the diagnosis of influenza by molecular biology.
- Offered distance learning course on clinical management.
- Expanded vaccination recommendation group with high vaccination coverage (above 80%).

Surveillance

The ILI sentinel surveillance system was created in 2000 and the SARS universal surveillance in 2009. In 2011 sentinel surveillance expanded to SARS in ICU and the Ministry of Health (MOH) offered financial support to states and municipalities for strengthening activities. Initially there were 59 sentinel units (US) and currently there are 319 ILI + SARS ICU US, and more than 60% (215/319) of the sentinel units are deployed. It is recommended to collect five samples of ILI patients weekly and samples from all hospitalized cases of SARS. Training, monitoring visit to the states and municipalities and meeting with the surveillance network, laboratories and health care were performed.

Laboratory

The laboratory network in Brazil has three NICs and 27 state labs, and 14% (51) of them perform molecular biology (RT-PCR in real time) diagnosis. Recently we have seen progress in the expansion of laboratory diagnosis with significant integration of surveillance activities and laboratory. CDC training on diagnostic molecular biology, phylogenetic analyzes and transport of samples were offered.

Laboratory Activities

- Tested 37,553 specimens from January to August 2013; 7,304 tested positive for influenza viruses.
- Standardized flows and deadlines for etiologic diagnosis in the influenza surveillance network.
- Diagnostic standardization for the laboratory network: supply and laboratory reagent offered by MS for the diagnosis of influenza by RT-real time PCR and indirect immunofluorescence (IIF).
- Provided air transportation of samples from the states to the NICs by MS laboratories.

- Systematic review and provision of computerized systems for epidemiological surveillance (SIVEP-Flu) and laboratory (GAL), with standardized and predefined information, avoiding error bias in subsequent data analyzes.
- Monitored visits to laboratories and sentinel units in the states and municipalities.

Preparedness

Preparedness activities to the seasonality of influenza and to a possible influenza pandemic: regional seminars, online clinical management course, distribution of educational materials, health care equipment purchase, surveillance training, provision of strategic stockpiles of antiviral, integration with the health care.

Training

- Conducted training on influenza surveillance for indigenous health.
- Conducted training on the information system SIVEP-Flu for 27 states.
- Attended training on biological samples transportation by WHO.
- Conducted training in molecular biology diagnostic to NICs by CDC.
- Attended training in phylogenetic studies by CDC Influenza.
- Conducted state seminars of preparedness for seasonal influenza.
- Hosted a meeting to update the influenza protocol treatment, with the medical societies.

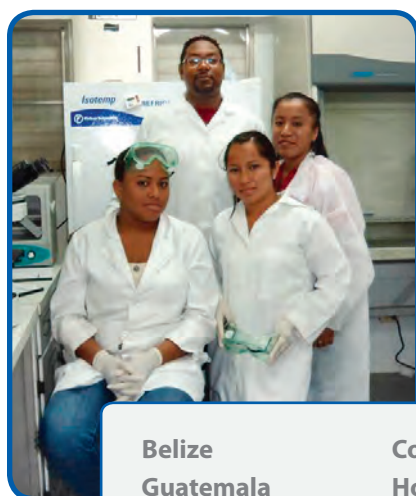
Special Project

Epidemiology Projects with the State of São Paulo, Brazil

During the summer of 2013, the Influenza Division hosted Dr. Ana Freitas Ribeiro, Director of the Surveillance Epidemiologic Center (CVE) for the state of São Paulo, the largest state in Brazil. As head of the CVE she is responsible for surveillance of all chronic and infectious diseases. She is also a PhD candidate in Epidemiology at the University of São Paulo, where her dissertation research focuses on the impact of pandemic influenza in the state of São Paulo. During her time with the Influenza Division, she collaborated on her PhD analyses as well as new collaborative projects between CVE-SP and CDC-Influenza Division.

Working with the Influenza Division, Dr. Freitas Ribeiro analyzed the impact of seasonal influenza vaccination among persons 60 years and older, on rates of influenza-associated mortality and hospitalization from 1994 to 2009 in São Paulo State to examine the impact of the introduction of seasonal influenza vaccination since 1999 among persons ages ≥ 60 years. Dr. Freitas and colleagues also conducted an analysis of increased reports of pH1N1 cases in São Paulo in 2013 and compared the pattern to the 2009 pandemic to examine how the profile of pH1N1 has changed over time. Both analyses are ongoing with Brazil.

Central America & Panama (CDC-CAP)



**Belize
Guatemala**



**Costa Rica
Honduras**



**Dominican Republic
Nicaragua**

**El Salvador
Panama**

Overview

Influenza program activities of the U.S. Centers for Disease Control and Prevention's (CDC) Regional Office for Central America provide support to eight countries: Belize, Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica, Panama and the Dominican Republic. Its main focus is to strengthen capacity to respond to pandemic influenza and to prevent and control seasonal influenza. This included improvement of influenza surveillance and laboratory capabilities, promoting the development of local pandemic plans, supporting targeted research projects, and building the evidence base for decisions on influenza vaccine program expansion.

Highlights

- Estimated hospitalization costs related to Severe Acute Respiratory Infections (SARI) case-patients in Guatemala, Nicaragua, and Honduras.
- Estimated influenza-like illness (ILI) incidence rates in Guatemala and Costa Rica.
- Estimated the prevalence of influenza and dengue co-infection in hospitalized patients in El Salvador.
- Started a clinical trial about efficacy of early oseltamivir treatment at hospital admission to reduce severity of illness among children in El Salvador and Panama.
- Prepared a generic protocol to estimate influenza vaccine effectiveness.
- Published a manuscript in the WHO Bulletin about the incidence of influenza-virus-associated severe pneumonia in children in El Salvador.

Surveillance

The Influenza Program supported the expansion of SARI surveillance and helped to standardize the influenza surveillance procedures regionally. The program also supported the development of electronic information systems for SARI, as well as for the national surveillance of respiratory diseases. A generic protocol for the estimation of the effectiveness of influenza vaccine was prepared and authorized; a pilot project was conducted. The incidence rates for ILI were estimated for Costa Rica and Guatemala population; additionally, direct hospital costs related to SARI patients care were also estimated in Guatemala, Honduras and Nicaragua. The Influenza Program conducted the annual assessment for influenza surveillance capacity in the region.

Surveillance Activities

- Supported the implementation of two sentinel sites for SARI in Guatemala and Panama.
- Provided technical assistance to SARI sentinel sites for developing and updating Standardized Operative Procedures (SOP) for influenza surveillance according PAHO-CDC guidelines.
- Developed, strengthened and migrated information systems into electronic systems for SARI surveillance in sentinel hospitals in Guatemala, Nicaragua and Panama.
- Conducted a surveillance capacity assessment for influenza surveillance in eight countries in the region. Standard instruments and procedures were applied during this assessment.

Laboratory

In Central America there are eight national laboratories diagnostic capacity for influenza and other respiratory viruses based on immunofluorescence, qRT-PCR and virus isolation. Most countries have already also decentralized immunofluorescence laboratories. The influenza program has supported the improvement of viral culture capabilities, provided reagents and supplies to these laboratories to further support their influenza surveillance. The Influenza Program also supported the development of web-based platform for automated management of data at national laboratories and National Influenza Centers (NIC). Also, technical assistance has been provided to develop laboratory SOPs. An assessment exercise was conducted to the Influenza laboratories in all the countries in the region. Standardized evaluation tools were applied throughout the region.

Laboratory Activities

- Renovated and secured equipment for virus culture at the National Influenza Center in Nicaragua.
- Provided reagents and laboratory supplies for immunofluorescence tests to the NICs in Nicaragua, Guatemala, Costa Rica and Dominican Republic.
- Provided technical assistance to establish an IFA laboratory for respiratory virus in Guatemala (Cobán) and Tegucigalpa (Honduras).
- Applied the laboratory tool throughout the Central American countries. Also, provided support during the assessment and influenza sentinel surveillance in eight CAR countries.
- Provided support for the implementation of the new Information System of Laboratory Surveillance in Honduras and Panama and BO technology in Costa Rica.

Preparedness

The Influenza Program supported the process of implementing the IHR (2005) in Central American countries, which drove the preparedness and response to pandemic influenza. The Inventory of Core Capabilities for Preparedness and Response for Influenza Pandemic in Central America exercise conducted in many countries provided quantifiable evidence of their progress. During 2012, the Influenza Program conducted the third capabilities inventory exercise, which has been conducted every two years since 2008. The inventory results revealed technical assistance was required in all countries, therefore, the program provided the necessary support to update or rewrite the anti-pandemic preparedness plan in each country.

The Influenza Program prepared a manuscript with the results of the inventory exercises practiced throughout the region in 2008, 2010 and 2012. Also, we provided support for the consolidation of the Electronic Surveillance Project in Panama, Guatemala and Costa Rica and the development of the Surveillance Web Platform.

Preparedness Activities

- Conducted the National Inventory of Core Capabilities for Pandemic Influenza Preparedness and Response (National Inventory-Scorecard) in eight countries of the region with the help of standardized evaluation tools.
- Provided technical support to update pandemic preparedness plan in CAR countries according results obtained from scorecard evaluation.
- Consolidated the web-based platforms for disease surveillance information systems.
- Supported the implementation of SAP Business Objects software for data integration in the Ministries of Health in Guatemala, Panama, and Costa Rica.

Training

- Conducted three workshops on direct and indirect cost estimation of hospital personnel who participated in the project on hospitalization costs for SARI cases in Guatemala, Honduras and Nicaragua.
- Conducted a regional workshop on the use of information technology for epidemiological surveillance, designed for Information Technology Specialists working for Ministries of Health in the region.
- Conducted a regional training course on prevention, treatment and research of acute respiratory disease in pediatrics for Guatemalan pediatricians.
- Conducted a clinical practice training course for El Salvador and Panama's Oseltamivir Clinical Trial study teams.
- Conducted training about influenza sentinel surveillance for epidemiologists, clinicians and laboratory specialists in Guatemala, Nicaragua and Honduras.
- Hosted the National Round Table and workshop to support the update of the national influenza surveillance guidelines of Nicaragua.
- Conducted training on how to prepare the protocol for the Influenza Vaccine Effectiveness Project which will be developed in El Salvador, Panama, Costa Rica and Honduras.

Publications

Clara et al. Estimated incidence of influenza-virus-associated severe pneumonia in children in El Salvador, 2008–2010. *Bull World Health Organ.* 2012 Oct 1;90(10):756–63. doi: 10.2471/BLT.11.098202. Epub 2012 Aug 6.

Mexico



Capital: Mexico City
Infant Mortality Rate: 16.26/1,000 live births
Population: 118,818,228 (July 2013 est.)



Overview

Since September 2006, CDC has supported influenza surveillance in Mexico through a cooperative agreement. The agreement has helped to strengthen federal, regional and local influenza surveillance sites by funding training, equipment and coordination of activities of laboratories and epidemiology units. The Mexican National Laboratory Network consists of a National Influenza Center (NIC), the Institute for Epidemiologic Diagnosis and Reference (InDRE) that coordinates training, quality control and reporting for 31 state laboratories and eight laboratories of health institutes. The cooperative agreement has assisted Mexico's Secretariat of Health (SOH) by increasing influenza laboratory capacity in Mexican states and improving diagnostic protocols.

Mexico's outbreak response begins with local-state level investigations that are then assisted, if needed, by the Mexican Federal SOH. This response system was instrumental during the pandemic and remains the cornerstone of binational collaboration during the investigation of public health events of international concern.

Highlights

- Reduced the number of sentinel sites from 740 to 700. Disease definitions were also reviewed and brought into alignment with PAHO and WHO protocols.
- Shared human-animal surveillance data on a more regular basis.
- Updated the National Plan for Preparedness and Response to Human and Animal Influenza.

Surveillance

Mexico's influenza surveillance system is based on local sentinel sites that are spread out in all 31 states. Over the course of the CDC cooperative agreement the surveillance network has grown; it started with less than 100 sites and now has grown to more than 700 units. Each year this sentinel network along with the influenza surveillance regulations, which are national and obligatory for all states, are revised by the National Epidemic Surveillance Committee.

The purpose of the units is to collect detailed information of all ILI cases and take laboratory samples from hospitals and primary health care centers to monitor influenza strains. Epidemiologic and laboratory data are collected at the local level and sent to centralized databases that facilitate rapid analyses, interpretation, and response to influenza activity throughout the country.

Mexico's National Epidemic Surveillance System, (SiNaVE), detects the time when influenza virus activity starts and when the season can be determined as active. For 2012–2013, the Directorate General of Epidemiology (DGE) used methods recommended by CDC Influenza Division staff to calculate ILI/SARI activity and seasonal baselines. For the 2012–2013 season, the national baseline established was 0.36% of ILI/SARI consultations with 12.26% flu positivity. Using the formulas to calculate this threshold assists Mexico with better using surveillance data to recognize the start of the influenza season each year.

Surveillance Activities

- Developed a weekly newsletter that is distributed to the national epidemiological network and shared with partners.
- Based on lessons learned from the 2009 influenza A (H1N1) pandemic, the SOH has updated and improved the quality of data that is collected in the Mexican National Influenza Surveillance System.

Laboratory

InDRE serves as a full-service national public health laboratory, performing surveillance and diagnostic-reference testing for a broad range of agents and diseases, including respiratory viruses, rabies and arboviruses. As Mexico's NIC, InDRE cultures influenza viruses, conducts real time qRT-PCR testing for respiratory samples and sequences viral isolates.

InDRE also provides oversight and proficiency testing for the national network of laboratories several times a year. It has also developed an ambitious program to grow capacity with a new building, built with international standards and increasing the laboratory's infrastructure with several BSL-3 laboratories.

Laboratory Activities

- Retained the capacity to do full antigenic and genetic characterization of influenza viruses as well as isolate influenza viruses at InDRE.
- Performed influenza testing through real-time qRT-PCR in all 31 labs in the National Public Health Laboratory Network.
- Detected four influenza cases with oseltamivir resistance mutation H275Y without epidemiological association and has reported them to the World Health Organization (WHO) according to International Health Regulations 2005 (IHR).
- Developed an online platform to centralize data access and improve the communication system between the 31 state laboratories and InDRE.
- Achieved perfect qualifications since 2010 on WHO's laboratory's performance assessment.
- Obtained international quality certification ISO-9001-2008.

Preparedness

The National Influenza Preparedness Plan was updated after the 2009 H1N1 pandemic and again in 2012–2013 following a Monitoring and Evaluation assessment with DGE, InDRE and CDC staff. The National Laboratory Network was fully strengthened with diagnosis protocols based in real-time qRT-PCR and viral culturing. Mexico is part of the North American Plan for Animal and Pandemic Influenza (NAPAPI), in partnership with Canada and the United States.

A pilot project is being developed to evaluate disease in both humans' and animals' routine communication and influenza information sharing between SENASICA and DGE has been established. In 2013, national influenza guidelines will consider a set of sentinel sites around farms to evaluate disease behavior in animals and humans.

Preparedness Activities

- Conducted a Monitoring and Evaluation of the National Inventory of Core Capabilities for Pandemic Influenza Preparedness and Response with CDC staff, InDRE, DGE to revise the National Pandemic Preparedness Plan.
- Updated the National Pandemic Preparedness Plan to include the coordination of local and state plans and activities.
- Equipped the rapid response teams (RRT) in each state in Mexico with medical doctors, epidemiologist, and laboratory staff.
- Reviewed the national stockpiles and medical equipment quantities in the event of a surge as part of the monitoring and evaluation of pandemic preparedness undertaken.

Training

Mexico's SOH hosted the following training activities in 2012:

- Updated the National Public Health Laboratory Network leaders with regard to pandemic coordination.
- Several local epidemiologists are now studying for their Master's Degree in Public Health with the National Institute of Public Health.
- Developed Level Two of the Incident Command System Course for federal staff, in cooperation with the Public Health Agency of Canada.
- Conducted regional and national meetings with the National Epidemic Surveillance System [SiNaVE] on influenza surveillance, preparedness and response.

Paraguay



Capital: Asunción

Infant Mortality Rate: 21.48/1,000 live births

Population: 6,623,252 (July 2013 est.)



Overview

Since August 2009, CDC has provided funds to the Paraguay General Direction of Health Surveillance via a cooperative agreement to help the Paraguay Ministry of Health (MOH) strengthen influenza surveillance. Fiscal Year 2012–2013 was the fourth year of the CDC's cooperative agreement with Paraguay. This project focused on strengthening surveillance systems and implementation of the generic protocol PAHO/CDC for influenza surveillance. This year the proposal was aimed at strengthening hospital units. The development of emergency plans and in-service training in order to respond to events of public health importance will improve the ability to respond to an influenza pandemic.

Highlights

- Strengthened SARI surveillance in seven sentinel hospitals.
- Generation of regular information, quality, systematic and timely data.
- Strengthening local capacity of epidemiological surveillance units and regional hospital acquired for the investigation of outbreaks and unusual events.
- Disseminated information to national (Weekly Epidemiological Bulletin) and international (PAHO Influenza Report) partners.
- Incorporated RT-PCR detection of influenza viruses and other respiratory viruses.

Surveillance

Paraguay has been using the PAHO generic protocol for Influenza surveillance. Since 2010 the country implemented the severe acute respiratory illness (SARI) surveillance protocol. Through their 10 sentinel sites, Paraguay collects SARI samples that are sent to their NIC for diagnosis of respiratory viruses by RT-PCR. Strengthening of surveillance at sub-national levels including rural areas was prioritized. The sentinel sites are representative of the country geographically. There are two sentinel laboratories which use the IFA technique for virus diagnosis. They send 100% of negative samples and 100% of Influenza positive samples to the National Influenza Center (NIC) for subtyping.

Surveillance Activities

- PAHO epidemiologists conducted supervisory visits to SARI sentinel sites.
- Local experts and epidemiologists updated ILI and SARI sentinel surveillance standards following WHO requirements and CDC recommendations.
- Developed and integrated software between epidemiology and laboratory for the national influenza team and the sentinel hospitals.
- Calculated baselines and alert thresholds for the influenza season.
- Improved data management capacity at each sentinel site.
- Improved research capacity for outbreaks and unusual events nationwide.

Laboratory

Virologic surveillance has been strengthened with the provision of reagents, supplies and [additional training] human resources. CDC and APHL have provided laboratory assessments and technical assistance as well. This is reflected in the increased number of samples tested for diagnosis of respiratory viruses, as well as an increased percentage of influenza viruses and detected isolates. The virus isolates were sent to CDC, obtaining good agreement with the preliminary results of the NIC, and relevant information about genomic characterization and antiviral resistance of strains. Through the support of experts from CDC, technical difficulties have been overcome both molecular tests such as viral isolates, which is corroborated by the results of quality external evaluations and consistency with the results of CDC. Technicians from Sentinel Centers have received training in the diagnosis of respiratory viruses by IFA, and adequate sampling techniques. They also participated in an External Assessment Program coordinated by the NIC. This allowed for timely virological diagnosis at sentinel centers, with over 1,000 samples processed in a year.

Laboratory Activities

- Analyzed 5,954 samples for diagnosis of influenza and other respiratory viruses last year.
- Provided CDC with 20 isolates.
- Set up of RSV and adenovirus diagnosis by real-time PCR.
- Differential diagnosis in severe cases (hMPV, rhinovirus, bocavirus, coronavirus).
- Set up of Flu A/H7N9 and MERS-CoV detection by real time PCR.
- Participated in WHO's EQAP for molecular detection of influenza virus, obtaining a 100% performance score.
- Completed supervisory visits to the laboratories of the Regional Hospital of Ciudad del Este and the Pediatric Hospital Acosta Ñu.
- Trained sentinel laboratory technicians in the diagnosis of influenza and other respiratory viruses by IFA.
- Completed two external evaluation panels.
- Trained NIC technicians on the proper use of respiratory filters (Fit Test).
- Conducted an assessment of the laboratory by experts from CDC and NHPL.
- Update Workshop on Virological Surveillance of Influenza and other respiratory viruses for Sentinel Laboratories and Laboratories from Private Sector.

Preparedness

The implementation of field epidemiology training resulted in the achievement of considerable advances in outbreak investigation in Paraguay. Notification was promoted via internet in most regions of the country and the process of forming rapid response teams at the local level continues.

Preparedness Activities

- Graduated the first cohort of epidemiologists who successfully completed field training.
- Prepared two sentinel sites to perform IFA technique.
- Strengthened the CNE with training and connectivity.
- Provided rapid response training to CNE's epidemiologists.

Training

PAHO and CDC continue to provide technical assistance and training to ensure the functioning of the sentinel surveillance system, quality of the surveillance data, prompt data analysis, and integration of the information between epidemiology and laboratory.

- Trained staff in 19 health facilities on basic epidemiology.
- Trained sentinel site staff on surveillance procedures in hospitals.
- Trained staff on the software of loading epidemiologic and laboratory data.
- Conducted three workshops where health professionals were trained on the proper collection techniques, storage and transport of influenza samples.

Research Projects

- Multi-centric evaluation of trivalent seasonal influenza vaccine effectiveness to prevent severe acute respiratory infection among high risk groups targeted for vaccination (REVELAC-i)

**see Research Section for additional information*

Peru



Capital: Lima

Infant Mortality Rate: 20.85/1,000 live births

Population: 29,849,303 (July 2013 est.)



Overview

The cooperative agreement Sustaining Influenza Surveillance Networks and Response to Seasonal and Pandemic Influenza began in August 2010. The Peruvian Ministry of Health (MOH) and DGE are working with the U.S. Centers for Disease Control and Prevention (CDC) under this agreement to strengthen surveillance and detection for seasonal, avian, and human influenza in the country. Peru's influenza surveillance system uses sentinel sites to identify ILI and SARI case-patients throughout the country. Laboratory testing for influenza takes place in the 15 regional laboratories, as well as the National Influenza Center (NIC), located in the National Institute of Health (INS) in Lima.

Highlights

- Implementation of enhanced surveillance of severe acute respiratory infections (SARI) in seven hospitals.
- Updated the national regulations for the surveillance of influenza and SARI in 2012. The health regulation entitled, "Directive Sanitary Epidemiological Surveillance of influenza, other respiratory viruses (OVR) and severe acute respiratory illness (SARI) in Peru" was implemented and published in the official gazette El Peruano on Friday, February 10, 2012.

Surveillance

In 2006, the MOH sub-committee for influenza surveillance invited the Virology Department of the U.S. Naval Medical Research Unit No. 6 (NAMRU-6) in Lima to assist in increasing surveillance coverage by establishing new sentinel sites in order to strengthen the surveillance program. Since then, NAMRU-6 has augmented the existing program by supporting the collection and processing of samples at new sentinel sites as well as providing these data to DGE and INS.

Sentinel surveillance is conducted in 57 health centers throughout the country. This includes both ILI and SARI surveillance. SARI surveillance is conducted in 35 hospitals. ILI surveillance is conducted in 22 units.

Surveillance Activities

- Conducted advocacy meetings to raise awareness regarding influenza to government organizations and the public.
- Conducted meetings to analyze the influenza surveillance system and methods for improvement.

Laboratory

Peru has 15 regional laboratories, all of which receive respiratory samples from influenza sentinel sites. Samples are tested by immunofluorescent assays (IFA), and those that are positive are then sent to the country's NIC in Lima for testing by RT-PCR. At the NIC, specimens are tested the same day they are received and results are reported within 72 hours. Influenza positive samples are also cultured in MDCK cells. Positive isolates are shared with CDC at least three times per year for further characterization.

Preparedness

Peru has rapid response teams (RRT) in the regional governments. They recently updated and disseminated specialized guides on influenza outbreak management to each regional unit.

Preparedness Activities

- Conducted a Monitoring and Evaluation of the National Inventory of Core Capabilities for Pandemic Influenza Preparedness and Response with PAHO and CDC to revise the National Pandemic Preparedness Plan.

Training

- Provided training to clinical staff, epidemiologists, and laboratory staff on monitoring of SARI.
- Provided training to information technology staff to manage and operate the web-based system that connects to all the sentinel units.

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WHO SOUTH-EAST ASIA REGION (SEAR)

WHO South-East Asia Region (SEAR) Overview

The U.S. Centers for Disease Control and Prevention (CDC) funds nine non-research bilateral influenza cooperative agreements in the South-East Asia Region (SEAR). Cooperative agreements with eight Ministries of Health (MOH) or institutions designated by the MOH build capacity to routinely identify, diagnose and respond to seasonal, avian and pandemic influenza. In addition, CDC supports the WHO Regional Office for South-East Asia (SEARO) via a cooperative agreement.

Six of the eight countries (Bangladesh, India, Indonesia, Nepal, Sri Lanka and Thailand) were awarded sustainability grants and are in varying stages of completion. These grants support the countries for additional five years. Bhutan and Maldives were awarded their first influenza capacity building grants in September 2013. Countries are expected to do the following: develop and maintain a surveillance system that allows countries to rapidly detect, identify and respond to seasonal, novel and pandemic influenza, participate in the World Health Organization's (WHO) Global Influenza Surveillance and Response System (GISRS), and create and implement a sustainability plan that phases out U.S. government funding.

Core activities include improving laboratory and epidemiologic capacity and infrastructure for influenza virologic and disease surveillance; developing and maintaining sentinel hospital-based surveillance for influenza-like illness and severe acute respiratory infections; integrating laboratory and epidemiologic influenza surveillance; developing and maintaining surveillance for cases and clusters of respiratory illnesses; and training local rapid response and containment teams.

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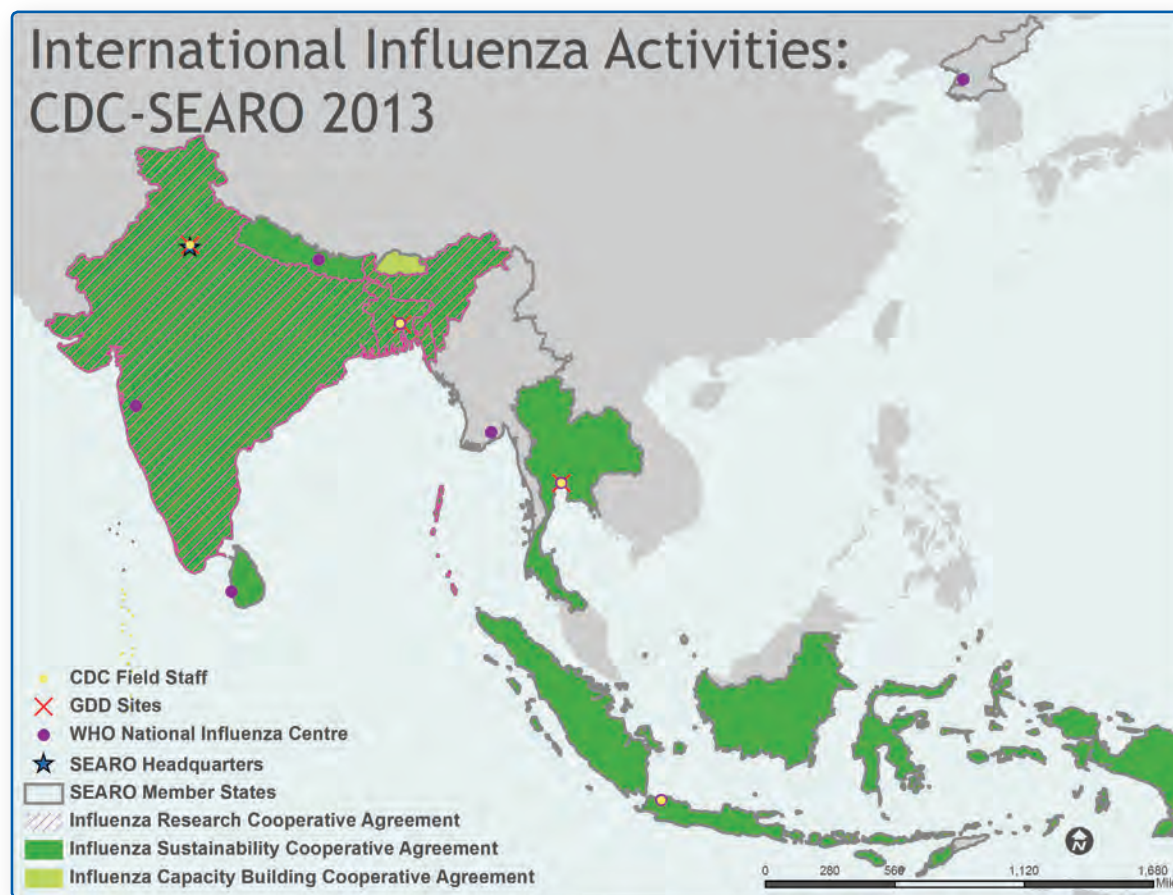
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WHO Regional Office for South-East Asia (SEARO)



Highlights

- Provided leadership and guidance during the recent H7N9 outbreak by updating member states on the status of the outbreak, issuing interim guidelines, and looking into stockpiling antivirals and creating vaccine deployment plans.
- Provided guidance to countries regarding seasonal influenza vaccinations.
- Conducted an Influenza Data Management Training for SEAR member states, in collaboration with CDC, to assist data managers and epidemiologists in improving influenza surveillance systems and analytical skills.

U.S. CDC Direct Support

In September 2006, WHO Regional Office for South-East Asia (SEARO) was awarded their first five-year influenza cooperative agreement, and is currently in their second five year agreement which began in 2012.

SEARO is located in New Delhi, India. The Office serves 11 countries; together their population exceeds 1.7 billion people. Member countries include Bangladesh, Bhutan, DPR Korea, India, Indonesia, Maldives,

Myanmar, Nepal, Sri Lanka, Thailand and Timor-Leste. Eight of the 11 countries are currently receiving CDC Influenza Division cooperative agreement funds: Bangladesh, Bhutan, India, Indonesia, Maldives, Nepal, Sri Lanka, and Thailand.

In 2012 and 2013, WHO SEARO staff provided training, support and technical assistance to member countries to strengthen preparedness, surveillance, response and laboratory capacity. WHO SEARO provides technical expertise, assistance and financial support to member states to strengthen their integrated influenza surveillance, to prepare for and effectively respond to influenza outbreaks and pandemics, to improve infrastructure and capacity of national influenza centres (NICs)/national influenza laboratories and to develop human resources. Responsibilities for these activities lay with SEARO's Disease Surveillance and Epidemiology (DSE), Blood Safety and Laboratory Technology (BLT) and Immunization and Vaccine Development (IVD) units.

Surveillance

SEARO with Prince Songkla University and U.S. CDC held an Influenza Data Management Training for SEAR member states in February 2013 to assist data managers and epidemiologists in establishing, maintaining and improving influenza surveillance systems and analysis. The course better familiarized participants with FluNet and FluID data bases for collecting epidemiological and virological data for the Global Influenza Surveillance and Response System (GISRS).

Surveillance Activities

- Established two positions in the SEARO vaccine preventable disease IVD Unit that support influenza through data management, emerging vaccine preventable disease surveillance and vaccine safety and quality.
- Traveled to Bhutan and Maldives to meet with staff to explain the benefits of working with CDC and to encourage them to apply for CDC influenza grants.

Laboratory

WHO SEARO continued to support efforts to strengthen laboratory infrastructure and build laboratory capacities to accurately and promptly diagnose influenza and monitor antiviral resistance. Eight countries in the region have functional NICs in part due to the technical and financial support provided to the countries through the cooperative agreement. Of these NICs, two have full capacity for influenza viral sequencing, the regional reference lab for influenza in Thailand and the global reference laboratory for H5N1 in Pune, India.

Laboratory Activities

- Provided support to the national laboratories in Bhutan, Maldives and Timor-Leste which now have polymerase chain reaction (PCR) capability to diagnose influenza and an interest in becoming NICs. The SEARO BLT unit organized appraisals of the three laboratories to identify gaps and recommend measures to build capacity towards designating the laboratories as NICs.
- Encouraged sharing of influenza laboratory data and will continue to foster information sharing within the Region.

Preparedness

The recent avian influenza A/H7N9 outbreak in China provided an impetus for the South-East Asia region to direct the attention of the member states to the need for ensuring preparedness for responding to novel strains of influenza with pandemic potential. Taking a leadership role at the height of the avian influenza A/H7N9 outbreak in China, SEARO updated its member states on the status of the outbreak, convened inter-departmental meetings to discuss plans for shaping the regional response, issued interim guidelines, discussed the possibility of mobilizing financial resources from different sources including CDC and looked into stockpiling antiviral medicines in order to prepare for an effective response to possible imported cases and cases due to local transmission. Attention was focused on revising national influenza pandemic preparedness and response plans including national pandemic vaccine deployment plans.

Preparedness Activities

- **Nepal**— At the request of the Government of Nepal, in August 2013, a SEARO staff member traveled to Nepal to support their national response to an upsurge in outbreaks of avian influenza A/H5N1 in poultry. SEARO met with the Ministry of Health, Ministry of Agriculture, FAO, CDC influenza grantees and other partners and provided recommendations on surveillance, risk assessment, outbreak response, communications and laboratory diagnosis.
- **India**— In the third meeting of the SEAR Immunization Technical Advisory Group (ITAG) held in 2012 in New Delhi, technical advisors reviewed the status of implementing the recommendations related to seasonal influenza adopted in the 2nd SEAR ITAG meeting.
- **Thailand**— Conducted their seasonal influenza vaccination campaign.
- **The Maldives**— Carried out their immunization campaign for Haj/Umra pilgrims. SEARO was technically consulted for selecting the most appropriate vaccine in terms of its antigenic match to circulating influenza strains in Saudi Arabia taking into account the mass gathering of pilgrims from different parts of the world.

Training

- Conducted an Influenza Data Management and Epidemiological Analysis Training Course, in collaboration with Prince Songkla University and CDC in Bangkok, Thailand (February 2013). Twenty three representatives from eight countries participated.
- Supported country participation in the International Conference on Human Infection with Novel Influenza Viruses in Beijing, China (August 2013).
- Conducted a joint meeting of NICs from the South-East Asia Region and the Western Pacific Region in Beijing, China (November 2013).

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Bangladesh



Capital: Dhaka
Infant Mortality Rate: 47.3/1,000 live births
Population: 163,654,860 (July 2013 est.)



Overview

The Institute of Epidemiology, Disease Control, and Research (IEDCR) in partnership with the International Centre for Diarrheal Disease Research, Bangladesh (icddr,b) conduct surveillance for emergent and zoonotic strains of influenza and for severe respiratory disease and influenza-like illness in the general population and in hospitals across Bangladesh. In addition, they participate in outbreak investigations of respiratory illness and conduct research studies on seasonal and avian influenza and other respiratory viruses (e.g., estimating disease burden and mortality through enhanced surveillance, assessing pharmacy dispensing practices for respiratory illness, developing and evaluating novel surveillance and diagnostic methods for respiratory diseases, and evaluating the effectiveness of intervention programs, including the use of influenza vaccine in high risk populations). Since 2007, CDC has provided resources, training, and technical support to laboratories at IEDCR and icddr,b to strengthen diagnostics capacity for influenza and other respiratory pathogens.

Highlights

- Estimated nationally representative influenza mortality rates using the enhanced surveillance platform in 2013.
- Leveraged and enhanced the national influenza surveillance platform to detect potential circulation of novel influenza A (H7N9) among poultry and suspected human cases of H7N9 or MERS-Coronavirus infection.
- Estimated the burden of disease in a cost-effective manner using the enhanced surveillance platform.

Surveillance

CDC funding enabled IEDCR and icddr,b to establish Bangladesh's first influenza sentinel sites. Together they have been conducting hospital-based influenza surveillance in 12 tertiary hospitals across the country since 2007. In FY13, the surveillance platform was enhanced by defining the catchment area of the participating hospitals and performing health utilization surveys in these areas. This allows Bangladesh to better estimate its influenza disease and economic burden. The current national influenza surveillance system identifies cases of SARI, ILI, and severe pneumonia in 19 sentinel sites. In addition, an event-based component of the surveillance system identifies clusters of severe disease, and all patients are screened for exposure to sick or dead poultry and tested for influenza A (H5N1) and for the novel H7N9 virus, as needed.

Surveillance Activities

- Collected and routinely tested specimens for influenza from 19 sentinel surveillance sites across the country.
- Continued routinely monitoring and investigating suspected influenza outbreaks.
- Provided detailed surveillance reports to CDC and WHO on a weekly basis during the influenza season
- Reported influenza surveillance results with monthly updates on the IEDCR website.

Laboratory

Since 2007 CDC has provided diagnostic support, resources, training and technical support to laboratories at IEDCR and icddr,b, resulting in strengthened capacity and improved diagnosis of influenza and other respiratory diseases. Influenza specimens (100–200 per year) are routinely sent to CDC for further molecular and antigenic characterization and vaccine strain selection.

In 2007, IEDCR was nominated as a NIC by the WHO and has routinely contributed specimens to the WHO GISRS. An upgrade of IEDCR's BSL-2 laboratory was completed in 2010. State-of-the-art equipment was purchased and the new BSL-2 laboratory is performing real-time and conventional PCR to identify seasonal influenza viruses, and H7N9, H9N2 and H5N1 influenza viruses. In FY 2013, a sequencer was procured and training of NIC staff is taking place. Plans are currently underway to increase the virus isolation and serologic testing capacity of the NIC.

icddr,b houses a modern molecular virology BSL-2 lab, tissue culture capacity, and an animal virology lab, as well as a certified BSL-3 laboratory where virus isolation and culture for highly pathogenic influenza strains can be performed.

Laboratory Activities

- Tested over 10,000 specimens from surveillance activities from October 2012–September 2013. Peak influenza circulation occurs during the rainy season, May–July.
- Integrated new sequencing capacity within several surveillance and research projects.
- Enhanced diagnostic capacity of partner laboratories for the detection of the novel H7N9 strain. icddr,b laboratory participated in the field testing of novel rapid serological assays for influenza-specific antibodies.

Preparedness

IEDCR, with key partners, has periodically updated their pandemic response and avian influenza plan with lessons learned from the pandemic. IEDCR has led several recent trainings for public health officials and health professionals on pandemic preparedness. An emergency operations center (EOC) was built and equipped to help centralize a government response during major outbreaks and pandemics. IEDCR, icddr,b, and the Department of Livestock Services (DLS) participated in joint avian influenza outbreak investigations following a One Health approach.

Preparedness Activities

- Conducted a second self-assessment for influenza pandemic preparedness and response using the standard CDC assessment tool in 2012; strengths and weaknesses were successfully identified.
- Responded to outbreaks and unusual health events or diseases reported directly or indirectly to the Director. National Rapid Response Teams (NRRT)

conduct outbreak investigations with the help of district rapid response and local Upazila rapid response teams. CDC supports the NRRT on suspected influenza outbreaks through engagement of CDC's field staff based in Bangladesh, via technical consultations with subject matter experts in Atlanta, and through provision of diagnostic reagents.

Training

IEDCR has held several trainings to strengthen Bangladesh's capacity to detect, survey, prevent and control influenza and novel pandemic threats.

- Conducted a two-day training on standard operating procedures (SOPs) for laboratory bio-safety and infection control of emerging infectious diseases (EIDs) [September 2013].
- Conducted a capacity building hands-on training course on SOPs for diagnosis of EIDs [September 2013].
- Conducted a dissemination workshop on a) re-assessment of present core alert and response capacities of IHR 2005 at ports of entry, and b) mapping of health risks and resources useful for implementation of IHR [September 2013].
- Conducted a workshop on establishing a laboratory network among public health laboratories [September 2013].
- Conducted training on preparedness, capacity building surveillance, laboratory support and response for zoonotic diseases [July 2013].
- Conducted training on web-based disease surveillance [July 2013].
- Conducted training on disease surveillance for Upazilla-level health officers and medical officers [March 2013].
- Conducted workshops on National Influenza Surveillance, Bangladesh in 2013 for: hospital managers on surveillance site management; surveillance officers on case selection and data and specimen collection; and medical technologists on specimen collection, preservation and transport.

Publications

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Bhutan

Capital: *Thimphu*
Infant Mortality Rate:
47/1,000 live births
Population:
725,296 (July 2013 est.)



Overview

Bhutan is a landlocked, remote country in South Asia located at the eastern end of the Himalayas. The existing national influenza surveillance system is a relatively new system with limited support.

The National Influenza Pandemic Preparedness Plan was developed realizing the threat posed by the H5N1 outbreak in poultry in neighboring countries in 2006. The plan was put into action during the H1N1 outbreaks in 2009 and the first H5N1 outbreak in domestic poultry in 2010.

The Public Health Laboratory (PHL) is the national focal point under the Ministry of Health for conducting and coordinating public health surveillance including influenza surveillance and laboratory testing.

Bhutan was awarded a CDC capacity building cooperative agreement, Surveillance and Response to Avian and Pandemic Influenza by National Health Authorities outside the United States in September 2013. The agreement aims to build and strengthen the national laboratory and surveillance capacity for severe acute respiratory infection (SARI) and influenza-like illness (ILI).

Highlights

- Awarded Capacity Building Cooperative Agreement.
- Established eight ILI surveillance sites in 2009 during the pandemic. Increased to 11 sites in 2010. In 2011, all sites began SARI surveillance.
- Began constructing a new PHL building which will expand influenza laboratory space including space for virus culture.
- Requested WHO approval to establish a National Influenza Center (NIC).

Maldives

Capital: *Malé*
Infant Mortality Rate:*
9/1,000 live births
Population:
393,988 (July 2013 est.)



Overview

Maldives is an archipelago in the Indian Ocean, consisting of a group of about 1,200 islands scattered over a distance of 800 km, of which 250 are inhabited. The islands are grouped into natural atolls, which are used as administrative demarcations. There are 21 administrative districts— 20 atolls and the capital, Malé. There are over 1 million tourist arrivals each year.

The Health Protection Agency (HPA), under the Ministry of Health is responsible for surveillance and response of communicable diseases, including influenza and other respiratory illnesses. Acute respiratory infections (ARI) are constantly the highest reported communicable disease category in Maldives. ARI surveillance (including influenza) is currently based on a passive syndromic system.

Maldives was awarded a CDC capacity building cooperative agreement, Surveillance and Response to Avian and Pandemic Influenza by National Health Authorities outside the United States in September 2013. The agreement aims to build and strengthen the national laboratory and surveillance capacity for influenza surveillance, establish protocols for pandemic preparedness and response and share information with WHO Global Influenza Surveillance and Response System (GISRS) for global pandemic preparedness.

Highlights

- Awarded Capacity Building Cooperative Agreement.
- Requested WHO approval to establish a National Influenza Center (NIC).
- Offered influenza vaccine for all persons travelling for Hajj and Umra pilgrimages.
- Participated in an ILI and SARI surveillance workshop in Thailand in 2013.

*Based on country estimates.

India



Capital: New Delhi

Infant Mortality Rate: 44.6/1,000 live births

Population: 1,220,800,359 (July 2013 est.)



Overview

CDC has supported capacity-building for surveillance since 2004, leading to improved characterization of circulating influenza viruses and capacity to rapidly detect novel viruses, including avian influenza viruses. CDC-supported laboratory training and preparedness workshops have strengthened India's response measures against seasonal, avian, and pandemic influenza. CDC also collaborates with Indian partner organizations on research to quantify influenza burden in India, evaluate the effectiveness of influenza vaccines in young children at increased risk for severe respiratory illness, and identify optimal timing for influenza vaccination in India to inform the development of national influenza vaccination policy.

Highlights

- Continued surveillance for A(H1N1)pdm09 viruses and genetic characterization of re-emerging H3N2.
- Conducted pre-monsoon influenza vaccination of children in Northern India for the first time, as longitudinal data on seasonality of influenza viruses persuaded the Drug Controller General of India (FDA equivalent) to permit importation of Southern Hemisphere (SH) vaccine for spring time vaccination.
- Contributed data for global pandemic influenza-related mortality estimates and global estimates for respiratory hospitalizations.
- Generated crucial data on respiratory morbidity among children and elderly in addition to providing platforms for new research projects.

Surveillance

Indian Council of Medical Research conducts sentinel surveillance at 10 surveillance sites throughout India which are generating crucial epidemiological and virological data. The National Influenza Center (NIC) at Pune has been sending timely isolates to CDC for antigenic analysis and has contributed cumulative weekly influenza surveillance data to the WHO FluNet website. Surveillance efforts have documented that influenza seasonality varied across India with peak influenza activity occurring during January–March in the northern most tip of the country and during the rainy season (August–October) in the rest of the country. Previously, India was only using Northern Hemisphere influenza vaccine, but these findings have led to importation of Southern Hemisphere vaccine for pre-monsoon vaccination of children in India.

Surveillance Activities

- Processed 12,687 samples during the year; 2,095 tested positive for influenza, of which 684(33%) were A (H1N1)pdm09, 951(45%) were A (H3N2), and 460(22%) were B viruses.
- Detected a resurgence of influenza A (H1N1)pdm09 during the winters of 2012–13 following a period of minimal circulation in 2011–12 winters, causing serious illness and fatalities.
- Participated in the Influenza Disease Burden in India study and established influenza-like illness (ILI) and febrile acute respiratory infection (FARI) case definitions that include measured or reported fever to provide an optimal balance between sensitivity and specificity for the identification of patients hospitalized with influenza.

Laboratory

Indian surveillance network members have trained extensively with CDC-Atlanta scientists on typing, sub-typing, PCR, real-time PCR, and reverse genetics techniques. The Indian network of surveillance sites now has ten sites equipped with RT-PCR to detect seasonal influenza viruses, including A (H1N1)pdm09. Four of these laboratories are also equipped to handle avian influenza.

Genetic characterization of viruses is carried out mostly at the NIC. All India Institute of Medical Sciences (AIIMS) has developed capacity to carry out virus neutralization assays and testing for cell-mediated immunity (CMI) and nutritional factors as part of a vaccine study.

Another virology laboratory became functional for influenza testing in Delhi; it provides support for testing thousands of samples collected under various HHS/CDC-supported influenza studies. CDC-developed technologies for individual respiratory virus detection as well as multi-pathogen detection using Taqman Low Density Array (TLDA) have been transferred to AIIMS. Laboratory studies of molecular mechanisms of influenza A and host cell interactions conducted with the International Centre for Genetic Engineering and Biotechnology (ICGEB) are leading to identification of unique host cell factors that may be manipulated by influenza A viruses.

Laboratory Activities

- Observed genetic characterization of circulating strain A(H1N1)pdm09 from India belonging to clade 7 with minimal changes in recent isolates.
- Generated a comprehensive database with full length HA and NA sequences for influenza A (H3) and influenza B viruses – data analysis is underway.
- Reviewed the real-time RT-PCR process for influenza testing at the newly operational laboratory at the International Clinical Epidemiology Network (INCLEN) Trust and helped fine-tune some of the quality aspects of testing.

Preparedness

HHS/CDC activities have focused on supporting pandemic influenza preparedness programs and helping advance the field of influenza research (seasonal, pandemic and avian) in India. Many of the preparedness activities related to increased awareness and response to minimize the risk of spread of human infections and disease were carried out with Ministry of Health and Family Affairs (National Center for Disease Control and the Indian Council of Medical Research) and WHO partners prior to 2009. These efforts contributed to India's ability to respond to the 2009 H1N1 pandemic. CDC continues to provide technical and laboratory support for ongoing surveillance activities.

Current activities are focused on influenza vaccination strategies, and increasing awareness and acceptance of influenza vaccine among health care providers. Support

from the U.S. Biomedical Advanced Research and Development Authority (BARDA) has led to increased influenza manufacturing capacity. Studies are being planned to look at the efficacy of indigenously produced live attenuated influenza vaccine (LAIV) in India.

Preparedness Activities

- Received license to import SH vaccine for vaccination prior to influenza peak due to evidence-based data on influenza seasonality.
- Reported very low acceptance rates from initial surveys in a tertiary care hospital, due primarily to limited knowledge about influenza vaccines. Discussions are underway to provide Influenza vaccinations to all health care providers within the federal government.
- Led production of LAIV monovalent pandemic H1N1 vaccine at the Serum Institute of India, Pune, and now in the process of producing trivalent LAIV.

Training

Consultations and Presentations

- Seasonal, Avian and Pandemic Influenza Control and Prevention Strategies; Identification of Gaps and Way Forward. Chaired by the Secretary-Department of Biotechnology and Co-chaired by Secretary-Department of Health Research, India: New Delhi (June 2013).
- Meeting of National Experts in the field of Influenza Surveillance-consultation for mortality estimate for influenza related deaths in India: New Delhi (May 2013).
- Influenza Burden Analysis Meeting: New Delhi (May 2013).

Trainings and Workshops:

- Hands on laboratory training on TLDA technology at INCLEN Trust Laboratories, New Delhi.

Publications

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Indonesia



Capital: Jakarta

Infant Mortality Rate: 26.06/1,000 live births

Population: 251,160,124 (July 2013 est.)



Overview

The overall goal of the influenza program in Indonesia is to establish a sustainable, comprehensive surveillance system that can identify and respond to seasonal, avian and pandemic influenza. CDC funding has supported routine influenza surveillance, the National Influenza Center laboratory and pandemic preparedness. In 2011, the Indonesia MoH, in collaboration with CDC and USAID, began piloting an enhanced surveillance project to better understand the burden of seasonal and avian influenza in the East Jakarta District. In addition to the ongoing influenza-like illness (ILI) surveillance, a national severe acute respiratory infection (SARI) surveillance system was established with CDC and Government of Indonesia (GOI) funding in 2013. Together these systems help identify circulating influenza viruses, and monitor severity and trends in several provinces in the country.

Highlights

- Established SIBI (Surveilans ISPA Berat Indonesia), the new national severe acute respiratory infection (SARI) surveillance system, in six hospitals in six provinces.
- Provided a model for harmonization of virologic and epidemiologic surveillance in one district, (East Jakarta Project).
- Integrated surveillance for the emerging influenza A (H7N9) virus and MERS-CoV via the SIBI platform and East Jakarta Project.

Surveillance

For SIBI surveillance, a protocol was developed based on the 2012 WHO Influenza Surveillance Standards. The system, which collects data on SARI cases, is used to determine the proportion of cases with influenza virus infection and those with severe illness, including pneumonia and death.

Since August 2011, the East Jakarta Project has provided rapid information about the epidemiology, clinical presentation and virus subtypes circulating in an urban area in one province in Indonesia. As of September 2013, 5,150 ILI cases and 3,200 SARI cases had been detected and tested for influenza.

Data from ILI surveillance, the East Jakarta Project and SIBI are routinely reported to the Global Influenza Surveillance Response System (GISRS).

Surveillance Activities

- **SIBI**— Selected six sentinel hospital sites in December 2012. All sites established a five-person SIBI team comprised of coordinating doctor, surveillance doctor, screening nurse, medical records officer and laboratory technician. Data collection began in April 2013 and 200 SARI cases were identified between April and September.
- **East Jakarta Project**— Conducted a health care utilization survey with partners (USAID, Strategies Against Flu Emergence Project, and Johns Hopkins) to help understand the health care utilization patterns and respiratory disease burden in communities.
- **ILI Surveillance**— Continued national ILI surveillance in 26 health care centers in 25 provinces. Uploaded data from ILI surveillance on the National Institute of Health Research and Development (NIHRD) website.

Laboratory

As of September 2013, the national outbreak detection surveillance system, (known as EWARS), was strengthened in 21 provinces. The system enables surveillance for 24 syndromes/diseases. Reporting is streamlined through the addition of electronic data reporting and feedback. Further, a situational analysis of laboratory involvement in outbreak detection, verification and investigation was conducted.

For the East Jakarta Project, an additional regional diagnostic laboratory, the Regional Environmental Health Laboratory (known as BTKL), was added to the surveillance system to test SARI specimens from the six sentinel hospitals. Training was provided to BTKL and the laboratory's RT-PCR capacity and protocols were upgraded. CDC provided technical support to NIHRD to strengthen influenza surveillance logistics, including cold chain management.

Laboratory Activities

- **EWARS**— Developed a laboratory mapping tool to determine Provincial Health Office utilization of laboratories in supporting outbreak verification and investigation with CDC technical assistance. A similar tool to assess laboratory capacity for diagnosing diseases under EWARS surveillance was developed.
- **East Jakarta Project**— Detected 5,150 ILI cases, of which 31% were influenza-positive; 3,200 SARI cases were detected and 14% were influenza-positive.
- **ILI Surveillance**— Detected 1,867 ILI cases, 525 (28.1%) samples were influenza-positive during October 2012–July 2013. Of the influenza-positive samples, 351 (18.8%) were influenza A and 174 (9.3%) were influenza B. The influenza A subtype most commonly detected as A (H1N1)pdm09. The GOI funded laboratory supplies for influenza testing.

Preparedness

CDC provided emergency response funds specifically for A (H7N9) and MERS-CoV preparedness in July 2013. Funds are being used to enhance existing surveillance systems' capacity for the detection of these emerging diseases.

Preparedness Activities

- Integrated travel history questions and surveillance for emerging influenza A (H7N9) and MERS-CoV diseases into both SIBI and the East Jakarta Project.
- Conducted a meeting in September 2013 with provincial health offices, SIBI coordinators and national stakeholders to discuss the latest A (H7N9) and MERS-CoV findings, review surveillance system data, and discuss how to use information arising from the system to inform policy.
- Funded reagents and supplies to enable additional RT-PCR, virus isolation and virus sequencing for these emerging infections.
- Established a web-based platform for SIBI to enable real-time reporting and feedback of data.

Training

- Conducted trainings on SARI surveillance in March 2013 for the six SIBI teams and the provincial/district health offices.
- Conducted refresher trainings for laboratory, hospital and health care center staff working on the East Jakarta Project in July 2013.
- Conducted scientific writing workshop for lecturers and researchers at Respati University, Jogjakarta.
- Conducted training in March 2013 on cold chain methods and RT-PCR machine maintenance for ILI surveillance regional laboratories.
- Conducted a Laboratory Management Information System Data Analysis and Quantification Workshop in November 2012.

Publications

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Nepal



Capital: Kathmandu

Infant Mortality Rate: 41.76/1,000 live births

Population: 30,430,267 (July 2013 est.)



Overview

Nepal is a mountainous country with most of its 27 million people living in rural areas. Nepal's geographic location, large amount of backyard poultry farming and poultry industry conditions put the country at high-risk for avian influenza outbreaks. Strong surveillance and epidemiology and laboratory capacity are particularly important to help detect and monitor seasonal influenza and any unusual events. Nepal's Patan Academy of Health Sciences (PAHS), a public health science university at Patan Hospital, was awarded Nepal's first influenza cooperative agreement in September 2009. The cooperative agreement has strengthened influenza surveillance in Nepal and has supported building capacity in the National Public Health Laboratory (NPHL)/National Influenza Center (NIC), the Patan laboratory and the sentinel hospital sites. Routine ILI and SARI surveillance at Patan Hospital provides consistently reliable and detailed epidemiologic and virologic influenza data. In September 2014, PAHS will begin a five-year sustainability grant in which they propose to review their current system, make adjustments and begin to establish a surveillance system that is sustainable over the long term.

Highlights

- Initiated routine SARI surveillance at Patan Hospital in January 2013.
- Initiated testing for influenza in a new molecular diagnostic laboratory at Patan Hospital in January 2013.
- Coordinated outbreak responses in coordination with Epidemiology and Disease Control Division (EDCD), the Ministry of Public Health (MOPH), and PAHS.

Surveillance

A network of partners consisting of the NPHL/NIC, Walter Reed Research Unit Nepal (WARUN) and PAHS oversee influenza sentinel sites that cover key geographic areas around the country, including areas with a significant poultry industry. PAHS oversees three hospital sites and one peripheral health facility. WARUN oversees two sites and NPHL with the assistance of the MOPH EDCD five sites. There is a strong collaborative relationship between the three surveillance partners who regularly share data, organize trainings together and support each other with technical assistance and resources when needed. A national Influenza Surveillance Network that includes animal health meets quarterly and on an as-needed basis.

Surveillance Activities

- Collected and analyzed ILI epidemiologic data from Patan Hospital since January 2010, and collected specimens from ILI patients at PAHS and peripheral sentinel sites since January 2011.
- Collected extensive denominator data, including the total number of out-patients and in-patients and the number of patients meeting the ILI and SARI case definitions at Patan Hospital.
- Maintained database and analyzed data from 2011, weekly, at PAHS.
- Managed sample collection and cold chain transport to the laboratory from peripheral sites.

Laboratory

PAHS now has a molecular laboratory, with real time RT-PCR, a virologist, and capacity to test ILI and SARI samples. They plan to operate as a unit of the NIC, sharing the influenza testing workload. NPHL was designated a NIC in April 2010. The molecular and virology laboratories are in a new BSL-2 facility where four staff are responsible for specimen extraction, real time RT-PCR detection, cell culture and virus isolation. In addition they have capacity to sequence and characterize by serological and real-time assay.

Laboratory Activities

- Initiated specimen testing at the new influenza molecular laboratory at Patan Hospital in January 2013. From January to August 2013, the lab received 82 samples. Of those tested, 19.5% were positive for influenza.
- Tested more than 2,000 samples for influenza in 2012. From January–July 2013, the NIC and PAHS tested 252 specimens from PAHS managed sentinel sites; 57 (23%) were positive for influenza.
- Submitted PAHS data and reports to the NIC and to the IHR focal point.
- Submitted 50 influenza isolates (35 A (H1N1) pdm09, 5 A (H3), and 10 B isolates) to NIID and the WHO CC, Japan in 2012 and 2013. The isolates were representative of different geographical locations, seasons and clusters of seasonal outbreaks.

Preparedness

In 2012 and 2013, Nepal has had several outbreaks of avian influenza in poultry. There has been a coordinated response with EDCD, the division responsible for outbreak responses that includes animal and veterinary health, medical, surveillance, risk communication, supervision and monitoring teams. During the outbreak response, PAHS staff have been actively involved with collecting and transporting to the NIC for testing human samples from poultry workers, exposed individuals and ILI symptomatic cases. To date, no human avian influenza A (H5N1) infections have been detected. The Government of Nepal is collaborating with several national and international partners on their response.



Representatives from CDC and Nepal during a laboratory assessment.

Preparedness Activities

- Developed routine simulation exercises to reinforce staff skills.
- Developed rapid response teams at district and sub-district levels, as well as remote areas.
- Acclimatized media personnel and other stakeholders to addressing disasters and/or outbreak situations.
- Trained nurses and doctors at sentinel sites to handle avian and seasonal influenza.
- Stockpiled Tamiflu so that when it is needed, it can be provided to health facilities and hospitals.
- Conducted the second self-assessment for influenza pandemic preparedness and response using the standard CDC assessment tool. Assessed areas of improvement and areas where more work is needed.

Training

- Provided technical support in the regional UN Food and Agricultural Organization Field Epidemiology Training for veterinarians.
- Attended the WHO/CDC Influenza Data Management Training in Thailand, February 11–15, 2013.
- Received reagents for respiratory syncytial virus (RSV) testing and PCR training for influenza and RSV.
- Received PCR and virus characterization training from Pune, India for one month.
- Conducted training for 400 hospital staff on infection prevention (ongoing until Dec 2013).
- Conducted training for nurses on surveillance definitions, selecting patients, maintaining the cold chain, and collection, storage and shipment of specimens at Nepalgunj Medical College in August 2013.

Publications

Molecular Epidemiology and Serological Characterization of Influenza Virus Infection in Nepal [abstract]. In: Options for the Control of Influenza Conference; September 5–10, 2013; Cape Town, South Africa.

Sri Lanka



Capital: Colombo

Infant Mortality Rate: 9.24/1,000 live births

Population: 21,675,648 (July 2013 est.)



Overview

The Epidemiology Unit of the Ministry of Health (MoH), the government agency responsible for communicable disease surveillance, control and prevention, was awarded their first influenza cooperative agreement in September 2009. During the grant period the country increased their routine influenza surveillance, laboratory, planning and communications capacities that enable them to better detect and respond to seasonal influenza and pandemic threats.

In September 2013, the Epidemiology Unit began a five-year sustainability grant in which they propose to review their current system, analyze and publish data, and develop a plan that helps them build and maintain a surveillance system that is sustainable over the long term. Key collaborating partners in the programme include the National Influenza Centre (NIC), Medical Research Institute (MRI), the Health Education and Promotion Bureau, and the Department of Animal Production and Health.

Highlights

- Initiated pilot testing of a web-based electronic information system that links data from the Epidemiology Unit, the NIC, and 20 sentinel hospitals.
- Revised the National Pandemic Vaccine Development Plan based on recent WHO recommendations and posted the plan online. The plan incorporates lessons learned while distributing vaccine during the 2009 H1N1 pandemic.

Surveillance

Human and animal influenza surveillance in Sri Lanka began in 2005 as part of their avian influenza preparedness program. With World Bank funding, the MoH established 20 sentinel hospitals, each of which set up influenza-like illness (ILI) surveillance. CDC funds have been used to help maintain ILI surveillance and establish and carry out severe acute respiratory infection (SARI) surveillance in three of the 20 sentinel sites.

Surveillance Activities

- Conducted site visits to monitor and supervise the influenza surveillance at seven selected sentinel hospitals.
- Initiated the pilot testing of a web-based electronic information system linking data from the Epidemiology Unit, the NIC and sentinel hospitals. Two nurses at each sentinel site were trained on the system. The system is operational as of October 2013, allowing for timely data sharing, analysis and results.
- Procured personal protective equipment (PPE), supplies and a refrigerator to store specimens for all ILI surveillance sites.

Laboratory

MRI was designated a WHO NIC in 1968. MRI also functions as the main national diagnostic laboratory in the MoH. The NIC has capacity to conduct real-time RT-PCR and viral isolation. NIC processed a total of 3,321 surveillance samples from sentinel hospitals and 800 more diagnostic samples from other hospitals.

Laboratory Activities

- Processed 1,721 ILI samples from 20 sentinel sites and 732 SARI samples from three SARI sites between Oct 2012–Aug 2013. Influenza positivity during this period ranged from 17.2% to 31.7% with highest positivity observed during Dec 2012–Jan 2013.
- Recorded higher than usual influenza positivity from both routine surveillance samples and diagnostic samples tested. Higher influenza activity was seen during March, April and May 2013 when compared to these months in previous years. Influenza A (H1N1)pdm09 viruses and influenza B viruses were predominant during this period.
- Conducted real-time and conventional RT-PCR and cultures for influenza viruses. Characterized seasonal/circulating influenza viruses by type and subtype, which included testing for influenza A (H5).
- Submitted seasonal influenza samples to WHO Collaborating Centre twice a year which fulfilled NIC requirements as outlined by WHO.
- Established a regional PCR laboratory at the Teaching Hospital in Kandy. This facility is the only laboratory outside of the NIC with the capacity to test samples for influenza by PCR.
- Procured essential laboratory equipment including RT-PCR equipment and a -20°C freezer for the new regional influenza laboratory at the Teaching Hospital in Kandy.

Preparedness

The Epidemiology Unit continues to provide guidance and strengthen human resource capacity and intersectoral collaboration for influenza preparedness and response.

Preparedness Activities

- Hosted capacity-building sessions on field epidemiology, new emerging diseases and outbreak investigations for Central and Regional-level epidemiologists.
- Revised the National Pandemic Vaccine Development Plan and posted it online. The plan includes sections on Management and Organization, Human Resources, Communication & Information, Vaccine Strategy and Post-Marketing Surveillance, Pandemic Vaccine Deployment, and Monitoring and Evaluation.
- Hosted monthly meetings to review the country's preparedness and response plans.
- Prepared partners and the Epidemiology Unit for the threat of MERS-CoV.

- Received MERS-CoV reagents from WHO and prepared to test samples.
- Conducted the second self-assessment for influenza pandemic preparedness and response using the standard CDC assessment tool in September 2012. Capacity increased in several areas since the first review in 2010.

Training

The Epidemiology Unit hosted and attended the following training activities:

- Trained infection control nursing officers who are responsible for ILI and SARI surveillance at sentinel hospitals. Training covered laboratory and epidemiological components of ILI and SARI surveillance, infection control and a new web-based information system.
- Conducted trainings on field epidemiology, including influenza surveillance and pandemic preparedness.
- Two epidemiologists attended a field epidemiology training course in India, July–October 2012 and another two epidemiologists attended July–October 2013.
- Participated in the Influenza Data Management Training Workshop (two epidemiologists and a virologist) in Thailand in February 2013.

Thailand



Capital: Bangkok

Infant Mortality Rate: 15.41/1,000 live births

Population: 67,448,120 (July 2013 est.)



Overview

Knowledge of the epidemiology of influenza in the tropics has increased substantially because of CDC's collaborative work in Thailand. The work CDC and the Thai Ministry of Public Health (MOPH) collaborated on led to the introduction of a seasonal influenza vaccine into Thailand's National Vaccination Program. During the 2009 H1N1 influenza pandemic, collaborative projects provided real-time data to help track the epidemic and assess risks. Thailand's aggressive changes in biosafety, community education, and prompt detection have eliminated outbreaks of avian influenza in the last several years. CDC also worked with WHO to create a regional stockpile of personal protective equipment and medicines for emergency outbreak response.

Highlights

- Purchased about 3.5 million doses of influenza vaccine for use in the public sector in 2013.
- Recommended seven high-risk groups for annual vaccination: health care personnel, persons with chronic disease, persons 65 years and older, pregnant women, obese persons, persons who are mentally disabled, children aged 6 months to 2 years.
- Evaluated vaccine coverage and vaccine effectiveness in the high-risk groups.

Surveillance

Thailand has a long-standing sentinel surveillance system for influenza (it was established in 2004). The system collects clinical specimens from sentinel sites around the country and routinely performs influenza virus analysis and monitoring for drug resistance, and submits viral isolates and isolates that cannot be subtyped to WHO Collaborating Centers. There are currently 10 established sentinel surveillance hospitals throughout the five regions of Thailand and the Bangkok Metropolitan area. Data from the systems are shared weekly, with partners and sites via a report posted on a public website. These data are used to inform decisions by policy makers. Using the strength of the existing influenza surveillance system, the Thai National Influenza Center (NIC) and Thai Department of Disease Control (DDC) have collaborated closely with WHO and CDC to expand the system to detect two novel viruses in SARI specimens; Middle East Respiratory Syndrome coronavirus (MERS-CoV) and influenza A (H7N9) virus. In addition, educational messages/fact sheets were updated using data from unusual outbreaks in-country and globally and distributed to executives at the MOPH.

Surveillance Activities

- Used the influenza surveillance system as the model for the establishment of a national surveillance system for emerging infectious diseases.
- Distributed weekly surveillance data and interpretive summary in Thai language via the NIC website and the Weekly Epidemiological Surveillance Report. Materials were used widely by public and private health care facilities as well as executive levels of the MOPH.

Laboratory

With regard to the sentinel influenza surveillance system, in 2012, the Thai NIC tested 3,590 specimens from patients with ILI and 721 from patients with SARI. Among the specimens from ILI patients, 760 (21.2%) were positive for influenza viruses (242 were influenza A (H1N1)pdm09, 97 were H3N2, and 421 were influenza B). Among the specimens from SARI patients, 91 (12.6%) were positive for an influenza virus (25 were influenza A (H1N1)pdm09, 20 were H3N2, and 46 were influenza B).

Laboratory Activities

- Conducted the annual scientific meeting for the Virology Association of Thailand.
- Circulated a weekly situational report and posted publically available data at <http://www.thainihnic.org/>.
- Analyzed influenza strain data from 2005–2012 to assess annual vaccine match and presented a poster on the results at an international conference.

Preparedness

In 2012, Thailand conducted their third self-assessment of the National Inventory of Core Capabilities for Pandemic Influenza Preparedness and Response. The first two assessments were in 2008 and 2010. With multiple time points, Thailand is better able to assess areas of improvement and where more work is needed. As expected, they scored highest in the area of laboratory capability followed by outbreak response. In 2013, Thailand published the third version of their pandemic preparedness plan called "The National Strategic Plan for Emerging Infectious Diseases (EIDs) 2012–2016" which expands beyond influenza to encompass threats from all emerging infectious diseases.

Preparedness Activities

- Conducted the third assessment of the National Inventory of Core Capabilities for Pandemic Influenza Preparedness and Response in May 2012.
- Organized a national workshop to develop the operational plan on preparedness, prevention and resolution of problems from emerging infectious diseases (EIDs) in March 2013.
- Used Thailand's Rapid Response Teams to promptly investigate possible cases of influenza A (H7N9).

Training

This past year saw the emergence of two new viral respiratory diseases, influenza A (H7N9) and MERS-CoV. To address these new concerns and educate the medical workforce, Thailand's Influenza Foundation partnered with the Ministry of Public Health for several trainings. In addition, the Thai NIC trained laboratory scientists in diagnostics.

- Conducted a scientific writing course in conjunction with the Influenza Foundation of Thailand for health care personnel (January 2013).
- Conducted a course for health care personnel on influenza A (H7N9), MERS-CoV and dengue virus with the Influenza Foundation of Thailand (June 2013).
- Attended a meeting on influenza A (H7N9) in Beijing (August 2013).
- Trained staff in the 14 regional medical science centers on new PCR diagnostics for H7N9 and MERS-CoV.
- Conducted a two-day workshop to review the proficiency test program (February 2013).

Publications

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Research Projects

- Randomized Controlled Trial of the Immunogenicity of Intramuscular versus Intradermal Trivalent Inactivated Split Virion Influenza Vaccine in HIV-infected Men who have Sex with Men in Bangkok, Thailand
- Pediatric Respiratory Infections Cohort Evaluation (PRICE)
- Influenza Vaccine Knowledge, Attitudes, and Practices in Pregnant Women and Their Providers in Thailand: A Vaccination Program Evaluation
- Influenza-Associated Mortality in Thailand, 2006–2011

**see Research Section for additional information*

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WHO WESTERN PACIFIC REGION (WPR)

WHO Western Pacific Region (WPR) Overview

Currently there are six bi-lateral Influenza cooperative agreements in the Western Pacific Region of Asia. These agreements area with Ministries of Health or institutions designated by the Ministry of Health work with CDC to build capacity to routinely identify, diagnosis, and respond to seasonal and pandemic influenza.

CDC direct country support via cooperative agreements has been established in the following countries:

- Cambodia
- China
- Mongolia
- Secretariat of the Pacific Community (SPC)
- Philippines
- Vietnam

In addition, CDC supports the WHO Regional Office for the Western Pacific (WPRO) via a cooperative agreement. Through this cooperative agreement, CDC indirectly provides assistance to the following additional countries:

- Fiji
- Laos
- Papua New Guinea

The core activities of our bi-lateral agreements and technical assistance are:

- To build sustainable national capacity for seasonal influenza, pandemic influenza and other emerging diseases and preparedness for implementation of the International Health Regulations 2005 (IHR)
- To make routine contributions of surveillance data to the WHO Global Influenza Surveillance and Response System (GISRS).
- To increase the geographic reach of WHO's GISRS.
- To provide earlier access to critical virus isolates from humans and birds for WHO GISRS.
- To increase the numbers of shipments and influenza isolates provided by WHO WPR influenza labs to WHO Collaborating Centers for analysis.
- To develop sustainable epidemiologic and virologic surveillance systems for severe influenza in order to gain understanding of the burden of disease from influenza in the WHO WPR.

In FY13, CDC expanded its cooperative agreement portfolio to include two new cooperative agreements with Vietnam and China to introduce or expand the use of seasonal influenza vaccines by public health programs outside the United States. The core activities include: conducting a needs assessment to identify barriers, developing a three-year action plan to introduce vaccines, implement the plan and introduce or expand vaccine use to the target population through a national policy.

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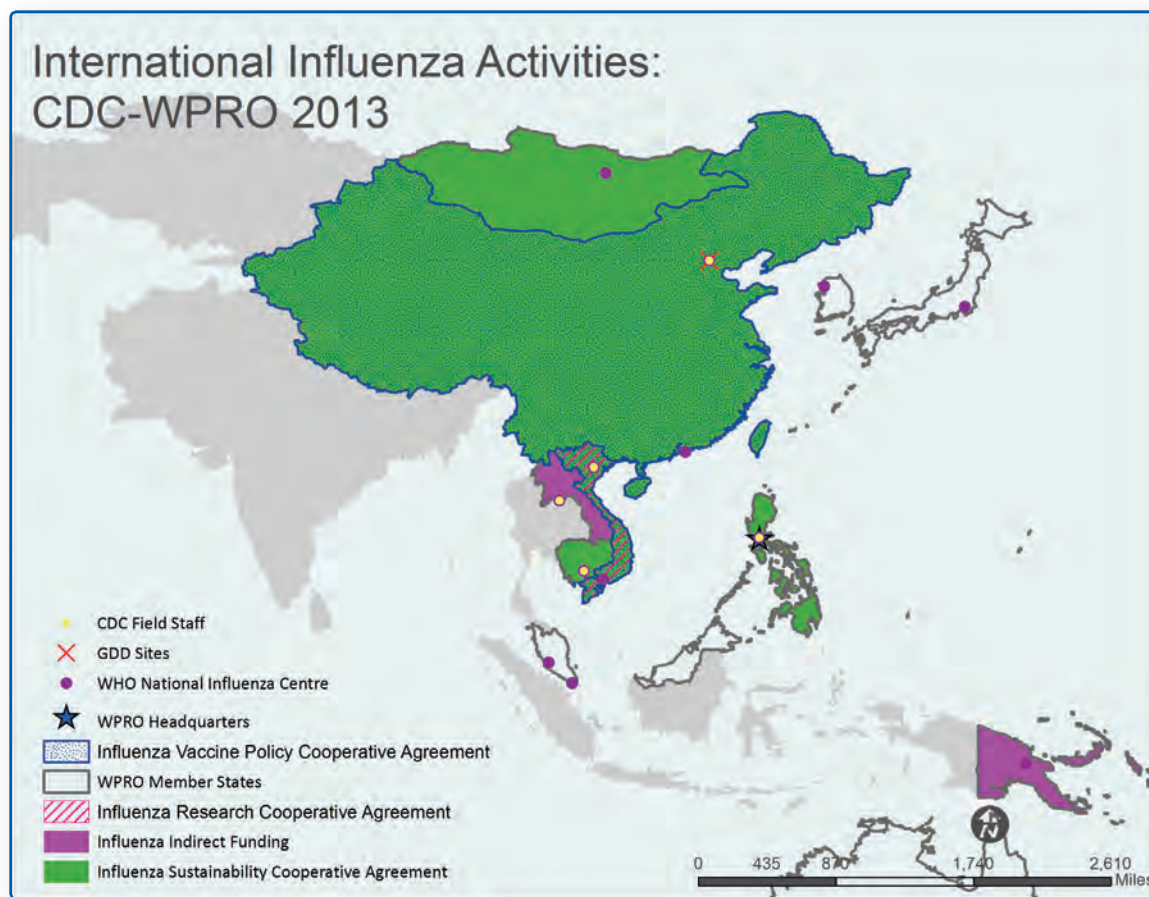
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WHO Regional Office for the Western Pacific (WPRO)



Highlights

- Ensured timely information collection, risk assessment and information dissemination to enable decision-making for H7N9 response.
- Upgraded EOC inaugurated on March 8, 2013 and activated for first time to serve as the common platform for command, control and coordination of A(H7N9) response.
- Conducted the first meeting on seasonal influenza vaccines in the WPR on Oct. 22–23, 2012 in Manila, Philippines emphasizing the importance of national level surveillance data to guide domestic influenza vaccine policies.

U.S. CDC Direct Support

The Regional Office for the Western Pacific (WPRO) is located in Manila, Philippines. The office serves 37 countries and areas that span from the northern hemisphere through the tropics and into the southern hemisphere. This region covers nearly one-quarter of the world's population with approximately 1.8 billion people.

Influenza surveillance has been established in many countries in the region. The Global Influenza Surveillance and Response System (GISRS) in the Western Pacific Region currently consists of 21 National Influenza Centres (NIC) in 15 countries, three WHO Collaborating Centres (CC) for Reference and Research on Influenza, one each in Australia, China, and Japan, two Essential Regulatory Laboratories, in Australia and Japan as well as an H5 Reference Laboratory in Hong Kong, China.

The Western Pacific Region (along with the South-East Asia Region) developed and uses the Asia Pacific Strategy for Emerging Diseases (APSED 2010) to provide a common framework to strengthen national and regional capacities to manage emerging diseases and public health threats, improve pandemic influenza preparedness and comply with the core capacity requirements of the International Health Regulations (2005). It includes components (such as surveillance and laboratory strengthening) that support the GISRS.

The five-year cooperative agreement between CDC and WHO WPRO, which began on September 30, 2011, has supported the implementation of APSED 2010, including influenza surveillance and response capacity development. The agreement also included funds directed to countries through WHO country offices in Cambodia, China, Fiji, Lao People's Democratic Republic, and Viet Nam.

Surveillance

As part of response for Avian Influenza A(H7N9), WHO activated an organization-wide mechanism involving the three levels of WHO–China Country Office, WPRO and Headquarters. The Emergency Response Framework provided overall guidance in line with the emergency management system and ensured adequate human resource surge capacity for monitoring and assessment of the event. The WPRO EOC was the common platform to coordinate the response. Timely information collection, risk assessment and information dissemination were vital to enable decision-making during the A(H7N9) response.

The first meeting on influenza vaccines in the WPR was held on October 22–23, 2012 in Manila. The meeting emphasized the importance of national level surveillance data to guide domestic influenza vaccine policies. It recognized that more data are needed to better understand burden of disease and influenza vaccine effectiveness and encouraged countries to undertake vaccine effectiveness studies and use WHO guidelines on developing a national vaccine deployment plan.

Surveillance Activities

WPRO

- Ensured timely information collection, risk assessment and information dissemination through the online Western Pacific Surveillance and Response Journal (WPSAR).
- Hosted the International Conference on Human Infection with Novel Influenza Viruses, in Beijing, China, August 2013.
- Supported two epidemiologists, a programme management officer, and a national professional officer in China and administrative support.

Cambodia

- Strengthened ILI surveillance at seven provincial sites and at the CDC department with weekly reports produced by each sentinel site and monthly respiratory disease bulletin produced and distributed to partners.
- ILI surveillance review, work plan development, an assessment of A(H5N1) situation, and quality assurance site-visits by national and provincial teams.

- Supported event based surveillance including human A(H5N1) cases.
- Conducted outbreak investigations by national and provincial rapid response teams and confirmatory testing for suspected influenza A(H5N1) cases. WHO was notified timely of human A(H5N1) cases through IHR mechanisms.
- Applied Epidemiology Training (AET) including data quality improvements
- Conducted indicator based surveillance including a CamEWARN review workshop in December 2012.
- Supported a medical officer, national professional officer and administrative support.

Lao People's Democratic Republic

- Fourth cohort of Lao FETP graduated in February 2013. Cohort Five began in February 2013.
- Conducted ILI and SARI sentinel surveillance in five provinces including workshops and site visits. A review meeting of all sites was held on November 22, 2012 and introduced new SARI case definitions and forms.
- Developed SARI case management guidelines including infection control and specimen collection. SARI surveillance and clinical management workshops in March and June 2013.
- Conducted an Annual Surveillance and Response workshop reviewed past activities and outbreaks.
- Supported an epidemiologist, national professional officer (FETP) and administrative support

Pacific Island Countries

- Heightened influenza surveillance through strengthening of syndromic surveillance.
- Supported NIC in Fiji and surveillance officers to Ministries of Health of Fiji, Solomon Islands and Vanuatu.
- Supported a medical officer, epidemiologist and surveillance coordinators.

Laboratory

Support was provided for expert visits, laboratory equipment and supplies in Cambodia, Lao People's Democratic Republic, the Pacific Island Countries and Viet Nam. Existing regional laboratory networks provided essential mechanisms for sharing laboratory information and providing diagnostic resources for A(H7N9) cases. The Chinese National Influenza Centre in Beijing shared virus isolates from the initial three cases with other WHO Collaborating Centres and related laboratories to facilitate development of diagnostic protocols for A(H7N9). As a result, a candidate vaccine virus was identified in a timely manner.

Laboratory Activities

WPR

- Conducted "Regional Training on Sequencing and Phylogenetic Analysis of Influenza Viruses for National Influenza Centres Laboratory Staff" at the WHO Collaborating Centre for Reference and Research on Influenza in Melbourne, Australia, April 29 – May 3, 2013.
- Provided technical guidance and support for development of a national public health diagnostic laboratory network work plan for infectious diseases in Mongolia.
- Supported laboratory officer in Vietnam and provided RT-PCR and supplies.

Cambodia

- Conducted laboratory testing for seasonal influenza, A(H5N1) and other samples at the Institute Pasteur de Cambodge and shipping to WHO CC.
- Procured laboratory supplies for testing for A(H7N9) and translation of materials on laboratory maintenance.

Lao People's Democratic Republic

- Laboratory influenza supplies including A(H7N9) were provided to the National Centre for Laboratory and Epidemiology (NCLE) in Lao PDR. NCLE continues to contribute to GISRS through submission of influenza isolates and samples to WHO CC. NCLE virology laboratory tested an average of 38 specimens/week for influenza during this reporting period (outbreak and surveillance specimens) and found the proportion influenza positive to range between 0–18%.
- The sequencing team composed of laboratory technicians from NCLE, the National Animal Health Centre (NAHC) completed their first full genome sequencing for avian influenza specimens from poultry.
- Repaired critical laboratory equipment at NCLE and supported a laboratory specialist.

Pacific Island Countries

- Enhanced laboratory-based influenza surveillance.
- Conducted IATA training in Papua New Guinea in June 2013.
- Supported laboratory specialist for Fiji NIC.

Preparedness

Capacities of IHR National Focal Points (NFPs) were strengthened and tested through IHR communication exercise. Another important exercise, PANSTOP, practiced, validated and strengthened various aspects of and procedures related to communication, coordination and decision-making to help countries determine whether initiation of a rapid containment operation is necessary to stop or slow the spread of an outbreak of influenza with pandemic potential. Other preparedness activities focused on infection prevention and control and support for local rapid response teams in Cambodia and Lao People's Democratic Republic.

Preparedness Activities

WPRO Regional

- Conducted the fourth annual IHR exercise (named "IHR Exercise Crystal") in December 2012 to test the functionality of the NFP system, ensure contact information was up-to-date and that protocols were clearly understood.
- Conducted the PANSTOP exercise in Vietnam, January 2013. The exercise involved the outbreak of a fictional respiratory disease in a northern province. As a result of the exercise, the Ministry of Health will revise its risk communications strategy to target multiple audiences with specific information suited to their needs.

Cambodia

- Conducted a training of trainers on infection prevention and control through Department of Hospital Services in December 2012.

Lao People's Democratic Republic

- Procured supplies (PPE, specimen collection equipment, etc.) for provincial rapid response teams.
- Meeting of the National Infection Control Committee in January 2013 revised and extended the National Infection Prevention and Control strategy to district level.
- Printed and disseminated the national Emerging Infectious Diseases Plan, 2011–2015.
- Supported an epidemiologist.

Training

WPR

- Conducted “Regional Training on Sequencing and Phylogenetic Analysis of Influenza Viruses for National Influenza Centres Laboratory Staff” at the WHO Collaborating Centre for Reference and Research on Influenza in Melbourne, Australia on April 29–May 3, 2013.

Cambodia

- Conducted refresher trainings on strengthening ILI sentinel surveillance in November 2012 and June 2013.
- Conducted a train-the-trainers session on infection prevention and control in December 2012.
- Conducted refresher training for village health volunteers in four affected provinces by H5N1 between March and April 2013.
- Conducted a workshop on H7N9 and MERS with participation from the Provincial Health Department, provincial clinicians, and Provincial Agriculture Department, July 2013.

Lao People's Democratic Republic

- Conducted two trainings using the “Basic Infection Prevention and Control (IPC) Training Package” developed in 2011 (50 participants trained to be IPC key staff).

Pacific Island Countries

- Conducted IATA training in PNG in June 2013.

Published Papers

Members of the Western Pacific Region Global Influenza Surveillance and Response System (in press). Seasonal influenza vaccine policies, recommendations and use in the World Health Organization's Western Pacific Region. WPSAR.

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Cambodia



Capital: Phnom Penh
Infant Mortality Rate: 52.7/1,000 live births
Population: 15,205,539 (July 2013 est.)



Overview

CDC has provided support to Cambodia to build human capacity and infrastructure for influenza surveillance, response, laboratory diagnosis, and pandemic preparedness. CDC's support has resulted in the establishment of a molecular laboratory at Cambodia's National Institute of Public Health Laboratory (NIPHL) capable of detecting influenza viruses, seasonal and avian, and other respiratory viruses. Influenza-like illness (ILI) surveillance, which began in 2006, is currently being monitored via six sentinel sites in six provinces. Additionally, all ILI samples are now tested at the National Institute of Public Health Laboratory. The laboratory is an active contributor to the WHO Global Influenza Surveillance and Response System (GISRS) and has diagnosed H5N1 in humans through this new system.

Highlights

- Received Year 2 and Year 3 awards under the current cooperative agreement as well as H7N9 supplemental funding to combat the spread of H7 in China.
- Completed structural enhancements for biosafety level (BSL) 2/2+ and cell culture rooms at NIPHL.
- Detected H5N1 infections for the first time since inception in both the influenza-like illness (ILI) and severe acute respiratory illness (SARI) surveillance systems in 2006 and 2009, respectively.
- Achieved perfect scores on Panels 11 and 12 of WHO's External Quality Assessment Project (EQAP) for the Detection of Influenza Virus Type A by PCR.
- Completed a CDC administered surveillance review in May 2012.

Surveillance

Since 2006, ILI surveillance in Cambodia has been supported by either or both of U.S. CDC's MOH and WHO cooperative agreements. ILI surveillance expanded to 13 sites in 2010 for improved geographical representation. Since January 2013, the number of sites has been reduced to six to increase surveillance efficiency and quality at a sustainable cost. Weekly upper respiratory samples of ILI patients have been tested for influenza viruses at IPC and NIPHL.

In 2009, under the first five-year U.S. CDC-MOH cooperative agreement, severe acute respiratory infection (SARI) surveillance was established at four referral hospitals in Phnom Penh, Kandal province, and Siem Reap province. Patients admitted for SARI are tested for influenza viruses and other respiratory viruses, bacterial pathogens and acid fast bacilli at NIPHL.

U.S. CDC-WHO cooperative agreement has also supported operational improvements of Cambodia's national communicable disease surveillance (CamEWAR) and event-based surveillance systems.

Surveillance Activities

- Maintained production of monthly MOH Respiratory Disease and Influenza Bulletin, which includes ILI, SARI and CamEWAR data.
- Shared SARI microbiologic isolate and antibiotic-resistance data with the Working Group on Community-Acquired Lung Bacteria and Antibiotics in Cambodia (CALIBAN).

Laboratory

Funding from the CDC-MOH cooperative agreement, together with close technical support and monitoring by the CDC Influenza Program in Cambodia and guidance from laboratory staff at the CDC Influenza Division, has resulted in significant strengthening of public health laboratory capacity at NIPHL. The molecular laboratory can perform real-time RT PCR for seasonal, avian (H5N1), and pandemic (nH1N1) viruses, in addition to conventional PCR for other respiratory viruses. Furthermore, NIPHL has added EV71 and H7N9 testing to its real-time RT PCR platform in 2012 and 2013, respectively.

In addition, funding from the CDC-WPRO cooperative agreement has supported testing for influenza at IPC and NIPHL. To further expand laboratory capacity at NIPHL, BSL2, BSL2+, and cell culture rooms have been added to allow for isolation and antigenic characterization of influenza viruses. Structural enhancements of these rooms were completed in October 2012, with equipment procurement, staff training, and laboratory operationalization scheduled for FY 2014.

Laboratory Activities

- Tested over 1,000 ILI samples for influenza since October 2012, and detected H5N1 infection for the first time since ILI surveillance was initiated in 2006.
- Completed structural enhancements of BSL 2/2+ and cell culture rooms.
- Implemented testing for EV71 virus.
- Achieved perfect scores on Panels 11 and 12 of WHO's EQAP for the Detection of Influenza Virus Type A by PCR.
- Performed screening and confirmatory H5N1 testing of suspect human cases.
- Tested outbreak investigation samples from close contacts of all confirmed human H5N1 cases.
- Performed culture/antibiotic sensitivity and/or Acid Fast Bacilli detection on over 1,300 SARI surveillance samples.
- Submitted ILI and/or SARI samples to WHO Collaborating Centers in Melbourne and Atlanta (from IPC and NIPHL).
- Tested nearly 1,200 SARI surveillance samples for influenza; a subset of these samples, approximately one third of these samples were tested for other respiratory viruses (RSV, PIV, hMPV, adenovirus).

Preparedness

Through the first five-year U.S. CDC-WPRO cooperative agreement, pandemic influenza preparedness and planning in Cambodia has been significantly advanced. Although activities in the current second five-year CDC-WPRO cooperative agreement do not include pandemic planning, multiple stakeholders involved with pandemic planning in-country have continued to build on efforts and outputs accomplished as a result of previous CDC cooperative agreement funding.

Training

- Conducted ILI and SARI refresher training workshops for staff members from all surveillance sites.
- Conducted SARI surveillance supervisory/on-the-job training visits to each site.
- Conducted a CamEWAR surveillance review workshop.
- Conducted refresher training on H5N1 for village health volunteers affected by human cases in four provinces.
- Conducted a workshop on H7N9 and MERS-Coronavirus for staff from provincial health departments, hospitals, and agricultural departments.
- Conducted on-the-job training for microbiology staff, technical school students and provincial health department laboratory staff on basic bacterial isolation/identification/ antibiotic susceptibility testing and laboratory safety.
- Conducted a train-the-trainer workshop on infection prevention and control.
- Conducted IATA training for NIPHL and U.S. CDC Cambodia staff in Phnom Penh.
- Attended the Data Management and Epidemiological Analysis for Influenza Course for WHO, NIPH, and other MOH staff involved with influenza surveillance data.

Publications

Chheng K, Carter MJ, Emary K, Chanpheaktra N, Moore CE, Stoesser N, Putschat H, Sona S, Reaksmey S, Kitsutani P, Sar B, van Doorn HR, Uyen NH, Van Tan L, Paris D, Blacksell SD, Amornchai P, Wuthiekanun V, Parry CM, Day NP, Kumar V. A prospective study of the causes of febrile illness requiring hospitalization in children in Cambodia. *PLoS One*. 2013 Apr 9;8(4):e60634.

Special Project

Tuberculosis Case Finding among Adults Hospitalized with Severe Acute Respiratory Illness (SARI) in Cambodia

This project was jointly conducted by the CDC Division of Tuberculosis Elimination, the CDC Influenza Program in Cambodia, NIPH, the Cambodia National Tuberculosis Program (CENAT), and three SARI surveillance sites. The primary objective of this project was to determine the impact of SARI surveillance as a novel method of TB case finding. To achieve this, data from all SARI cases ≥ 15 years of age reported between December 2009 and April 2012 who were tested for acid fast bacilli (AFB) were analyzed. The project found high TB prevalence (12%) among SARI cases, demonstrating the potential role of SARI surveillance in enhancing TB case finding in Cambodia.

China



Capital: *Beijing*
Infant Mortality Rate: *15.2/1,000 live births*
Population: *1,349,585,838 (July 2013 est.)*



Overview

For more than 20 years, U.S. CDC has supported the Chinese National Influenza Laboratory in monitoring seasonal and novel influenza viruses with pandemic potential. The U.S. CDC, China CDC, and the MOH are combining expertise on pandemic influenza preparedness, influenza surveillance, and rapid response to prevent, identify, and control influenza. Through the collaboration with the CDC, the China National Influenza Center (CNIC) has been designated a World Health Organization Collaborating Center (WHO CC) for Reference and Research on Influenza. The CDC cooperative agreement supported the establishment of environmental surveillance to estimate the rate of infection with highly pathogenic avian influenza viruses among occupationally exposed populations, and to investigate the distribution of influenza strains circulating in all 31 provinces.

Highlights

- Worked with CDC, WHO and other partners in identifying and responding to the first H7N9 outbreak in the world.
- Invited experts from CDC Atlanta to discuss the H7N9 situation in China and to provide guidance on surveillance data analysis, protocol development, and vaccine development.
- Implemented a joint response between CDC Atlanta and China CDC to ensure a better understanding of H7N9 surveillance and outbreak investigation leading to faster identification and implementation of effective control and preventive measures.

H7N9 Update

On March 31st, 2013, Chinese health authorities reported the first human infection with avian influenza A (H7N9) virus to the World Health Organization. During the spring and summer of 2013, H7N9 influenza A virus caused more than 130 human infections and 40 deaths in China. The preliminary epidemiologic and virologic analyses suggest live poultry markets as a likely source of infection, and the number of new cases declined significantly after the closure of live bird markets.

Since October 2013, new H7N9 cases have re-occurred in southern and eastern China. Human cases have been reported at an increasing rate. As of January 14, 2014, a total of 172 human cases of avian influenza A(H7N9) have been confirmed in the Mainland. So far, there is no sign of sustained human-to-human transmission. China remains vigilant on surveillance and situational analysis, has reinforced case management and treatment, as well as continuing efforts aimed at strengthening health education and communication.

U.S. CDC continues to cooperate with the Chinese counterparts on H7N9 prevention and control, including providing technical assistance on risk assessment of H7N9 human infections, improving protocols and questionnaires for case-control studies and assessing the surveillance of pneumonia of unknown etiology.

The second wave of H7N9 infections is well under way amid preparations for the Lunar New Year, January 2014. U.S. CDC will continue liaising with the Chinese counterparts for H7N9 updates, and provide assistance as necessary.

Surveillance

The CDC cooperative agreement supported improvements to the influenza-like illness (ILI) surveillance capacity of China CDC providing support in carrying out nucleic acid detection and egg-based virus isolation in network laboratories, by providing hands-on training, as well as providing intensive laboratory assessments. CDC continues to support antigenic, genetic and drug resistance surveillance, in part, to develop improved vaccine strain selection. In addition, the cooperation continues to support environmental surveillance to estimate the rate of infection with H5N1 and H9N2 avian influenza viruses among occupationally exposed populations, and to investigate the distribution of avian influenza strains circulating in Live Bird Markets (LBM) in all 31 provinces.

Surveillance Activities

- Expanded the genetic and antigenic characterization and determination of drug resistant viruses collected through the ILI surveillance system.
- Shared representative viruses with other WHO CCs in a timely fashion.
- Established environmental surveillance to estimate infection with H5N1 and H9N2 avian influenza virus among occupationally exposed populations and examined the distribution of these strains in LBMs across the country.
- Improved the influenza surveillance information system.

Laboratory

In FY 2012 & 2013, the CNIC and CDC worked closely together to enhance ILI surveillance quality and CNIC's capacity to better support their 409 network laboratories.

At the national level, ten senior staff participated in international meetings and trainings and received training on surveillance data analysis, influenza detection technology, scientific writing and other relevant topics in order to enhance CNIC's capacity to fulfill the requirements and responsibilities as a WHO CC.

Laboratory Activities

- Shipped influenza virus strains to other WHO CCs.
- Continued laboratory quality improvement at both national and provincial levels following the 2009 expansion of the laboratory network.
- Initiated vaccine seed selection and a preparation platform.
- Helped selected network laboratories successfully conduct egg-based virus isolation.
- Developed a reference kit for network laboratories in order to evaluate PCR kits used in surveillance.
- Participated and presented at international meetings, playing a greater role in global influenza control.

Training

- Supported two training workshops on Influenza Laboratory Detection Techniques in Chengdu, Sichuan, July 30–August 3, 2012 and in Hefei, Anhui, August 13–17, 2012 for approximately 160 key technicians from 80 network laboratories.
- Supported a training workshop on influenza and avian influenza laboratory detection techniques in Beijing for 40 key technicians from 20 network laboratories (July–August, 2013).
- Supported hands-on training at CNIC for 12 technical staff members from network laboratories.
- Visited the Centre for Health Protection of Hong Kong where CNIC received ISO 15189 medical laboratories accreditation.
- Instructed CNIC staff on developing the platform for influenza vaccine candidate strain selection (March 2013).
- Invited to visit CDC's Influenza Division to collaborate with the Influenza Sequencing Team on a project to employ Next Generation Sequencing platforms to analyze H7N9 clinical samples (August–September 2013).

Publications

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Lao People's Democratic Republic (PDR)



Capital: *Vientiane*

Infant Mortality Rate: *56.13/1,000 live births*

Population: *6,695,166 (July 2013 est.)*



Overview

In Laos, CDC is building capacity for avian, pandemic, and seasonal influenza preparedness by strengthening laboratories, surveillance, outbreak response, capacity building initiatives, infection control guidelines and best practices, clinical case management, and pandemic planning. CDC technical investments have led to: recognition of seasonal influenza as a public health problem; reliable laboratory capacity to detect influenza; data sharing of viral data with WHO Global Influenza Surveillance and Response System (GISRS); and improvements and expansion nationwide of the influenza-like illness (ILI) and severe acute respiratory illness (SARI) surveillance networks. Testament to capacity enhancements has been shown by WHO recognition of the National Center for Laboratory and Epidemiology as a designated National Influenza Center (NIC) in August 2010. Capacity building beyond influenza has strengthened the International Health Regulations as practiced in Laos, and enabled Laos's first time laboratory detection of human anthrax and circulating dengue subtypes.

Highlights

- Adopted seasonal influenza vaccination policy into the National Immunization Program (NIP) agenda.
- Added dengue surveillance onto ILI/SARI surveillance platform; enabled recognition of dengue epidemic.
- Conducted second annual seasonal influenza vaccine campaign targeting 100,000 persons from prioritized groups: pregnant women, elderly, chronically ill and health care workers.

Surveillance

The Virological ILI/SARI Surveillance Network in Laos consists of eight hospital sites throughout the country, supported by the CDC-WHO Collaboration and managed by the National Center for Laboratory and Epidemiology (NCLE), a WHO designated National Influenza Coordinating Center (NIC). Additionally, CDC partners with Oxford Welcome Trust (and NCLE) in Non-Malaria Fever Surveillance (NMFS) with focus on influenza in a febrile disease surveillance activity, involving one hospital in Luangnamtha in the north and Saravan in the south.

Surveillance Activities

- Found no evidence of spread of H5N1 from Cambodia bordering to the south, and H7N9 from China bordering to north.
- Attributed over 40% of febrile disease episodes from NMFS to influenza. Current analysis will yield measures of under-reporting (in FY 2014).
- Seasonal Trends and Circulating viral sub-strains (and phylogenetic analysis) provide the requisite background information for influenza vaccine activities in 2013.
- Graduated fourth FETP class, with an alumni network of 39 training epidemiologists throughout the country.
- Completed the first "full genomic sequencing" activity in Laos, describing the phylogenetic evolution of H5N1 from 2004–2009.
- Initiated feasibility assessment of seasonal influenza vaccinations in pregnant women on birth outcomes/ measures.

Laboratory

NCLE with support from the CDC-WHO Collaboration carries out RT-PCR based laboratory testing, using a WHO prescribed diagnostic algorithm. External Quality Assessment Project (EQAP) results carried out in Hong Kong proved 100% testing reliability for FY 2013.

Laboratory Activities

- Adapted protocol from the Thai NIH continues to maintain cell lines for cell culture work in producing viral isolates.
- Contributed ~300 viral influenza isolates to the WHO Global Influenza Surveillance and Response System (GISRS).
- Received H7N9 primers/probes; incorporated into the NCLE diagnostic algorithm.
- Received 1,513 influenza samples [Influenza B positive = 111 samples (7.34%); influenza A/H3 positive = 31 samples (2.05%); influenza A/pdmH1N1 positive = 42 samples (2.05%); influenza A/unttype positive (low virus titre) = 1 sample (0.07%); Negative = 1,328 samples (87.77%)].
- Investigated nine suspected influenza outbreaks from October 12 to August 16, 2013 in which NCLE received 69 samples.
- Investigated suspect influenza outbreaks which were attributed to the following: Influenza B (Vientiane Capital, Attapeu and Sekong); Influenza A/H3 (Xayaboury and Sekong); Influenza A/pdmH1N1 (Phongsaly); and Negative for Influenza (Pongsaly, Champassak and Sekong).
- Conducted a laboratory review with assistance from the Alaska State Laboratory in May 2013, assisted with providing guidance in the use of new H7N9 primers/probes.
- Completed full genomic sequencing of H5N1 animal isolates from sampling six outbreak clusters to describe the phylogenetic evolution of H5N1 from 2004–2009.

Preparedness

The CDC-WHO Collaboration partnered with NCLE and the Ministry of Health (newly formed clinical working groups) revised SARI clinical management, specimen collection and processing guidelines, and disseminated to all hospitals throughout the country.

Special Project

Laos Vaccine Donation Project

During Fiscal Year (FY) 2013, CDC facilitated a vaccine contribution with bioCSL (Australia) that provided 100,000 targeted groups (pregnant women, elderly, chronically ill and Health Care Workers (HCW)). Operational deployment costs provided by CDC enabled training and vaccine distribution in selected districts/provinces throughout the country. There were no adverse events following immunization (AEFIs) recognized through conventional NIP monitoring.

Supplemental funds made available through WHO Laos valued at \$250,000 will be used to support regional training activities add two additional SARI sites in addition to the existing ILI (eight sites) and SARI (five sites) surveillance network, and allow for procurement of additional reagents and materials for laboratory testing purposes.

Preparedness Activities

- Supported series of clinical working group guideline development meetings.
- Produced 1,500 posters for disseminating new SARI virological surveillance guidelines to health centers, district and provincial hospitals, and national hospitals in all 17 provinces.
- Carried out three regional training workshops to disseminate new SARI virological guidelines from February/March to June 2013, in Luangprabang, Bolikhamxay, and Champassak.
- Revised SARI collection guidelines to capture H7N1 cases.

Training

- Supported Annual Field Epidemiology Training (FET) workshop in March 2013 in Khammouan Province.
- Supported Annual Meeting Workshop on Surveillance and Response of Notifiable Selected Diseases in April 2013.
- Supported Annual ILI/SARI workshop meeting in April 2013.

Publications

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Mongolia



Capital: Ulaanbaatar
Infant Mortality Rate: 34.78/1,000 live births
Population: 3,226,516 (July 2013 est.)



Overview

Influenza-like illness (ILI) has been a serious public health challenge in Mongolia since the 1970's, due to rapid growth in population size and urbanization. Mongolia's National Influenza Center (NIC) was established in 1974 and joined the WHO Global Influenza Surveillance and Response System (GISRS) in 1978. As a result of political and economic transition, the system suffered serious damage in the 1990's. In 2004, Mongolia began working with CDC's Influenza Division to increase the capacity of their influenza surveillance, laboratory and preparedness activities. This partnership restored the system and improved its quality. Surveillance sites routinely enter ILI data into Mongolia's web-based Flu Information System (FIS). FIS allows the surveillance sites to access laboratory results from their own sites and to see surveillance summary reports in real time. The country has also developed a special program for the real-time, online reporting of influenza and ILI events where patient data is linked to specimens sent to the NIC from surveillance sites.

Highlights

- Established a working group to develop a sustainability plan for the influenza surveillance system consisting of representatives from national and local levels.
- Calculated ILI rates for the Mongolia Provinces of Dornogovi, Dornod, Uvurkhangai, Selenge and Khovd for the first time and samples have been tested.
- Conducted influenza genome sequencing for seasonal influenza viruses which has become a routine activity.

Surveillance

Mongolia has established outpatient and inpatient information in their Influenza Sentinel Surveillance Sites (ISSS). The ISSS information of Influenza-like Illness data is routinely entered into FIS. Mongolia has developed and installed an on-line program (FLULAB 1.0) to provide information on database samples, laboratory testing protocols, inventory system for reagents, and supplies.

Surveillance Activities

- Using Skype, improved communications for weekly audio-conferencing from the NIC to all local ISS sites. These calls include pediatricians from the National Center of Maternal and Child Health to provide advice to clinicians on the clinical management of severe acute respiratory infection (SARI) cases in the sentinel hospitals.
- Reported 22,297 SARI cases (8.6% of all admissions) with 36 (0.2%) deaths registered from thirty seven hospital-based ISSSs.
- Provided technical assistance visits to sentinel sites in the Sainshand and Zamyn-Uud soums of the Dornogovi Province and Baganuur, District of Ulaanbaatar city. The NIC team included virologists, epidemiologists, and researchers from the Virology Department, Tohoku University's School of Medicine in Japan.

Laboratory

Influenza virological surveillance in Mongolia is based on weekly collection of samples from ISSSs and from the detection and identification of influenza viruses by real-time RT-PCR. The influenza positive specimens were inoculated on MDCK cells and the HA, NA and M genes of representative isolates were sequenced and submitted. The susceptibility of viruses to NA inhibitors (oseltamivir and zanamivir) were examined by chemoluminescent assay using the NA-Star kit and sequence analysis on NA gene if the IC50 value increased. Randomly selected samples from influenza negatives were tested by real-time multiplex PCR for other respiratory viruses.

Achieving 100% accuracy during assessment testing, the Virology Laboratory (VL) at the NIC joined the WHO External Quality Assessment Project. The VL participating in Influenza Performance Evaluation Program conducted by U.S. CDC, Atlanta was also 100% accurate. The VL was assessed using the International Influenza Laboratory Capacity Review Tool developed by CDC and the American Public Health Laboratory (APHL). Following the assessment, APHL and CDC provided technical assistance designed to improve laboratory capacity.

The specialists from Mongolia NIC have done follow up visits to the regional laboratories in Orkhon, Darkhan-uul provinces and provided technical assistance on testing protocol, primers & probes, RNA extraction, and software program of the RT-PCR equipment used by each laboratory. Through CDC project funds, the VL and National Center of Communicable Diseases (NCCD) have provided the necessary reagents, kits and laboratory supplies for use in the regional virology laboratories.

Laboratory Activities

- Processed approximately 300–600 specimens per month during peak influenza season, dropping to around 50 per month outside the normal influenza season.
- Conducted surveillance testing year round.
- Collected specimens at a number of hospitals and sentinel sites within Ulaanbaatar City and from two regional laboratories and sentinel sites located elsewhere in the country.

Preparedness

The Mongolia NIC has provided technical assistance to health care facilities and relative agencies to prepare for influenza A (H7N9) and MERS-CoV infections. Revised guidelines developed by WHO have been translated into Mongolian.

Preparedness Activities

- Conducted a Laboratory Capacity Review in 2013.
- Translated the WHO document Pandemic Influenza Preparedness: Framework (PIP Framework) into Mongolian and published it in Mongolian Journal of Infectious Disease Research.

- Established regional virology laboratories in Khovd and Dornod Provinces in July 2013 with the procurement of RT-PCR machines, centrifuges and some accompanying devices - conducted surveillance testing year round.
- Provided reagents, kits and laboratory supplies for regional virology laboratories for the 2012–2013 season.

Training

- Provided training on laboratory diagnosis of A (H7N9) avian influenza for laboratory specialists of NCCD, National Center for Zoonotic Diseases (NCZD), Veterinary Laboratory and Regional Virology laboratories (15 participants).
- Participated in regional training on sequencing and phylogenetic analysis of influenza viruses for National Influenza Center laboratory staff in Melbourne, Australia, supported by WHO Western Pacific Regional Office (WPRO).
- Organized a workshop on the calculation of tolerant limits for Dornogovi, Dornod, Uvurkhanga, Selenge and Khovd Provinces and obtained results for use in epidemiological analysis.
- Attended the WHO Consultation Meeting on Global Influenza Surveillance in Switzerland, Geneva.
- Attended the Influenza Data Management and Epidemiological Analysis Training Course in Phnom Penh, Cambodia.

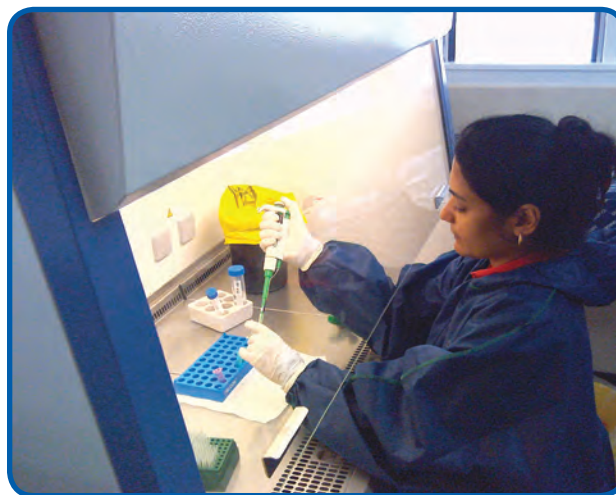
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Secretariat of the Pacific Community (SPC)



Overview

The Secretariat of the Pacific Community (SPC) is an international organization with a membership of 22 Pacific Island Countries and Territories (PICT). SPC, through its Public Health Division, is the focal-point of the Coordinating Body of the Pacific Public Health Surveillance Network (PPHSN), a joint initiative of SPC and the WHO, which is dedicated to targeted communicable disease control and surveillance, including influenza. The cooperative agreement between SPC and CDC began in 2005 and supports the development of influenza surveillance networks across a vast area, including both the North and South Pacific. In August 2010, an additional five-year extension was awarded to SPC to further develop the existing surveillance systems and address the challenge of pandemic preparedness.

Highlights

- Strengthened relationships between PICTs and reference laboratories in the region and among local PICT sentinel sites.
- Enhanced H7N9 surveillance in Fiji and Guam Public Health laboratories through the provision of equipment and enhanced testing capacities by providing laboratory supplies.

Surveillance

In 2010, PICTs began implementation of a standard syndromic surveillance system with the assistance of WHO and SPC, comprising four core syndromes including influenza-like illness (ILI). The system is designed to provide data that can be used to fulfil the obligations of countries under the International Health Regulations (2005). Project staff have been actively working to integrate ILI sampling into the syndromic surveillance system in each country with the aim of improving the number and quality of specimens that are collected from patients. This has been achieved by advocating for the use of sentinel surveillance sites for both syndromic and influenza surveillance.

Surveillance Activities

- Conducted several supervisory visits in PICTs to review the influenza sentinel surveillance system, update national plans, and promote the integration of virologic and epidemiologic data at the country level.

Laboratory

LabNet is the three-tiered public health laboratory network of the PPHSN: (i) level one (L1) laboratories receive specimens directly from clinicians and where possible, conduct initial screening tests (e.g. influenza rapid tests), (ii) level two (L2) laboratories receive specimens from L1 laboratories (and may also receive specimens directly from clinicians), for first-level confirmation testing (e.g. influenza RT-PCR testing) and (iii) level three (L3) laboratories are internationally recognized reference laboratories for definitive diagnostic testing and further analysis of specimens (e.g. influenza subtyping, sequencing and virus isolation). Reference laboratories of PPHSN continue to provide influenza diagnostic testing for all specimens sent from PICT L1 laboratories. This service is provided at no cost to the country shipping the specimens provided that the corresponding laboratories comply with the International Air Transport Association (IATA) shipping requirements. A technical working body (TWB) facilitates and coordinates the development of LabNet.

Laboratory staff have continuously been certified or re-certified (biannually) to ensure shipments of all biological specimens across the Pacific comply with IATA regulations. This has been achieved by collaboration between SPC and PIHOA in the North Pacific Region.

Laboratory Activities

- Supported laboratory-based influenza surveillance through technical assistance and the procurement of equipment and laboratory supplies to enhance local testing capacities.
- Facilitated transport of shipments of samples to identified reference labs for confirmatory testing.
- Conducted several laboratory trainings with regional partners focused on screening tests and enhancing sample transfers.
- Provided training on laboratory diagnosis and algorithms related to influenza and other outbreak prone diseases in the Pacific Region to several national laboratories.
- Conducted a regional LabNet meeting will be held in Noumea at SPC Headquarters (September 2013).

Preparedness

The Fiji Centre for Communicable Disease Control at the Mataika House and Guam Public Health Laboratory have been able to enhance their H7N9 surveillance capabilities with the emergency supplemental funds received earlier this year. Both Level II laboratories have the ability to provide confirmation of influenza through molecular diagnosis. They are both strategically situated should neighbouring PICTs need assistance with confirmation tests. Shipping biological specimens in the Pacific is an expensive process. Building the capacity in both Level II laboratories within the Pacific ensures timely and reliable laboratory results are sustained with the assistance of partner agencies is the goal of SPC PPHSN Laboratory Network.

Training

- Conducted microbiology enhancement and influenza laboratory-based surveillance training in Samoa and American Samoa.
- Contributed to IATA training in Fiji.
- Organized regional LabNet meeting in Nouméa with participants from all PICTs.
- Attended the Data Management and Epidemiologic Analysis for Influenza Data in the Western Pacific Region in Phnom Penh, Cambodia.

The Philippines



Capital: Manila

Infant Mortality Rate: 18.19/1,000 live births

Population: 105,720,644 (July 2013 est.)



Overview

The Philippines' Research Institute for Tropical Medicine (RITM) and Department of Health were awarded a five-year capacity building cooperative agreement in 2005. The cooperative agreement enabled the establishment of an influenza surveillance network with 44 sentinel sites, both health centers and outpatient departments in tertiary level hospitals, distributed across 12 of the 17 regions in the country. The partnership also supported the development of severe acute respiratory infection (SARI) surveillance in 16 health centers and seven hospitals in an urban setting, to establish the burden of disease associated with influenza. RITM is also the Philippines National Influenza Center (NIC). CDC and RITM entered into a second five-year agreement in 2009 to ensure sustainability of the RITM as a NIC and to plan for the continued existence of the surveillance network.

Highlights

- Reduced the number of regions with influenza-like-illness (ILI) surveillance sites by 30%, while maintaining a high quality of NIC operations and representativeness of influenza surveillance information.
- Re-established and strengthened relationships with key stakeholders regarding the sustainability of national influenza surveillance.
- Began to integrate ILI and SARI surveillance into the existing Philippine Integrated Disease Surveillance and Response (PIDSR) System through the National Epidemiology Center (NEC).

Surveillance

With a view towards sustainability, the regions of the Philippines with ILI sentinel sites were downsized from 12 (out of 17) regions to five with a total of 33 health centers and hospital sites (down from 47 in 2012), maintaining high quality virologic surveillance operations and representativeness of influenza surveillance data. Virologic information is regularly sent to the Department of Health (NEC and the National Center for Disease Prevention and Control (NCDPC)) as well as shared with the WHO Global FluNet.

Building on the experience of the NIC in its Flu-BOD study, the NIC and NEC have begun discussions and planning for expanding the SARI surveillance and establishing this in the government tertiary hospitals that host the subnational laboratories in order to cover the severe end of the spectrum of Influenza disease. Surveillance guidelines for SARI, under the existing PIDSR system, have been discussed with regional surveillance units and are now being finalized. The quality and efficiency of sentinel site performance is verified through regular monitoring visits and through a set of process and outcome indicators.

Surveillance Activities

- Reported a total of 2,817 SARI cases from five sentinel hospitals.
- Revised the ILI Case Report Form into a one-page format based on CDC recommendations.
- Revised the SARI Case Report Form to include the recommended minimum required information.

Laboratory

The RITM-NIC continued to perform a full array of culture-based and PCR-based testing producing high quality results to support surveillance activities for influenza and other respiratory viruses. It likewise continued to improve its technical capacity.

The NIC continued to send unsubtypable isolates and representative isolates, for quality assurance, to the WHO Collaborating Center (CC) in Melbourne. In 2011, 141 isolates were shipped. The NIC continues to participate in the WHO External Quality Assessment Project and has consistently attained 100% in these proficiency panels.

Laboratory Activities

- Improved turn-around time from receipt of specimen to result transmittal by shifting the algorithm of testing from pure virus isolation to pre-screening by influenza PCR followed by virus isolation.
- Collected specimen from 2,860 ILI cases from October 2012 to August 2013 from 33 sentinel sites in the country. Of the specimens collected, 2,468 (86%) were screened using RT-PCR and 828 (29%) were subsequently subjected to virus isolation.
- Isolated influenza from 108 (13.04%) specimens while 364 (13.75%) influenza-positive cases were detected by RT-PCR.
- Detected Influenza A and B by RT-PCR in eight (0.97%) and 46 (5.55%) cases, respectively. Influenza virus was isolated in eight of the 829 specimens tested.
- Continued to provide proficiency testing for subnational laboratory staff. Panel Five was administered from June to October 2012, with three of five laboratories obtaining 100%.

Preparedness

CDC support has assisted in the continuous development of the Philippines' national preparedness plan. To coordinate influenza preparedness activities, the Philippines' Department of Health has four major committees including: a planning committee, an operations committee, a logistics committee and a finance committee. Each committee works on developing guidelines and making recommendations concerning influenza such as quarantine and isolation at points of entry, containment, mitigation, vaccine purchases and guidelines for prioritization and rapid response teams (which are currently being reviewed).

Preparedness Activities

- NCDPC, in coordination with NEC and NIC, is currently preparing guidelines for clinical management and infection control of novel respiratory pathogens. NEC has prepared interim surveillance guidelines for these emerging infectious diseases.
- Coordinated with CDC and WHO to successfully establish PCR testing for novel respiratory pathogens.
- Optimized real-time PCR for Influenza B in the laboratory. This is in preparation for developing influenza real-time PCR testing capacity in the five (5) subnational laboratories established in 2009 at the height of the pandemic influenza AH1N1.
- Trained physicians and nurses of the Bureau of Quarantine for nasopharyngeal and oropharyngeal swabs (NPS/OPS)/sputum specimen collection as part of preparedness efforts for novel respiratory pathogens (MERS-CoV, Influenza AH7N9).

Training

- Attended the Data Management and Epidemiologic Analysis for Influenza Data in the Western Pacific Region in Phnom Penh, Cambodia.
- Conducted a refresher training course for Influenza Surveillance Officers (December 2012).
- Revised the training module for the collection of swabs (NPS/OPS) and provided additional training to all sentinel site staff.
- Conducted a series of training courses on specimen collection for novel respiratory pathogens— organized by the Bureau of Quarantine in coordination with the NIC.

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Vietnam



Capital: *Hanoi*

Infant Mortality Rate: 19.61/1,000 live births

Population: 92,477,857 (July 2013 est.)



Overview

Since 2006, CDC has supported Vietnam's National Influenza Surveillance System to conduct continuous active and passive surveillance for influenza-like illness and severe acute respiratory illness caused by seasonal, pandemic, and animal-origin strains of influenza. CDC strengthened Vietnam's pandemic preparedness plans and communication strategy to quickly detect influenza viruses and to respond rapidly. Working with the Ministry of Health (MOH), Ministry of Agriculture and Rural Development (MARD) partners, CDC conducts research on influenza and other zoonotic diseases to better define the transmission of viruses between species.

Highlights

- Awarded Vaccine Policy Cooperative Agreement.
- Received supplemental funding for H7N9 activities—MOH, National Institute of Hygiene and Epidemiology (NIHE); MARD, Department of Animal Health (DAH).
- Initiated NIHE CoAg activities: AHI Longitudinal; second Burden of Disease study (BOD)—Initiated DAH CoAg activities: Inception workshop; Trainings; Cross-sectional study.
- Completed NIHE CoAg activities: Animal Human Interface (AHI) Pilot Extension-South; Co-evolution; Household Health Utilization Survey.
- Assisted with the Global Health Security (GHS) Demonstration Project.
- Supported HHS Secretary and CDC Director visits and provided FETP assistance in Vietnam.

Surveillance

In 2005, CDC entered into a five-year cooperative agreement (CoAg) with the Vietnam MOH/NIHE to establish a National Influenza Surveillance System (NISS). Developed primarily as an outpatient surveillance system for influenza-like illness (ILI), the system has supported up to 15 sites that are strategically located throughout the country's four geographic regions. The system also includes nationwide passive surveillance that detects cases of severe viral pneumonia (SVP) in hospitals, including the majority of Vietnam's confirmed human H5N1 cases. A second five-year cooperative agreement in 2010 expanded surveillance to include inpatient severe acute respiratory infection (SARI). Currently there are 10 ILI surveillance sites and four SARI surveillance sites in NISS, of which four ILI and SARI sites (in the same hospitals) are funded by this cooperative agreement. The Vietnam MOH supports sustainability of this initial CDC-supported program by funding the remaining six ILI sites for FY 2012–2013.

Surveillance Activities

- Continued to monitor and provide support for NISS during the primary influenza season in Vietnam, including optimum times for vaccination.
- Incorporated antigenic characterization and antiviral resistance surveillance into the NISS.
- Provided the "Influenza Weekly Update Vietnam" (a report of influenza surveillance activity, including ILI, SARI, and SVP).

Laboratory

Vietnam has two National Influenza Centers (NIC); NIHE/Hanoi and Pasteur Institute of Ho Chi Minh City (PI-HCMC). NIHE and PI-HCMC continue to provide influenza virus samples to the WHO Collaborating Center (CC) in Atlanta.

The AHI Program collaborates with the National Center for Veterinary Diagnosis (NCVD) of DAH/MARD, which provides poultry samples to CDC Atlanta for review and analysis. The human and animal samples provide information on the influenza virus types, characterization, and evolution in Vietnam, and also contribute to the knowledge of influenza viruses and anti-viral resistant strains in Asia.

CDC helps build laboratory capacity at PI-HCMC by supporting the training of a NIC staff member in advanced molecular analyses at CDC Atlanta. Experts from CDC and the Association of Public Health Laboratories (APHL) conducted influenza laboratory assessments at both NICs, DAH's influenza laboratories at NCVD and at the Regional Animal Health Office (RAHO) 6.

Laboratory Activities

- Tested 3,586 ILI samples from NISS outpatient sentinel sites from October 1, 2012–August 18, 2013, with an influenza positivity rate of 19%.
- Tested 901 SARI samples from NISS inpatient sentinel sites from October 1, 2012–August 18, 2013, with an influenza positivity rate of 17%.
- Tested 134 samples from persons with severe unexplained pneumonia from October 1, 2012–August 18, 2013, detecting 29 (22%) cases caused by seasonal influenza strains and 2 (1%) cases of avian influenza A(H5N1).
- Provided 52 influenza virus specimens to the WHO CC in Atlanta from NIHE and PI-HCMC in 2012.
- Conducted formal influenza laboratory capacity reviews at both NICs and at two animal health laboratories (NCVD and RAHO 6, of DAH/MARD) in May–June 2013.
- Conducted four site visits to the influenza laboratory under the regional public health institutes participating in the NISS.

Preparedness

The Influenza and AHI Programs at CDC Vietnam, through their support of CDC's Global Health Security (GHS) Demonstration project, provided leadership and technical expertise to the Laboratory systems and Emergency Operations Lanes of the GHS. This included ensuring that the already established CDC Influenza platform in Vietnam was a part of the considered enhancements to MOH's public health preparedness, including for the International Health Regulations. Specifically, this potentially allows the use of the SARI and SVP surveillance systems in consideration for current and future GHS support as well as for MOH enhancements to respiratory disease surveillance and to response preparedness.

Preparedness Activities

- Supported both GHS Laboratory Systems and Emergency Operations Lanes with IP/AHI staff.
- Enhanced existing systems of GHS Laboratory Systems to include the consideration for multiple respiratory pathogen discoveries, including avian and human influenza viruses.
- Enhanced the GHS Emergency Operations Center to include the monitoring of on-going infectious disease activities, including respiratory disease epidemiology and laboratory reports, in preparation for responding to emergency events.
- Assisted in the development and delivery of emergency operations and management training.

Training

- Supported 12 training sessions with a total of 326 public health and animal health staff at CoAg study sites, in the use of data collection tools, and techniques for human and animal specimen collection, storage and transportation through the MARD/DAH Research CoAg.
- Supported one laboratory staff member from PI-HCMC to attend training on enhanced molecular analyses of the influenza virus in CDC Atlanta.
- Recommended and facilitated four staff members (by IP/AHI Programs) from NIC/NIHE, NIC/PI-HCMC, NCVD and RAHO 6, to attend the Regional Training Workshop on Sequencing and Phylogenetic Analysis of Influenza Viruses in Melbourne, Australia.
- Recommended and assisted two epidemiologists, from NIHE and PI-HCMC, to attend the CDC/WPRO Data Management Training in Phnom Penh, Cambodia.
- Supported the Vietnam FETP, including assisting with the development of training modules, classroom training sessions and mentoring, and providing technical review of abstracts, presentations, and manuscripts presented by the fellows at meetings and conferences.

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MEETINGS, TRAININGS, & WORKSHOPS

FY 2012

3rd Annual African Network for Influenza Surveillance and Epidemiology (ANISE) Meeting

Location: Nairobi, Kenya

Dates: February 1–3, 2012

Goals: The goal of the meeting was to share and promote the use of standardized surveillance methods in the regions among laboratorians, epidemiologists, veterinarians and other public health practitioners involved in influenza related public health activities or influenza research in Africa.

Agenda: The three day meeting included plenary sessions, breakout sessions, and poster presentations. The meeting included the following scientific themes: Burden of Disease, Virologic Surveillance, Co-Infections and Other Respiratory Diseases, and Vaccines and Other Interventions. Representatives from 12 African countries provided updates on their national influenza surveillance systems. Additional highlights from the meeting included the poster presentations and roundtable discussions.

Outcome: The meeting brought together 170 participants representing 30 countries, including 24 African countries. Additionally, members from organizations such as the WHO, Institut Pasteur, and the U.S. Army Medical Research Unit (USAMRU-Kenya) in Kenya attended and provided updates. Out of the 82 abstracts that were submitted, 17 were selected for oral presentations and 58 were selected for poster presentations. The meeting was a success and provided attendees an opportunity to present their data and share best practices.



Group photo from the 3rd Annual ANISE Meeting in Nairobi, Kenya.

Improving Influenza Laboratory Management Practices Training Course

Location: Bangkok, Thailand

Dates: February 27–March 2, 2012

Goals: The training course was designed to help laboratories achieve, maintain, and improve global influenza surveillance systems by presenting various laboratory management topics to influenza laboratory managers and staff.

Agenda: The format for the course was a combination of lectures, demonstrations, and hands-on exercises. This format allowed participants to gain knowledge and information for implementation within their laboratories. Course topics included: Human Resources Basics, Biosafety for Lab Managers, Quality Assurance and Quality Control, Inventory Management, Specimen Collection and Processing, Laboratory Testing and Test Result Reporting, and NIC Designation. During the course, participants toured the laboratories of the National Institute of Health (NIH) of Thailand. They also listened to presentations on Thailand's Influenza Surveillance Network and their BSL-3 Laboratory.

Outcome: The participants learned how to describe key aspects of laboratory biosafety including risk assessment, incident management and BSL-3 (biosafety level three) security practices. Additionally, participants learned how to develop strategies to implement Quality Assurance and Quality Control best practices, describe and develop an inventory management system, describe specimen collections and processing best practices for influenza detection, and they learned the roles and responsibilities of becoming and/or maintaining a National Influenza Center (NIC) designation.



Improving Influenza Laboratory Management Practices Training Course – Group Photo.

FY 2013

Indian Ocean Commission (IOC) Influenza Surveillance Training Workshop

Location: Pointe aux Piments, Mauritius

Dates: January 21–25, 2013

Goals: Several countries from the IOC (Comoros, Reunion, Seychelles, Mauritius and Madagascar) demonstrated an interest in establishing and maintaining influenza surveillance with the goal to build capacity to detect, diagnose, and respond to influenza and other respiratory diseases. CDC, the Association of Public Health Laboratories (APHL), Mauritius MOH, Institut Pasteur (IP)-Madagascar, and the IOC developed a training course to help the ministries of the IOC achieve, maintain, and improve global influenza surveillance systems by teaching epidemiologists and laboratorians the methods and practices of establishing and maintaining influenza sentinel surveillance.

Agenda: The workshop was taught in a “hands-on” manner using a combination of lectures, group discussion, and on-site instruction. Day one and day four of the course focused on overall topics applicable to both epidemiologists and laboratorians. For day two and day three the participants were divided into two groups, epidemiologists and laboratorians, which allowed for more in-depth instruction and discussion. Each group also participated in hands on instruction: the epidemiologists toured a hospital to learn about their sentinel surveillance system and the laboratorians performed the CDC influenza assay at the university laboratory.

Outcome: All participants strongly agreed that the workshop was very valuable. The most valuable component was developing network connections. A majority of participants indicated that after completing the workshop they would be able to analyze data and use it for empowered decision making as well as utilize new contacts within the IOC network to respond to unexpected or crisis events. Participants also indicated that they would be able to identify strategies to help overcome public health laboratory management challenges and to create a plan to increase team effectiveness in their laboratories.



Group photo from the workshop.

International Influenza Networks Meeting

Location: Scottsdale, Arizona

Dates: January 14–16, 2013

Goals: To increase awareness of global work, share data, best practices, and lessons learned surrounding influenza networks.

Agenda: While essential topics such as partnership, building capacity, and information sharing were covered, integration and sustainability were focal points of a majority of discussions. Participants were able to gain a better understanding of the influenza focused networks and their respective strengths through a series of five panel presentations. The panels were divided up according to the network's areas of focus such as human surveillance, education/advocacy, animal surveillance and research, laboratory and clinical/research. The panelists shared network goals, information generated and the unique attributes including current strengths and gaps. Group exercises were also a significant part of the meeting. The participants were given a charge each day during the group exercise and reported back to the larger group with their findings.

Outcome: More than 60 government officials, leaders from various influenza focused networks and representatives from the private sector convened in Scottsdale for the first International Influenza Networks Meeting. Over 35 networks were represented. Successes from the meeting include exposure to existing networks and their activities and a better understanding of gaps and challenges.



Group photo from the International Influenza Networks Meeting in Scottsdale, Arizona.

Regional Data Management Training Courses

Working with various organizations in the World Health Organization (WHO) Regions as well as WHO Region Offices, the Extramural Program Office of the Influenza Division provided technical support and trainers for courses on data management and analysis for cooperative agreement partners in various World Health Organization (WHO) Regions.

The primary goal of the course was to help data managers and epidemiologists establish, maintain, and improve influenza surveillance systems by teaching data management and analysis methods. The course format was a mixture of short lectures and hands-on exercises which allowed participants to gain knowledge and skills to use with their own data and teams. Course topics included: building a database from scratch; data entry controls and data cleaning; quality assurance and control; data analysis; collection and analysis of risk factor data; understanding of the utility of baselines, risk ratios, and odds ratios in data interpretation; and presenting and reporting data for public health action.

In partnership with the National Institute for Communicable Disease (NICD) the first Data Management Training Course for influenza surveillance data managers/epidemiologists was held in Johannesburg, South Africa. The training course was held at the NICD Training Facility on November 14–18, 2011.

Location: Johannesburg, South Africa

Date: November 14–18, 2011

Summary: There were 30 participants representing 20 African countries (Angola, Burkina Faso, Cameroon, Côte d'Ivoire, Egypt, Ghana, Kenya, Madagascar, Mali, Malawi, Mauritania, Morocco, Nigeria, Republic of Congo, Rwanda, South Africa, Tanzania, Togo, Uganda, and Zambia) and 12 instructors from various agencies such as CDC, NICD, WHO AFRO and WHO Headquarters. The course was offered in both English and French. During the course, the participants toured the NICD Data Management Centre. The tour provided the participants with a look at how NICD enters, stores and utilizes data. Many participants thought the Centre's processes were very effective and wanted to see if they could implement some of the methods used within their countries.



Dr. Richard Njouom presenting on data management techniques used in Cameroon.



South Africa Data Management Training Course— Group photo.

The Extramural Program Office of the Influenza Division in collaboration in the WHO South East Asia Region (SEAR) supported a training, February 11–15, 2013 in Bangkok, Thailand.

Location: Bangkok, Thailand

Date: February 11–15, 2013

Summary: A total of 23 participants from eight countries (Bhutan, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand and Timor-Leste) as well as instructors from agencies including CDC, the World Health Organization Collaborating Center, the WHO Regional Office for South-East Asia (SEARO) and Prince of Songkla University participated in the course. On the last day of training, course participants shared information on their own surveillance systems and shared some of their current reports and analysis. Discussion of individual needs and plans for improvement of surveillance systems were discussed.

The third session with the World Health Organization (WHO) Regional Office hosting cooperative agreement partners in the WHO Eastern Mediterranean Region (EMR) was held April 21–25, 2013 in Cairo, Egypt.

Location: Cairo, Egypt

Date: April 21–25, 2013

Summary: A total of 27 participants from 14 countries (Afghanistan, Egypt, Iraq, Jordan, Lebanon, Morocco, Oman, Pakistan, Palestine, Qatar, Somalia, Sudan, Tunisia, and Yemen) as well as instructors from agencies including CDC, NAMRU–3, WHO Headquarters Office, the WHO Regional Office for the Eastern Mediterranean (EMRO) participated in the course. Extramural team members, worked with WHO EMRO to design the course to meet the specific needs of region participants.

On the last day of training, course participants presented their data to their peers and making a case for the future funding needs of their program. The exercise was designed so participants could practice presenting data to decision makers responsible for funding. Presenters obtained feedback on both the presentations and their individual presentation skills. Discussions were lively and informative.



Attendees working on exercises during the SEARO course in Bangkok.



Attendees working on exercises during the EMRO course in Cairo.

Immediately following the EMRO course, the WHO Regional Office for Europe (EURO) requested a modified version of the data management course. The course was held on May 1–3, 2013 in Nijmegen, Netherlands. The course was revised to focus more on the concepts of epidemiologic analysis and understanding the utility of baselines, risk ratios and odds ratios in data interpretation. The intent was to build analytical skills using Microsoft Excel as a data collection tool. Additionally, WHO EURO presented and discussed study results from a University of Nijmegen study to which countries had contributed data.

Location: Nijmegen, Netherlands

Date: May 1–3, 2013

Summary: A total of 12 participants from seven countries (Albania, Armenia, Belarus, Georgia, Kyrgyzstan, Russian Federation and Ukraine) as well as instructors from agencies including CDC, WHO EURO and Nijmegen University participated in the course. The course was conducted in English and Russian (via simultaneous translation) for participants.

The course format was changed due to the limited instruction days. The format remained a mixture of short lectures and hands-on exercises allowing participants to gain knowledge and skills. Course topics included: building a database from scratch; data entry controls and data cleaning; quality assurance and control; data analysis; collection and analysis. The more advanced concepts of risk factor data; understanding of the utility of baselines, risk ratios, and odds ratios in data interpretation; and presenting and reporting data for public health action were introduced on a limited basis. Based on participant questions and requests, the focus of the class was instruction on building a basic Access database and instructions on how to analyze data in Excel and creating a descriptive graph.



Attendees listening to a presentation during the Data Management course at Nijmegen University.

The Council of State and Territorial Epidemiologists (CSTE) in collaboration with the Ministry of Health, Côte d'Ivoire and the U.S. Centers for Disease Control and Prevention (CDC) conducted a Data Management and Scientific Writing Workshop held in Abidjan, Côte d'Ivoire. The purpose of the workshop was to provide guidance and structure to the journal writing process, empowering participants to complete and produce quality data for manuscript/abstract writing and publication.

Location: Abidjan, Côte d'Ivoire

Date: May 2–24, 2013

Summary: Burkina Faso, Côte d'Ivoire, Ghana, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone and Togo each sent participants to the workshop. The 13 participants were chosen based on their involvement with influenza surveillance activities in their respective countries. Facilitators/mentors from agencies including CDC, CSTE, and NAMRU-3, as well as the CDC Côte d'Ivoire Country Office participated in the workshop. The format remained a mixture of short lectures and hands-on exercises. Participants were especially pleased to have a mentor assigned to them to assist them as they developed their abstracts and/or manuscripts.

At the conclusion of the workshop, each participant had developed an abstract ready for submission to an upcoming conference. Eleven of the 13 participants submitted an abstract to the Options for the Control of Influenza Conference held September 2013 in Cape Town, South Africa. All 11 abstracts were accepted by the Options Conference. Additionally, the participants were able to develop a relationship with a mentor to provide technical assistance on an ongoing basis for finalization of a manuscript.



Group photo from the Data Management and Scientific Writing Workshop in Abidjan.

A final data management course had the Extramural Program Office partnering with CSTE and the WHO Collaborating Center, Australia, to conduct a program in Phnom Penh, Cambodia on July 29–August 2, 2013.

Location: Phnom Penh, Cambodia

Date: July 29–August 2, 2013

Summary: There were 22 participants representing nine Western Pacific countries (Fiji, New Caledonia, Vietnam, Vanuatu, Mongolia, Laos, Cambodia, Papua New Guinea, and Philippines) and six instructors from various agencies such as CDC, CSTE, WHO CC and the Maldives Ministry of Health. Throughout the course, participants engaged in discussions around issues within their countries and how to solve the problems. During the last day participants presented their data to their peers and received feedback on the presentations and their individual presentation skills.

An end of course evaluation was conducted for each session. Feedback indicated that all participants agreed the materials presented will help them perform their jobs better and they appreciated the interaction with the facilitators and other participants. They felt the content covered was appropriate for the class and overall the course was worth the time they spent. The information shared during the training course will help countries improve data collection, management, and analysis and contributes to the overall goal of building capacity to establish strong influenza surveillance systems throughout the various regions.



Group photo from the Data Management and Epidemiologic Analysis for Influenza Data Course in Phnom Penh, Cambodia.

MONITORING & EVALUATION TOOLS

Monitoring & Evaluation Tools

Under the cooperative agreements made between the U.S. Centers for Disease Control and Prevention's (CDC) Influenza Division and its partner countries, the Division supports the monitoring and evaluation (M&E) of activities associated with international Influenza program implementation. The purpose of M&E in this context is to:

- Demonstrate accountability for the resources used by programs to key stakeholders; CDC and the countries which receive funding.
- Document each country's capability and capacity for influenza surveillance, diagnostics and pandemic preparedness in order to:
 - » Identify program strengths and opportunities for improvement.
 - » Provide a mechanism to measure progress toward defined objectives and thereby demonstrate meaningful improvement in public health function over time.
- Guide ongoing investment in influenza surveillance, diagnostics and pandemic preparedness globally.
- Inform strategic and programmatic planning for countries and target technical assistance provided by CDC.
- Standardize and systematize practices.
- Identify good practices that can be shared between countries.

The Influenza Division has developed three tools which are described below. Countries participate voluntarily in these assessments.

National Inventory of Core Capabilities for Pandemic Influenza Preparedness and Response (National Inventory)

Purpose: The National Inventory of Core Capabilities for Pandemic Influenza Preparedness and Response (National Inventory) is a comprehensive tool by which countries can systematically and quantitatively measure their capability and capacity to respond to an influenza pandemic.



Structure and Content: The National Inventory covers 12 distinct domains, defined as 'core capabilities' and each capability is assigned a composite score based on the quality, coverage and timeliness of four related indicators. For example, the core capability of 'Infection Control' is measured by determining performance in the following indicators (i) standards of infection control by level of health-care system (ii) integration of infection control training for staff (iii) availability of logistical resources for infection control and (iv) level of institutionalization of infection control efforts. The end-points for the core capabilities are not identical which allows for variation in public health priorities across countries with differing resource constraints. Countries repeat the assessment every two years to monitor changes in pandemic preparedness. For a copy of the National Inventory, please visit www.cdc.gov/flu/international/tools.htm.

Implementation: In 2008, 40 countries completed baseline self-assessments, facilitated by CDC staff. A further 12 countries participated in late 2009 and early 2010 to establish baselines. By the end of 2010, 36 of the initial 40 countries completed a repeat assessment to monitor changes in their level of pandemic

preparedness since 2008. In 2012, 33 out of the 36 countries were able to complete a third assessment to continue to track changes in their level of pandemic preparedness. 10 of the 12 countries that established 2010 baselines also completed their first re-assessment in 2012.

Outcomes: All of the countries improved their scores between 2008 and 2012 indicating an overall improvement in pandemic preparedness for each country over the period.

- The biggest improvements in pandemic preparedness capabilities were made between 2008 and 2010 whereas between 2010 and 2012 four capabilities improved, six remained the same and two decreased although they remained higher than the 2008 level (Figure 1).
- Among the 12 core capabilities for pandemic preparedness, countries scored 'routine influenza surveillance' capability highest in 2008, 2010, and 2012, and scored 'health sector pandemic response' lowest in 2008, 2010, and 2012.

Further to this:

- The assessments in 2008 helped countries to identify and target areas for preparedness improvement which in turn strengthened their ability to respond to the 2009 H1N1 pandemic.
- At the same time, the 2009 outbreak offered an enormous opportunity for countries to test their pandemic response with the outcomes captured when they repeated the tool in 2010.
- The assessments in 2012 helped countries identify whether improvements in 2010 were sustained.
- Identifying areas for Influenza improvement is also enhancing capacity-building for other infectious diseases as well as encouraging compliance with International Health Regulations 2005 (IHR).
- Using the tool to document progress is helping countries to collaborate with different partners & advocate for continued support.

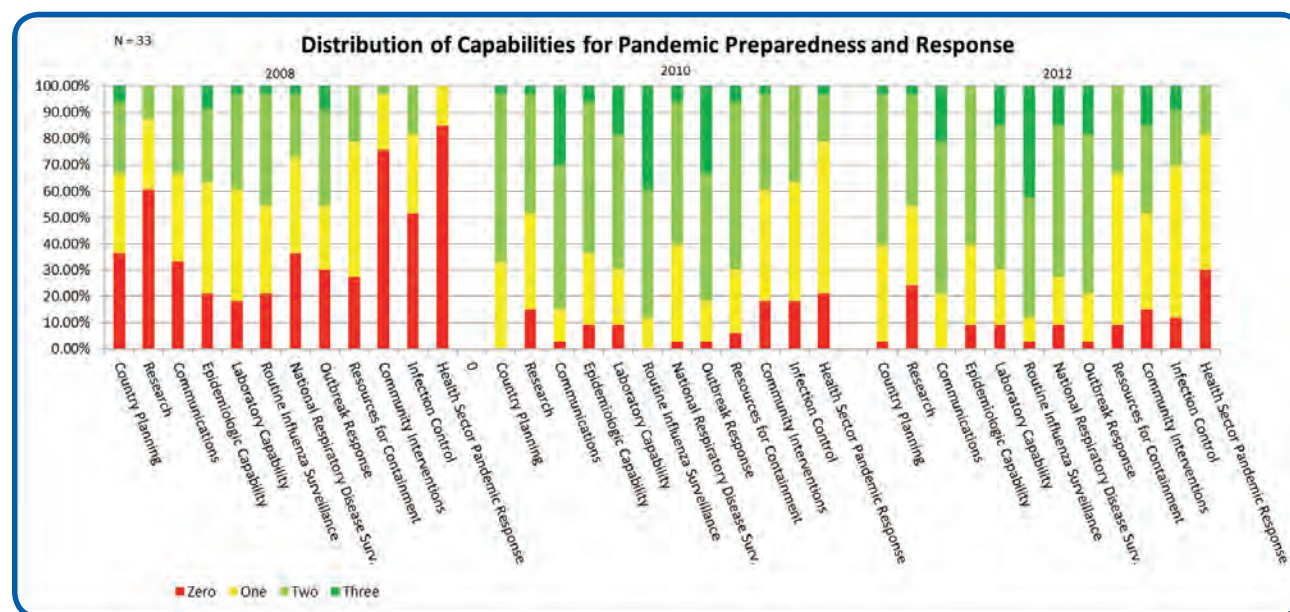


Figure 1. Change in Pandemic Preparedness Core Capability Scores between 2008 and 2012.

International Influenza Laboratory Capacity Review Tool

Purpose: The goal of the International Influenza Laboratory Capacity Review Tool (Lab Tool) is to support good laboratory management and practice. It is designed for assessing the capability and capacity of an influenza laboratory to perform high quality influenza diagnostics.



Structure and Content: The Lab Tool is a series of questions divided into nine sections for assessing laboratories across a wide variety of influenza laboratory functions including, general laboratory functions, virology and molecular biology techniques, availability and maintenance of equipment, specimen handling, collection and reporting, staff training, laboratory safety and methods for quality assurance and quality control. The results from these sections form the basis of laboratory capacity summary reports and recommendations for countries. The structure and content of the tool was updated in 2011 based on a first round of assessments and comments gathered from assessors. For a copy of the tool, please visit www.cdc.gov/flu/international/tools.htm.

Implementation: Between September 2009 and September 2013, 42 national laboratories in 39 countries completed laboratory assessments, facilitated by staff from CDC and the Association of Public Health Laboratories (APHL). Thirteen (13) of the 42 countries underwent repeat assessments in the same period.

Outcomes: The tool has highlighted overall laboratory strengths while recommendations are provided by reviewers where opportunities for improvement present themselves. For example, a training needs assessment based on the first 26 laboratories reviewed, identified six country laboratories in the Africa region that do not perform virus isolation; all expressed interest and readiness to receive technical assistance in these methods. Likewise, across all regions, many countries received specific recommendations for improving the biosafety of their laboratories. As a consequence, APHL, CDC, and the National Institute for Communicable Diseases in South Africa delivered a course on “Improving Influenza Laboratory Management Practices”, in Johannesburg in 2011. In 2012, a second course was delivered in Bangkok with the support of CDC, APHL, and The National Institute of Health in Thailand and the WHO Collaboration Center in Melbourne and China.

Analytic Framework: During FY 2011, CDC and APHL further developed the Lab Tool by adding a quantitative component to the analysis of data collected. A quantitative analysis can be presented visually allowing quick identification of the status of an influenza laboratory’s capacity. It can also provide a standardized approach to tracking changes in laboratory capacity over time. Approximately 150 questions have been selected for analyzing laboratory capacity across eight categories which have been identified as critical to the functioning of a national influenza laboratory. The eight categories for analysis include: National Influenza Center (NIC) Criteria, Laboratory Management, Biosafety, Quality Assurance and Quality Control, Molecular Biology, Virology, Specimen Handling, Collection, and Reporting and Equipment. Each selected question has been assigned one point. The points are aggregated by category and converted to a percentage performance measure. Beginning in 2012, the quantitative analysis will be included in summary reports. Data collected in 2009 through to 2011 was analyzed using the new analytic framework. Figure 2 shows aggregate scores for laboratory capacities among all participating countries from 2009 to 2011.

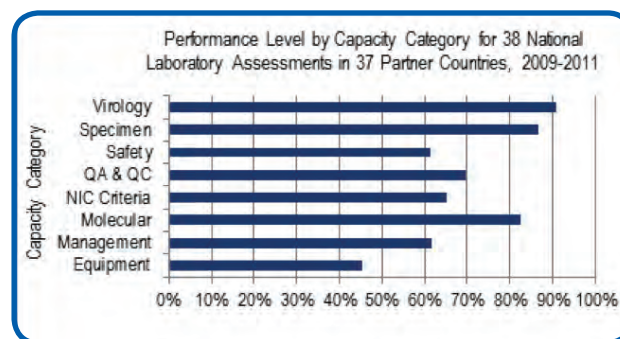


Figure 2. Performance level of laboratory capacities.

International Influenza Surveillance Assessment Tool

Purpose: The International Influenza Surveillance Assessment Tool is designed to standardize and systematize the review of national surveillance systems. The tool helps CDC and partners to clarify the objectives and structure of their surveillance systems, such that recommendations and technical assistance can be targeted to meet system goals such as, conducting data quality checks and establishing built-in laboratory and epidemiologic data integration.



Structure and Content: The tool consists of six checklists covering national, central and sentinel site levels and covers all ILI and SARI related surveillance. For example, it includes a review of data management, analysis and reporting procedures. The tool uses a standard format for creating surveillance capacity summary reports where recommendations for countries can be provided. For a copy of the tool, please visit www.cdc.gov/flu/international/tools.htm.

Implementation: Between March and September 2010, the surveillance tool was piloted in three countries by CDC staff, with an additional seven reviews completed later that year. In FY 2011, a further eight countries underwent surveillance reviews. That year, CDC's Influenza Division also entered into a cooperative agreement with the Council of State and Territorial Epidemiologists (CSTE) who have provided epidemiologists to assist with conducting reviews in partner countries. In FY 2012, 20 countries participated in a review of their surveillance system.

Outcomes: The tool has served to highlight overall surveillance strengths and challenges with recommendations for improvement in the 38 countries reviewed to date. Recommendations have included: weekly and quarterly analysis of risk factor data, dissemination of data to stakeholders, and better coordination between national staff and sites.



INFLUENZA RESEARCH

Influenza Research

BANGLADESH

Hospital Based Human Influenza Surveillance

icddr,b collaborates with the Institute of Epidemiology, Disease Control and Research (IEDCR) of Government of Bangladesh for the implementation of this influenza surveillance in 12 tertiary care hospitals from all six administrative divisions of Bangladesh.

Study Aims and Objectives:

- To identify individuals and clusters of people with life threatening infections or severe respiratory disease caused by influenza virus and other respiratory pathogens.
- To characterize the diversity of strains of influenza in circulation in Bangladesh.

Approach: Sentinel influenza surveillance in 12 hospitals. In each surveillance hospital, physicians systematically identified patients aged ≥ 5 years with severe acute respiratory illness (SARI), or patients aged < 5 years with severe pneumonia (SP), or presenting as outpatients with influenza-like illness (ILI). Staff collect demographics and clinical history data and respiratory specimens for real time reverse transcription polymerase chain reaction (rRT-PCR) influenza testing.

Timeline: Surveillance was initiated in May 2007 and is ongoing.

Progress and Findings: During May 2007–August 2013 we collected 19,964 specimens. Among them, 2,912 (14.6%) tested positive for influenza virus. Among the influenza positive cases, infection due to influenza A and B were 1,984 (68%) and 924 (32%) respectively. Among the influenza A positive cases 137 (7%), 928 (47%) and 922 (46%) were due to A/H1, A/H3 and A(H1N1)pdm09 respectively. The highest flu positivity was observed among those of 5–14 years of age. Before the 2009 pandemic, we observed distinct influenza peaks from May to September. But after the pandemic, there is no distinct seasonality observed.

During October 2012–August 2013 we collected 3,115 specimens. Among them 552 (17.7%) tested positive for influenza. Among the influenza positives, most were infected with influenza A (478/87%). Among the influenza A positives highest frequency was due to A/H3 (306/64%). Among the collected specimens most were from ILI cases (1,333 /43%). The highest influenza positivity was among SARI cases (257/24%) and the lowest among SP cases (42/6%).

Conclusion: Influenza affects all age groups in Bangladesh, but most frequently those between 5 to 14 years old. Both influenza A and B are circulating in Bangladesh. Among the influenza A type, most prevalent circulating sub-type is A(H3). No human cases of H5N1 infection have been detected through this surveillance. Influenza seasonality may have altered after the 2009 pandemic.

Related Published Paper: Zaman RU, Alamgir ASM, Rahman M, Azziz-Baumgartner E, Gurley ES, et al. (2009) Influenza in Outpatient ILI Case-Patients in National Hospital-Based Surveillance, Bangladesh, 2007–2008. PLoS ONE 4(12): e8452. doi:10.1371/journal.pone.0008452.

Dispensing Practices and Impact of Educational Intervention for Acute Respiratory Illness among Drug Sellers, A Pilot Study in Bangladesh

Pharmacies are the primary source of health advice and medicines in Bangladesh but very little information is available regarding availability of oseltamivir as well as medication purchase patterns and drug dispensing practices in pharmacies for respiratory illness. Thus, this pilot study was undertaken to collect this data as well as to assess the adoption of treatment guidelines for acute respiratory illness by pharmacies in Dhaka city.

Study Aims and Objectives:

- To describe medications provided for acute respiratory illness (ARI) by drug sellers in pharmacies across Dhaka, Bangladesh.
- To describe factors driving patients' for health care seeking from pharmacy.
- To assess the availability of oseltamivir in pharmacies.
- To develop and assess the adherence and sustainability of an educational intervention for the empirical treatment of acute respiratory illness through pharmacies in Dhaka, Bangladesh.

Approach: icddr,b in collaboration with the government of Bangladesh and funding from CDC is conducting this cross sectional and interventional pilot study among 100 randomly selected pharmacies in Dhaka city. Field staffs acting as surrogate relatives of patients suffering from ARI with different clinical scenarios were deployed to each of the selected pharmacies to assess dispensing practices. Availability of oseltamivir at each selected pharmacy was also surveyed. Real-life pharmacy customers were interviewed to explore health care seeking drivers. After assessment of dispensing practices, a training manual for an educational intervention to improve the knowledge of the drug sellers for the management of ARI was developed with government and medical association partners. Pharmacists were trained and follow-up assessments will be performed to assess the adherence of the drug sellers to the training material and the sustainability of the educational intervention.

Timeline: May 2012–December 2013.

Progress and Findings: Among 100 selected pharmacies; none had oseltamivir available for sale during the survey. Drug sellers dispensed drugs for the patient in 64% of the field staff visits as surrogate relatives, recommended that the patient be seen by a physician in 31% of the visits and refused to give drugs without the patient present in 6% of the cases. Among all the dispensed drugs, acetaminophen was the most frequently dispensed drug (40%), followed by antibiotics (37%), antihistamines (30%), and bronchodilators (17%). According to WHO management guidelines for ARI, 70% of the dispensed drugs were inappropriate but not harmful, 23% were appropriate, 5% could not be judged appropriate or inappropriate (herbal medicine) and 2% were inappropriate and potentially harmful.

Conclusion: Drug sellers were unfamiliar with and did not stock oseltamivir. Their dispensing practices for ARI were often not in accordance with ARI management guidelines.

Related Published Papers: In Progress.

Surveillance for Human Infections with Avian Influenza A Viruses among Live Bird Market Workers and Their Household Members in Dhaka City Area, Bangladesh

Live bird market (LBM) workers in Bangladesh are at risk of avian influenza A virus (AIV) infection due to ongoing circulation of these viruses among market poultry and their occupational exposure. LBM workers handle, slaughter and process poultry and offal, mostly without personal protective equipment. We initiated active influenza surveillance among a closed cohort of LBM workers and their household members to identify human cases of AIV infection, to detect circulating AIVs and to assess serological evidence of AIV infections.

Study Aims and Objectives:

- To identify live bird market workers and their household members infected with avian influenza A viruses.
- To characterize avian influenza A virus strains causing human infections and to compare them to strains currently circulating among poultry in live bird markets.
- To assess the serological evidence of avian influenza infection among live bird market workers and their household members.

Approach: Surveillance was implemented in 16 LBMs with ongoing avian influenza surveillance of poultry since 2009. Among LBMs, four are wholesale (operating 24 hours/day) and 12 are retail. We enrolled 750 workers and 1,830 household members proportionately from each market through random sampling, based on the total number of LBM workers. Enrolled workers were visited twice a week at the market to determine if they or their household members experienced illness compatible with AIV infection since the last visit. A possible case of AIV infection was defined as: fever (subjective, measured or reported) and/or any respiratory signs or symptoms or conjunctivitis. For all possible cases, nasopharyngeal and oropharyngeal and conjunctival (if conjunctivitis was present) swabs were collected in viral transport media. The samples were tested by real-time RT-PCR (rRT-PCR) for influenza viral RNA and further subtyped if positive for influenza A (H1N1pdm09, H3, H5, H9). Acute (<7 days since illness onset) and convalescent serum (>21 days after acute serum collection) were collected from laboratory-confirmed influenza A participants and tested for influenza H5N1 and H1N1pdm virus specific antibodies by microneutralization and hemagglutination inhibition assays.

Timeline: This project was initiated in February 2012 and is ongoing.

Progress and Findings: From February 2012 to September 2013, a total of 1,183 poultry workers or their household members experienced illness compatible with AIV infection. Of 1,183 swab samples tested, 107 (9%) tested positive for influenza A and 25 (2%) tested positive for influenza B by rRT-PCR. Of 107 samples positive for influenza A, 33 (30%) were subtyped as H1N1pdm09, 23 (21.5%) as H3, 15 (14 %) as H9N2, 10 (9%) as H5N1, 19 (18%) were unsubtypeable, and 4 (4%) were inconclusive. No worker with detectable H5 viral RNA developed severe illness.

Thirty paired (acute and convalescent) blood samples have been collected from the influenza A+ cases for serological testing by hemagglutination inhibition and microneutralization assays. Among available paired serum testing results from 15 participants, including two with H5 viral RNA detected in respiratory specimens, none demonstrated seroconversion to H5N1, four LBM workers had evidence of H5N1-specific antibodies suggesting previous infection, and three had evidence of seroconversion to H1N1pdm09 virus.

We have shared the positive H5N1 results with the Government of Bangladesh and CDC. All avian flu positive samples were shipped to CDC for further characterization.

Conclusion: Among symptomatic poultry workers in Bangladesh LBMs, we detected seasonal influenza A and B viruses, and viral RNA from AIVs, including H5 and H9. Use of serological testing on paired serum can help to assess acute infection versus exposure to AIVs and inform the interpretation of detection of AIV RNA in LBM poultry workers exposed to AIVs. Surveillance in LBMs is useful for detecting and monitoring persons with occupational exposure to AIVs and increasing understanding of transmission of AIVs at the animal-human interface.

Incidence of Influenza-associated Mortality in Bangladesh, 2010–2012

Influenza-associated mortality estimates can help assess the burden of disease, identify high risk groups and assist policy makers determine if an annual influenza immunization should be a prioritized public health intervention.

Study Aims and Objectives:

- To estimate the incidence of influenza-associated mortality in Bangladesh during 2010–2012.
- To describe health seeking behavior for severe acute respiratory illness (SARI).

Approach: During July to December 2012, we randomly selected 22 unions, the smallest administrative units in Bangladesh, from the catchment areas of 11 tertiary hospitals and collected mortality data in the unions. We employed a social networking approach to identify people who died in these unions in May 2010 to April 2012. We interviewed the household members, who had taken care of the decedents during their illness and asked about decedent's demographics, medical history, symptoms, and health seeking 14 days before death. For children aged <5 years, we classified a death as being associated with acute respiratory illness (ARI) if caregivers reported that decedents developed sudden onset fever and cough or difficulty breathing within 14 days of death. For people aged ≥5 years, we classified a death as being associated with ARI if caregivers reported that decedents developed sudden onset fever and cough or sore throat within 14 days of death. As part of the ongoing national hospital based surveillance in 11 hospitals, physicians routinely collected throat and nasopharyngeal swabs from case-patients. We only considered swabs from children <5 years who presented with fever and cough or difficulty breathing with one danger sign; and from patients presented with fever and cough or sore throat if aged ≥5 years. We tested the samples for influenza and its subtypes. To calculate the incidence of influenza-associated mortality, we multiplied the monthly proportion of samples from the hospitals that were laboratory-confirmed for influenza in May 2010 to April 2012 by the number of decedents in the community with a history of sudden onset of ARI 14 days prior to death, and divided this numerator by the age-specific 2011 census population of the unions.

Timeline: May 2012–February 2013.

Progress and Findings: We identified 10,043 deaths; 1,191 (12%) were associated with ARI. Of those who died with ARI, 150 (13%) were children <5 years, 30 (2%) were aged 5–19 years, 211 (18%) were aged 20–59 years and 800 (67%) were aged ≥60 years; 738 (62%) were males. A total of 360 (13%) patients were laboratory-confirmed for influenza; the proportions of samples that were confirmed for influenza among people aged ≥5 years were 19% and 4% among children <5 years. The annual cumulative incidence of influenza-associated mortality was 11.1 (95% CI 10.4–11.7) per 100,000 population for all ages. The annual incidence of influenza-associated mortality among children <5 years was 3.7 (95% CI 3.1–4.3); for people

aged 5–19 years it was 1.3 (95% CI 0.8–1.8); for 20–59 years it was 5.3 (95% CI 4.6–6.1) and for persons aged ≥60 years the incidence was 108.5 (95% CI 101.1–116.0) per 100,000 persons. After extrapolating the incidence rate to the 2011 census population of Bangladesh, the estimated deaths associated with influenza were 15,989 (95% CI 14,981–16,853) per year among all ages; it was 12,503 (95% CI 11,650–13,367) among ≥60 years annually.

Conclusion: The highest burden of influenza mortality in Bangladesh appears to be among persons aged ≥60 years. Vaccination among elderly persons may reduce the burden of influenza in the country.

Related Published Papers: In Progress.

Identifying Zoonotic Transmission of Swine-borne Diseases in Bangladesh

Zoonotic infections from swine pose a worldwide public health concern because of their potential to infect humans and lead to pandemics. In addition, pigs are potential pathogen reservoirs and amplifiers for transmission. Through this study, we would like to understand zoonotic transmission of influenza and rotavirus viruses in swine and swine raisers, as well as to create a platform to conduct surveillance on swine-borne zoonoses in Bangladesh.

Study Aims and Objectives:

- To establish active surveillance to identify and characterize influenza A viruses in pigs and rotavirus strains circulating in piglets
- To detect pathogens of zoonotic origin in pig raisers (influenza A viruses and rotavirus)
- To create a platform to explore pathogen transmission between pigs and people.

Approach: To understand zoonotic transmission of influenza A viruses, icddr,b in collaboration with the government of Bangladesh and funding from CDC has been conducting swine surveillance in two pig raising communities and one pig slaughterhouse. We have been collected nasal swab samples from the pigs regardless of their health status in two pig raising communities in two sub-districts of Rajshahi (Bangladesh) to identify current subtypes and strains of influenza viruses in circulation. We are also conducting surveillance in a pig slaughterhouse in Gazipur district, where nomadic, and backyard raised pigs are brought from all over the country. Simultaneously, we are collecting nasal and throat swabs of those showing influenza-like illness (ILI) symptoms among the pig raiser household members in the two pig raising communities for detecting circulating influenza viruses. The samples are tested by real-time RT-PCR (rRT-PCR) for influenza viral RNA and further subtyped if positive for influenza A. The viral genomes will be sequenced to characterize the diversity of the viruses identified in humans and in pigs. We are also investigating the prevalence of antibodies against influenza A viruses in pigs and the pig raisers and compare with a non-pig raising population. To identify circulating rotavirus in the pig population, we have been sampling piglets (under two months of age) with diarrhea. Rotavirus will be identified by real time RT-PCR and the viral genome for further characterization by sequencing. Additionally, we have been conducted surveillance to identify children (less than five years) in the pig raising communities having diarrhea and look for rotavirus in their stool samples. Rotaviruses will be detected and sub-typed by rRT-PCR. Pig rotavirus strains will be compared with human strains identified in the pig raising community as well as through a hospital based surveillance in Bangladesh to detect possible interspecies transmission.

Timeline: Initiated in June 2013 and ongoing.

Progress and Findings: So far, we have collected 220 pig nasal swab samples, of which 160 have been tested and found 11 samples positive for influenza A (H3). We have also collected nasal and throat swabs samples from 27 ILI patients and among them we have tested six samples and found one sample positive for influenza A (H3). We have also collected 200 serum samples from the primary pig caregivers and abattoir workers but these have not yet been tested. We have collected three stool samples from the under five children with diarrhea and these sample are under laboratory processing. We have also collected two fecal samples from the piglet with diarrhea and the samples are under laboratory processing. Sample collection, processing and testing are ongoing.

Incidence of Influenza-associated Respiratory Illness among Pregnant Women in Bangladesh

Physiological changes during pregnancy puts pregnant women at increased risk for severe influenza infections and associated complications. Several studies have documented severe influenza infections in pregnant women including excess maternal mortality and loss of pregnancy. To our knowledge, there are no data describing burden of influenza among pregnant women and limited data on health impact of influenza on pregnant women during pregnancy and on infant birth weight and gestational age in Bangladesh.

Study Aims and Objectives:

- To assess the burden of seasonal influenza infection in pregnant women in Bangladesh.
- To assess the health impact of maternal influenza illness with pregnancy related complications and growth of young infants including neonates in Bangladesh.

Approach: We have been conducting this study in eight upazillas (sub-district) in Bangladesh. We identified pregnant women from the community with the help of female welfare assistants (FWA) who identify pregnant women during their door to door visit in the villages. Subsequently icddr,b field staff visited the pregnant women's household and enrolled the women in the study. After enrolment, we followed up each participant once a week over phone or through household visit. Whenever any participant mentioned having influenza-like illness (ILI) during follow-up contact, the trained field staff collected nasal swab from that participant. The swab specimen was sent to icddr,b virology lab for influenza testing. When any participant informed about her delivery, the field staff visited the household within three days of delivery to collect the weight of newborn, to enroll the newborn in this study and then started to follow-up of the newborn until six months of age for episodes of ILI.

Timeline: May 2013–September 2013.

Progress and Findings: We completed identification and enrollment of study participants during May–June 2013. We enrolled a total of 1,912 pregnant women in this study. Of those, we have been communicating with 1,811 participants once a week to identify any episode of ILI from July 2013 to second week of September 2013. We had to drop 101 participants, primarily due to migration to areas outside of the study site and a few refused to be contacted. Currently there are 1,210 pregnant women and 610 young infants under follow-up. We collected nasal specimen from 81 pregnant women who reported to have ILI and of 81 specimens, five (6%) had detectable influenza virus RNA. We have not yet identified any ILI episode among neonates.

Conclusion: This study data would describe the burden and suggest if maternal influenza infection has health impact on pregnant women and on infants in low-income settings such as Bangladesh. Moreover, the data may also help in targeting influenza vaccines for pregnant women in Bangladesh to reduce influenza burden and associated complications during the pregnancy period as well as indirectly the very young infants.

Characterization of Children Hospitalized with Respiratory Illness in Bangladesh

Limited data is currently available on the burden of influenza and other respiratory illness in Bangladesh. This study aims to characterize the burden of viral respiratory illness, particularly for illness requiring hospitalization, as well as to identify potential risk factors for severe illness in children under five years of age.

Study Aims and Objectives:

Aim

- Estimate the burden of childhood viral respiratory illness in Bangladesh.

Objectives

- Determine the incidence of medically attended influenza and other respiratory viral illness in children aged <5 in Bangladesh.
- Understand the seasonality of childhood respiratory viral illness in Bangladesh.
- Identify the risk factors for severe influenza and other respiratory viral illness in children.
- Explore the causal association between respiratory viral infection and symptomatic illness.
- Determine the association between micro nutritional deficiencies and severe influenza and other respiratory viral infections in children.

Approach: Hospital-based surveillance in combination with health utilization survey.

We have ongoing surveillance in four hospitals which will act as the main platform for the study. Twice every month research physicians enroll children admitted in the hospitals residing in the primary catchment areas of the hospital. Children age <5 years with any of the following two and/or more symptoms: fever, cough, difficulty breathing consistent with pneumonia or respiratory distress syndrome are eligible for the study. Investigators collect information on existing chronic medical condition, symptoms, treatment prescribed, and outcome of each hospitalized children. We collect throat and nasal swab samples from these children. All the respiratory samples collected are being tested for influenza A and B, RSV, metapneumovirus, adenovirus, parainfluenza viruses and rhinovirus by real-time RT-PCR. Findings will be compared 1:1 to children of the same age with influenza-like illness who visit the outpatient department but are not admitted.

In addition we have been collecting respiratory specimens from asymptomatic hospitalized children from January 2012, which will help us better understand the causal association between influenza infection and respiratory illness. We have also started collecting blood samples from children with and without respiratory symptoms for micronutrient testing which includes Vitamin A, D and Zinc from January 2013 which will help us better understand the role of these micronutrient on influenza infection.

Timeline: October 2010–September 2014.

Progress and Findings: We have completed four years of data collection from children presenting with acute respiratory symptoms at the outpatient and inpatient department of four sentinel surveillance hospitals in Bangladesh where the study is being conducted. Between October 2010 and January 2013 we have collected data and respiratory samples from 400 hospitalized children and 1,400 children attending the outpatient department with acute respiratory symptoms. The data collection will continue until September 2014.

Based on the analysis of three years of data we estimated the incidence of ambulatory influenza illness per 100 children per year at 13.3 (95% CI 10–20) in 2011 and 11.3 (95% CI 9–19) in 2012. Similarly, incidence of hospitalized influenza illness per 1,000 children per year was 0.5 (95% CI 0.09–1.2) in 2011 and 0.3 (95% CI 2–4.3) in 2012. In addition incidence of hospitalized RSV illness per 1,000 children per year was 3.58 in 2011 and 3.16 in 2012. Similarly the incidence was 1.46 and 0.73 for parainfluenza viruses and 1.28 and 0.27 for human metapneumovirus viruses. We will conduct the risk factor analysis at the end of the study period in 2014.

A monthly report is disseminated to co-investigators and collaborators within icddr,b, the Government of Bangladesh and CDC.

Conclusion: The surveillance has been providing crucial information in terms of frequently occurring respiratory viral infection in children, a group who are at higher risk of morbidity and mortality associated with influenza and other respiratory viral infections. In addition, the data may also help in targeting influenza vaccines for children at risk in Bangladesh.

DOMINICAN REPUBLIC

Needle-Free Cutaneous Jet Injection of Reduced-Dose Influenza Vaccine in ≥ 6 to < 24 -Month Old Children in the Dominican Republic

Most developing countries cannot afford influenza vaccines (INF) to protect their populations. One potential strategy to lower cost is to reduce antigen mass and deliver into intradermal (ID) or intramuscular (IM) tissues. To that end, a controlled, randomized study in the Dominican Republic used jet injection, avoiding the risks and drawbacks of conventional needle-syringe (NS) to determine whether immune responses suggesting protection can be induced safely in young children by reduced 0.1 mL ID doses of INF administered ID with an investigational, disposable-syringe jet injector (DSJI), or IM by conventional NS, compared to standard 0.25 mL IM doses by NS.

Study Aims and Objectives:

- Assess non-inferiority for seroconversion (SC), seroprotection (SP), geometric mean titer (GMT) or GMT foldrise (GMTFR) of two 0.1 mL INF doses ID by investigational spacer on a Biojector® 2000 DSJI, or by two 0.1 mL doses IM by NS, compared to two full doses IM of 0.25 mL in controls.
- Determine the tolerability of local and systemic reactions of INF delivered ID by DSJI, compared to full-dose IM.

Approach: A total of 450 healthy participants ≥ 6 and < 24 months of age were recruited at the national children's hospital in Santo Domingo. Consented eligibles received two doses one month apart of trivalent, inactivated Vaxigrip® INF (Sanofi-Pasteur) in randomly-allocated investigational study arms ID-JI-0.1 (n=150) or IM-NS-0.1 (n=150), or in control arm IM-NS-0.25 (n=150). Investigators were blinded to allocation; unblinded nurses vaccinated in a closed room without parents present.

Timeline: Phase I patients first enrolled in October 2006. Data collection from final Phase II subjects occurred in November 2009. After serologic assays and data cleaning, the DSMB unblinded the investigators in quarter two of 2013.

Progress and Findings: Unblinded analyses of the Total Vaccinated Cohort found systemic reactions generally mild and similar among all study arms, while local reactions – although mostly mild – were more frequent in the ID-JI-0.1 arm. Moderate pain occurred on either injection in 3% (5/150) of ID-JI-0.1 subjects and 1% (1/150) of IM-NS-0.25 controls. Severe pain occurred in 2% (3/150) and 1% (2/150), respectively.

The immunologic endpoint of non-inferiority was not achieved for SC, SP, GMT, or GMTFR against H1N1, H3N2, or B vaccine antigen type by either the ID-JI-0.1 or IM-NS-0.1 reduced-dose study arms, compared to IM-NS-0.25 controls. All immune measures were lowest for ID-JI-0.1, intermediate for IM-NS-0.1, and highest for IM-NS-0.25. For example, post-dose-1-and/or-2 SC rates for H1N1 were 57.1%, 67.1%, and 73.6%, respectively. For H3N2, SC was 44.6%, 62.4%, and 79.7%, and for type B, 64.6%, 72.5%, and 87.8%, respectively.

Conclusion: Causes for inferior immune responses of jet-injected cutaneous delivery are hypothesized and being analyzed, including “wet” injections (noted in 26 [17%] of 150 ID-JI-0.1 subjects), which may result from variable operator technique, jet-cartridge bubbles, and short plunger stroke for 0.1 ml. The safety profile was tolerable and not a contraindication for this technique.

EL SALVADOR

Characterization of Influenza Co-infection, Dengue Fever and Other Respiratory Viruses in Patients Hospitalized in El Salvador

Prospective cohort.

Study Aims and Objectives:

- Assess the utility of the dengue and severe acute respiratory infection case-definitions during the rainy season in El Salvador.

Approach: We describe the influenza laboratory confirmed cases among dengue case-patients admitted in four hospitals, in El Salvador, during 2012 rainy season.

Timeline: 2012–2013.

Progress and Findings: We found that dengue case-patients were more likely to test positive for influenza (19% CI95% 12–26%) than severe acute respiratory case-patients (10%, CI95% 6–14%). The prevalence of influenza-dengue co-infection was 1%.

Conclusion: Health officials should explore the diagnosis of influenza and the potential value of empirically treating dengue and/or SARI case-patients with oseltamivir during influenza season, especially in those cases with respiratory signs or severe disease.

GHANA

Health Facility–based Surveillance for Influenza and Other Respiratory Viruses in Residents of Shai–Osudoku and Ningo–Prampram Districts, Ghana

After the 2009 influenza pandemic, data on acute respiratory infections started being gathered in Ghana from nascent hospital-based surveillance. Knowledge of the epidemiology of influenza and other respiratory virus infections will assist in producing reliable estimates of disease burden.

We will document the occurrence of influenza-like illnesses (ILI) and hospitalized severe acute respiratory infections (SARI), and the proportion attributable to influenza infection. These data will be combined with health utilization data to estimate the burden of influenza in the Shai–Osudoku and Ningo–Prampram Districts (SONPD).

Study Aims and Objectives:

Aim

- To describe the epidemiology, etiology and outcome of ILI and SARI caused by influenza and other respiratory pathogens.

Objectives:

- Establish enhanced health facility-based surveillance for outpatient ILI cases, hospitalized SARI cases, and deaths caused by influenza and other respiratory pathogens in SONPD.
- Measure the incidence, prevalence, demographic characteristics (including age, sex, ethnicity, and socioeconomic status), clinical spectrum and outcomes for outpatient ILI cases, hospitalized SARI cases, and deaths due to influenza and other respiratory pathogens.
- Identify etiologies of ILI cases, SARI cases, including deaths attributable to influenza and other respiratory pathogens using routine methods (Polymerase Chain Reaction and culture).
- Determine risk factors for severe influenza.
- Evaluate case definitions for influenza and other respiratory pathogens in the SONPD.

Approach: We intend to estimate the incidence of influenza infection in the SONPD via health facility-based prospective surveillance.

Timeline: This cooperative agreement between CDC and the Noguchi Memorial Institute for Medical Research was awarded October 2012 and continues being funded. The first sample for this study was collected February 2013.

Progress and Findings: The study is effective and has been successful thus far. Participants are recruited from nine sites; seven in SONPD, one in Lower Manya District and one in North Tongu District with the total number of outpatient consultations also being collected from additional eight public health facilities in SONPD. Data and sample collection are ongoing, progressively being analyzed and yet to be published.

Conclusion: The results of this study will assist the Ministry of Health/Ghana Health Service and the global scientific community to generate effective policies based on reliable estimates of the burden of influenza and other respiratory infections. Furthermore, it will also be an essential step in establishing a strong platform for additional studies, which will help to better understand the epidemiology of influenza and other respiratory viruses not only in Ghana but in the African region.

Related Published Papers: Pending.

INDIA

Addressing Emerging Infectious Diseases in the Republic of India: Influenza Disease

This HHS/CDC cooperative agreement was established for five years (9/2008–9/2013) to estimate the burden of disease related to influenza virus infection in India, through a population-based longitudinal study at three sites with demographic surveillance systems.

Study Aims and Objectives:

- Estimate the incidence of laboratory-confirmed influenza among persons hospitalized with acute respiratory illnesses and acute exacerbations of chronic medical conditions.
- Determine risk factors for severe disease due to influenza, including underlying chronic conditions, demographics, smoking, and socio-economic status.
- Estimate the annual mortality rate due to severe respiratory disease and influenza in the population.

Approach: Persons living in the DSS areas in one of the two study areas (Ballabgarh and Vadu) that seek inpatient medical attention and meet the study enrollment criteria are enrolled, and clinical and epidemiologic information and respiratory specimens are collected from all consenting persons. Each site is also conducting a community-based survey, to gather health care utilization data as well as household risk factors and socioeconomic status. Additionally, outpatient screening and enrollment was done to estimate the burden of non-hospitalized medically attended influenza disease.

Timeline: April 2009–September 2013.

Progress and Findings:

The proportion of patients with laboratory-confirmed influenza was higher at Vadu than Ballabgarh during all study years (21% vs. 5%, $p < 0.05$ in 2010; 18% vs. 5%, $p < 0.05$ in 2011; 23% vs. 5%, $p < 0.05$ in 2012).

- Annual acute medical illness hospitalization rates were similar at both sites (Vadu: 101.3 to 224.7 per 10,000; Ballabgarh 86.0 to 126.2 per 10,000), whereas annual influenza-associated hospitalization rates were 5–9 fold higher in Vadu (20.3–51.6 per 10,000) compared to Ballabgarh (4.4–6.3 per 10,000).

Conclusion:

- >5,000 hospitalizations recorded with influenza positivity ranges from 7–21%.
- Rates of hospitalization vary significantly and almost 1/5 hospitalizations due to influenza occur during peak monsoon season.
- Incidence of Influenza varied between sites (6–44/10,000).
- Annualized incidence rate in Vadu comparable to rates in US.
- Age specific differences from site to site.

Related Published Papers:

Gupta V, Dawood F, Rai S, Broor S, Wigh R, Mishra AC, Lafond K, Mott J, Lal RB, Krishnan A. Validity of clinical case definitions for influenza surveillance among hospitalized patients: results from a rural community in North India. *Influenza Other Respi Viruses*. 2012 Jul 16. doi: 10.1111/j.1750-2659.2012.00401.x.

Chadha M, Hirve S, Dawood F, Lele P, Sambhudhas S, Deoshatwar A, Juvekar S, Lafond K, Lal RB, Mishra AC. Burden of seasonal and pandemic influenza-associated hospitalization during and after the 2009A(H1N1)pdm09 pandemic in a rural community in India. *PLoS One*, 2013 May 15;8(5):e55918.

Hirve S, Chadha M, Lele P, Lafond KE, Deoshatwar A, Sambhudhas S, Juvekar S, Mounts A, Dawood F, Lal R, Mishra A. Performance of case definitions used for influenza surveillance among hospitalized patients in a rural area of India. *Bull World Health Organ*; 90:804–812, 2012.

Moorthy M, Samuel P, Peter JV, Vijaykumar S, Sekhar D, Verghese VP, Agarwal I, Moses PD, Ebenezer K, Abraham OC, Thomas K, Mathews P, Mishra AC, Lal RB, Muliylil J, Abraham AM. Estimation of the Burden of Pandemic A(H1N1)pdm 09 in Developing Countries: Experience from a Tertiary Care Center in South India. *Plos One*, 7:e41507, 2012.

Nair H, Brooks A, Katz M, Roca A, Berkly JA, Madhi SA, Simmerman MA, Gordon A, Sato M, Howie S, Krishnan A, Ope M, Lindblade KA, CaroseneLink P, Lucero M, Ochieng W, Kamimoto L, Dueger E, Bhat N, Vong S, Theodoratou E, Chittaganpitch M, Chimah O, Balmaseda A, Buchy P, Harris E, Evans V, Katayose M, Gaur B, O-Callaghan-Gordo Goswami D, Arvelo W, Venter M, Briesse T, Tokarz R, Widdowson M-A, Mounts A, Breiman RF, Feiken DR, Klugman KP, Olsen S, Gessner BD, Wright PF, Rudan I, Broor S, Simoes EAF, Campbell HA. The global burden of respiratory infections due to seasonal influenza in young children: a systematic review and meta-analysis. *The Lancet* 378:1917–30, 2011.

Spectrum of Respiratory Virus Infections in Acute Respiratory Tract Infection (ARI) among Children in India

This study has been carried out by utilizing the hospital based surveillance to estimate the incidence of influenza in Ballabgarh, Haryana.

Study Aims and Objectives: To estimate burden due to pneumonia, important viral (such as influenza, Respiratory Syncytial Virus) and bacterial causes (*H. Influenzae* and *Streptococcus Pneumoniae*) of acute respiratory infections and drug sensitivity patterns of the causing agents in a rural community.

Approach: Specimens collected from under 5 children of SARI cases from July 2009–June 2011 were tested for various pathogens using a real-time RT-PCR.

Timeline: July 2009–June 2011.

Progress and Findings: Analysis of 245 specimens revealed 127 (52%) had presence of one of the respiratory virus, including high prevalence of RSV (20.3%), followed by Rhinovirus (17%) and PIV3 (4%) and influenza (7%).

Conclusion: This study provides evidence that respiratory viruses singly or in mixed infections are detected in >50% of medically attended hospitalized children from a rural community in India using sensitive detection methods like RT-PCR. These findings will help guide efforts to reduce the disease burden due to viral ARIs in developing countries.

Related Published Paper: Broor S, Dawood F, Pandey BG, Saha S, Gupta V, Krishnan A, Rai S, Erdman D, Lal RB. Respiratory viruses are associated with a substantial proportion of hospitalizations among children aged <5 years in rural northern India. *Clinical Infectious Disease. Journal of Infection* (In press).

Epidemiological Study of Respiratory Pathogens in ARI among Children and Elderly in India

Acute respiratory infections (ARI) are a major cause of morbidity and mortality among children globally, with the greatest number of deaths occurring in developing countries. While estimates of total episodes of ARI and incidence of hospitalization due to pneumonia in India have been generated, no study has been carried out to date to systematically identify etiological agents in a population-based setting.

Study Aims and Objectives:

- Estimate the incidence of ALRIs among children (under 5 years) and elderly (over 60 years).
- Assess the relative burden of select viral and bacterial respiratory pathogens associated with ARIs.
- Characterize the clinical spectrum of ARI associated with identified bacterial and viral pathogens.
- Document the antimicrobial sensitivity pattern of major respiratory pathogens isolated from ARI patients.
- Quantify with a societal perspective the economic burden associated with morbidity due to ARI in under-fives and elderly.

Approach: A surveillance platform was initiated in August 2012 in four villages in Ballabgarh Block of Haryana State in North India, with a population of 2,754 children below 10 years. All children are screened weekly for presence of any respiratory symptom (cough, sore throat, ear ache/discharge, nasal discharge/congestion, shortness of breath, respiratory difficulty) or hospital admissions. World Health Organization (WHO) standard case definitions are used for ARI, including upper (AURI) and lower respiratory infections (ALRI), and pneumonia are used. Those identified by screening are assessed clinically by trained nurses. Records of those hospitalized are reviewed by medical officers. Throat and/or nasopharyngeal swab are collected from children meeting these case definitions, and tested for both bacterial and viral pathogens. Urine samples are also collected from pneumonia cases for pneumococcal antigen testing.

Timeline: August 2012–August 2016.

Progress and Findings: After initial pilot runs, the platform became fully functional on 14th August 2012. Until 28th March 2013 (90,031 child weeks of surveillance) 10,561 ARI cases have been reported, giving an incidence rate of 6.1 per child year. Four hundred thirty-four (434) cases of ALRI were diagnosed, giving an ALRI incidence rate of 0.25 per child year. Of the 429 cases tested for Influenza, 20 were positive (10 for H1N1pdm09; nine for Influenza B and one for H3). Of the 295 samples tested for bacteriology, 20 were positive for *S. pneumoniae*, 15 for *staph aureus* and three for *H. influenzae*. None of the 201 control specimens were positive for influenza and only one tested positive for *Strept. pneumoniae*. Tests for other viruses and urinary antigens are still to be carried out.

Conclusion: A fully functional population-based surveillance platform has been set up which is providing useful information on epidemiology and etiology of ARI in this cohort. This platform can serve as a potential vaccine trial site in future.

Related Published Paper: Nair H, Simões, EA, Rudan I, Gessner BD, Azziz-Baumgartner E, Zhang JS, Feikin DR, Mackenzie GA, Moisi JC, Roca A, Baggett HC, Zaman SM, Singleton RJ, Lucero MG, Chandran A, Gentile A, Cohen C, Krishnan A, Bhutta ZA, Arguedas A, Clara AW, Andrade AL, Ope M, Ruvinsky RO, Hortal M, McCracken JP, Madhi SA, Bruce N, Qazi SA, Morris SS, El Arifeen S, Weber MW, Scott JA, Brooks WA, Breiman RF, Campbell H; Severe Acute Lower Respiratory Infections Working Group. Global and regional burden of hospital admissions for severe acute lower respiratory infections in young children in 2010: a systematic analysis. *Lancet*. 381:1380–90, 2013.

Direct and Indirect Protection by Influenza Vaccine Given to Children in India

Through collaboration between the All India Institute of Medical Sciences (AIIMS), CDC, University of Denver and the University of Alabama, a study to determine whether immunization of young children with trivalent influenza virus vaccine (TIV) protects immunized children and older non-immunized household members is being conducted in three villages near New Delhi, India. Children aged 6 months–10 years are randomized at the household level to receive TIV or Inactivated Polio Vaccine (IPV) (the control vaccine) and weekly household surveillance for febrile acute respiratory illness (FARI) is conducted among all household members.

Study Aims and Objectives:

- Measure direct protection of children by influenza vaccine.
- Measure indirect protection against influenza among family members of influenza vaccine recipients.
- Define contribution of influenza virus to illness within three villages in rural Ballabgarh.
- Assess risk factors for more severe disease due to influenza virus.
- Establish surveillance system for influenza virus infections that will be used to assess outcomes in subsequent influenza virus vaccine study.

Approach: A prospective, household randomized, controlled, observer-blinded study is being conducted in three peri-urban villages outside of Delhi, India. The vaccination of children aged 6 months to 10 years with either Trivalent Influenza Vaccine (TIV) or the control vaccine (IPV) will be carried out for five years, followed by weekly household surveillance for febrile acute respiratory illness (FARI) to assess the efficacy of influenza vaccination. Additionally, a small subset of vaccinated children (n=200) will be enrolled to measure their immune response to vaccination and risk factors affecting immunogenicity.

Timeline: September 2008–September 2014.

Progress and Findings:

- Enrollment, vaccination, and surveillance activities have been successfully implemented since October 2009 with high annual rates of vaccine acceptance (~90% of 3,700 eligible children) in every round, and exceptionally high rates of community acceptance for surveillance enrollment (90% of 18,000 persons consented to participate for weekly surveillance).
- Between November 2009–November 2012, 28,955 FARI cases have been sampled and influenza positivity was identified among 3,251 (11.2%) across all age groups.
- While predominant circulating strain in 2009 was A/H1N1pdm09, co-circulation of both influenza B and A/H1N1 pdm09 was observed in 2010. In 2011, A/H3N2 was predominant strain but in 2012, A/H1N1pdm09 re-emerged with no case of A/H3N2; Inf B co-circulated during both these years accounting for half of influenza positive cases.

- Influenza seasonality in Delhi coincides with rainy season in July, and evidence from the study was used to change the vaccination timing to pre-monsoon using SH strains from the earlier winter timing in November using NH strains.

Conclusion:

- Enrollment and immunization rates for Influenza vaccine are high, reflecting on high community acceptance.
- Likely no benefits of vaccination in first year (due to vaccine mismatch).
- Emergence of pandemic H1N1 emphasized the importance of multi-year studies of influenza vaccine.
- Weekly FARI surveillance in 18,000 villagers providing incidence data.
- Measurement of cell mediated immune response and nutritional factors in subset of the participants.
- Vaccine efficacy for first year estimated but further analysis needed.

Related Published Papers:

Sullender W, Fowler K, Anand K, Gupta V, Moulton L, Lafond K, Widdowson M-A, Lal RB and Broor S. Design and initiation of a study of the direct and indirect effects of influenza vaccine given to children in rural India. *Vaccine*, 30:5235–5239, 2012.

Fowler K, Broor S, Sullender W, Gupta V, Purakayastha DR, Widdowson MA, Lal RB, Krishnan A. Incidence rate of symptomatic 2009A/H1N1 and seasonal influenza infection in a rural Indian community. *Int J Infect Dis*. 2013 Sep 12. doi:pii: S1201–912(13)00265–8. 10.1016/j.ijid.2013.08.005. [Epub ahead of print]PubMed PMID:24103331.

Broor S, Sullender WS, Fowler K, Gupta V, Widdowson M-A, Krishnan A, Lal RB. Demographic Shift of Influenza A(H1N1)pdm09 during and after Pandemic, Rural India. *Emerg. Infect. Dis*. 18:1472–1475, 2012.

Understanding Host Innate Immune Responses against Influenza A Virus: An ICGEB-CDC Collaboration

Influenza virus has evolved complex translational control strategies as part of an innate defense mechanism exhibited by the infected cell. The influenza virus on the other hand has evolved complex cap-dependent translation initiation mechanisms and involve the recruitment of both viral and host-cell proteins to preferentially synthesize viral proteins and prevent activation of antiviral responses.

Study Aims and Objectives:

- To explore cellular factors that are activated or involved with influenza virus (including H5N1) replication, assembly or release.
- Study viral-host factors associated with influenza pathogenesis.

Approach: We undertook a comprehensive analysis of these viral and host interactions to better understand the viral drift resulting in a molecular evolution that results in its adaptability to infect different hosts. Discovering these new host-viral protein-protein interactions hold great promise for further research leading to new anti-viral targets.

Timeline: 2009–2014.

Progress and Findings:

- The NP protein of Influenza A viruses (H1, H3, H1pdm09) downregulates the PKR pathway via interaction with HSP-40 (PLoS One published).
- The Influenza A virus Neuraminidase protein via upregulation of Src signaling thereby enhancing cell survival through interaction with CEACAM6. (JBC, submitted).
- Influenza A virus Nucleoprotein interacts with Clusterin and inhibits its anti-apoptotic function, likely by preventing Bax movement into the mitochondria. This may lead to Cytochrome c release from mitochondria and subsequent induction of apoptosis.
- Role of Actinin-4, a cytoskeleton scaffolding protein postulated to be involved in viral trafficking within an infected cell. Actinin-4, being a cytoskeleton protein can be hypothesized to facilitate transport of viral components during entry and exit of viral particles and can possibly have a role in intracellular trafficking of viral components thus controlling viral assembly and budding.

Conclusion: Complex interplay of viral proteins with innate host factors likely will uncover unique pathways that can be exploited for anti-viral approaches.

Related Published Papers:

Tripathi S, Cao W, Sharma K, Patel JR, Ranjan P, Katz JM, Cox NJ, Lal RB, Sambhara S, Lal SK. Influenza A virus Nucleoprotein induces cell death in human lung epithelial cells by targeting Clusterin. *Cell Death & Disease* 2013 Mar 28;4:e562. doi: 10.1038/cddis.2013.89.

Sharma K, Tripathi S, Ranjan P, Kumar P, Garten R, Deyde V, Katz JM, Cox NJ, Lal RB, Sambhara S, Lal SK. Influenza A virus nucleoprotein exploits Hsp40 to inhibit PKR activation and eIF2 α phosphorylation. *PLoS One*. 6:e20215. 2011.

Sharma S, Mayank A, Tripathi S, Patel JR, Gaur P, Katz JM, Cox NJ, Lal RB, Sambhara S, Lal SK. Influenza A virus Nucleocapsid protein interacts with a cytoskeleton scaffolding protein α Actinin-4 to regulate viral replication and transcription. *PLoS One*. 6:e20215. 2011.

Gaur P, Patel JR, Sharma S, Ranjan P, Gangappa S, Katz JM, Cox NJ, Lal RB, Sambhara S, Lal SK. Influenza A virus neuraminidase protein enhances cell survival through interaction with CEACAM6. *J. Biol. Chem*, 287(18):15109–17, 2012.

Severe Acute Respiratory Infection (SARI) among Children Less than Five Years of Age: Use of TAC Multiple Pathogen Detection Platform in International Influenza Program Sites (TAC-KID)

The study is a prospective case-control study aimed at understanding the etiology of severe respiratory disease among hospitalized children less than five years of age in a tertiary level hospital in Delhi, India.

Study Aims and Objectives:

- Estimate the prevalence of selected viral and bacterial respiratory pathogens among children less than five years of age hospitalized with SARI and among children without respiratory illness over a 12 month period.

- Describe the seasonality and compare the etiology of SARI among children less than five years of age.
- Identify risk factors for severe acute respiratory infection by etiology and compare by site among children less than five years of age.

Secondary Objective:

- To compare laboratory findings from TaqMan array cards to standard laboratory wet assay procedures.

Approach: The study will enroll case children less than five years of age who are hospitalized with SARI and control children who are visiting outpatient clinics but not experiencing an infectious illness. The proposed study will seek to enroll cases and controls over a 12 month period.

Timeline: July 2013–June 2014.

Progress and Findings: The study has just started enrolling patients.

This study is part of multi-site study; other sites are in Malawi, Peru and South Africa.

Cost of All-cause and Influenza-associated Acute Respiratory Infections in North India

Acute Respiratory Infections (ARI) are important causes of mortality and morbidity, especially among children. Data on the economic burden of ARI are important to guide policy decisions about options for ARI prevention, such as national recommendations for available vaccines against pneumococcus and influenza. However, the economic burden of ARIs is not well documented in India where a large proportion of the population incurs out of pocket expenditure for medical care.

Study Aims and Objectives:

- Evaluate costs to patients for medically-attended (outpatient and inpatient) episodes of ARI in select public and private hospitals in and around Delhi, India.

Approach: A cross-sectional survey was conducted among patients attending the outpatient departments or hospitalized at three public and eight private hospitals. Participants were asked about direct medical costs (costs of consultation, investigations, and medications), non-medical costs (travel, food, etc.) and indirect costs (loss of wages) for treatment of ARI episodes. Nasopharyngeal swabs were taken only from hospitalized children (<10yr) and elderly (>60yr) patients and tested for influenza viruses by RT-PCR. Data on the cost of outpatient services and hospital beds for public hospitals were obtained from the World Health Organization-Choosing Interventions that are Cost Effective (WHO-CHOICE, 2011) and these costs were added to costs reported by patients to calculate total direct medical costs of hospitalization; all costs were converted to 2013 US dollars using the Wholesale Price Index (WPI) of India.

Timeline: September 2012–March 2013.

Progress and Findings:

- A total of 523 patients were enrolled, including 309 outpatients and 214 hospitalized patients.
- The median direct and indirect costs to the patient per outpatient ARI episode were US\$ 3.8 (IQR 2.70–9.69) and US \$1.9(IQR 1.9–3.8) for public facilities and US \$9.5 (IQR 4.0–28.0) and US \$3.8 (IQR 1.9–3.8) for private facilities.

- Compared to hospitalizations at public facilities, total costs (medical and non-medical) were higher at private facilities (US \$117.6 IQR 70.9–283.5 versus US \$236.31, IQR 155.0–375.0); medical costs alone were also higher (US \$92.4, IQR 56.2–198.3 versus US \$203.5, IQR 140.4–336.8).
- In contrast, caregiver's median wage loss due to hospitalization was lower at private facilities (US \$19.1; IQR 15.2–25.2) than at public facilities (US \$28.8; IQR \$19.1–61.1), likely due to longer hospitalization.
- Of the 112 hospitalized patients, 6 (5.4%) had respiratory specimens positive for influenza viruses.

Conclusion: The economic impact of ARI episodes in India is substantial, with a single hospitalization costing more than the monthly per capita income (US \$114.5) in India. These results are from one site, and point to the need for generation of such estimates from other parts of the country.

Divergent Patterns of Circulating Influenza Viruses in Two Regions of Northern India: When Does Equator Not Define Hemisphere?

Distinct patterns of pandemic 2009A/H1N1 (pH1N1) influenza were observed recently in the two northern regions of India (500 miles apart), with Srinagar having peaks of influenza activity in the winter season (January–February 2009) and the Delhi region in monsoon times (July–August 2010).

Study Aims and Objectives:

- To reassess the seasonality of influenza in two cities in north India to and allow better recommendation of appropriate vaccination timing for these cities in India.

Approach: A total of 4,652 patients presenting with influenza-like illness (ILI) at the tertiary care centers of SKIMS, Srinagar (n=2,126) or AIIMS, New Delhi (n=2,526) were enrolled from January 2011 to December 2012. Nasopharyngeal swabs were tested by real time-PCR for seasonal and pandemic influenza viruses. Sequence analysis was carried out.

Progress and Findings:

- Influenza positivity was higher (375/2,126; 17.6%) in Srinagar, than in Delhi (239/2,526; 9.46%).
- Distinct seasonality and subtypes patterns were observed in these two cities: Srinagar had peaks in January–March with predominant strains being A/H1N1pdm09 in 2011 and A/H3N2 in 2012, followed by resurgence of A/H1N1pdm09 in November–December 2012.
- In contrast, Delhi has peak influenza circulation in July–September with co-circulation of A/H3N2 and influenza B in 2011 and A/H1N1pdm09 in 2012.
- For both years we observed that a co-circulating subtype in Delhi area precedes than that of Srinagar area, suggesting a remarkable difference in distribution of circulating influenza viruses at these two centers.
- In addition, influenza seasonality in Srinagar (34.090N) matched the pattern observed in temperate climate, whereas Delhi with monsoon in July–September and a latitude of 28.660N which is just 500kms from Srinagar revealed influenza during summer months (July–September).

Conclusion:

- Thus India, though physically located in northern hemisphere, has distinct seasonality related to the latitude location of the city.

- While cities with temperate seasonality will benefit with vaccination in October–November, cities with peaks in monsoon season in July–September will likely benefit with vaccination in May–June of every year.

Related Published Papers:

Koul P, Khan U, Bhat K, Saha S, Broor S, Lal RB, Chadha M. Recrudescence Wave of A/H1N1pdm09 Influenza Viruses in Winter 2012–2013 in Kashmir, India. PLOS Currents Outbreaks. 2013 Sep 26. Doi:10.1371/currents.outbreaks.f1241c3a2625fc7a81bf25eea81f66e6.

Broor S, Krishnan A, Roy DS, Dhakad S, Kaushik S, Mir MA, Singh Y, Moen A, Chadha M, Mishra AC, Lal RB. Dynamic patterns of circulating seasonal and pandemic 2009A (H1N1) influenza viruses from 2007–2010 in and around Delhi, India. PLoS One. 7:e29129, 2012.

Koul PA, Muneer MA, Bali NK, Chawla-Sarkar M, Sarkar M, Kaushik S, Khan UH, Ahmad F, Garten R, Lal RB, Broor S. Pandemic and seasonal influenza viruses among patients with Acute Respiratory Illness in Kashmir (India). Influenza Other Respi Viruses. 5(6):521–527, 2011.

KENYA

Ongoing Population-based Surveillance for Influenza and Other Respiratory Diseases in Nairobi and Kisumu, Kenya

The Influenza Program in collaboration with the International Emerging Infections Program (IEIP) under KEMRI/CDC conducts population-based disease surveillance (PBDS) for severe acute respiratory illness (SARI) and influenza-like illness (ILI) in two sites in Kenya; Kibera, an informal urban settlement in Nairobi, and Lwak, a rural community in western Kenya. Approximately 25,000 residents are enrolled in each of the two sites.

Study Aims and Objectives:

- Characterize etiologies of acute respiratory illness in a rural community and an urban community in Kenya.
- Evaluate the burden of medically attended and home-reported influenza and other respiratory diseases.
- Provide a platform to evaluate interventions such as antivirals or vaccines.

Approach: Community interviewers visit each household bi-weekly to ask residents questions about illness symptoms in the past week. In addition, residents have access to a free clinic, where surveillance is conducted for respiratory illness, including influenza, and a number of other disease syndromes. Patients meeting the case definition for SARI and ILI have a nasopharyngeal and oropharyngeal specimen collected. Specimens for SARI and ILI are tested at the KEMRI/CDC laboratory in Nairobi for influenza and other viral pathogens using real time RT-PCR.

Timeline: Surveillance for respiratory illness in the two sites began in 2006. Scientific presentations and publications from this surveillance platform are described further below.

Progress and Findings: Influenza virus has been shown to circulate year-round with a peak in activity generally between July and October of every year. During peak season the percent of outpatient ILI and hospitalized SARI patients testing positive for influenza approaches what has been observed during

winter seasons in temperate climates. From January 2008 to December 2012 the average rate of influenza-associated hospitalization (inpatient SARI) was 3.6(95% CI 2.3–75.5) per 1,000 person-years in children <5 in Lwak. The average rate of influenza-associated medically-attended SARI (inpatient and outpatient) in children <5 was 13.6 (95% CI 10–18.5) per 1,000 person-years in Lwak and 20.2(95% CI 16.4–24.9) per 1,000 person-years in Kibera. The average rate of influenza-associated medically-attended ILI in children <5 was 67.5(95% CI 59.9–76.1) per 1,000 person-years in Lwak and 45.5(95% CI 39.3–52.6) per 1,000 person-years in Kibera. Few children who had laboratory-confirmed influenza were diagnosed with influenza by the treating clinician in the inpatient (0%) or outpatient (2.5%) settings. 55% of children in Lwak and 99% of children in Kibera meeting the SARI case definition were treated as outpatients. Outpatient influenza-associated SARI cases in Lwak and Kibera were as likely as hospitalized influenza-associated cases to be hypoxic ($p=0.48$) and to be diagnosed with pneumonia ($p=0.11$).

Conclusion: The burden of influenza-associated hospitalization in Kenyan children from 2008–2012 was 1.2–10 times higher than estimates of influenza-associated hospitalizations in the US States of Oregon and Michigan from 2008–2011. Many children who had an IMCI danger sign were not hospitalized and the SARI case definition applied was fairly stringent, which may indicate that the true burden of influenza-associated severe disease in Kenyan children is much higher than current estimates suggest. Few clinicians diagnosed children with influenza despite the presence of a global pandemic during the reporting period. Influenza-associated disease remains under-recognized in Kenyan children. In general at both sites, rates of influenza-associated illness are highest among children <2 years old and lowest among adults ≥ 50 years old.

Related Published Paper: Katz MA, Lebo E, Emukule G et al. Epidemiology, Seasonality, and Burden of Influenza and Influenza-Like Illness in Urban and Rural Kenya, 2007–2010. *J Infect Dis.* 2012 Dec 15;206 Suppl 1:S53–60. doi: 10.1093/infdis/jis530.

Hospital-based Surveillance for Multiple Respiratory Pathogens in Nyanza Province, Kenya

The Influenza Program in collaboration with the CDC Global Disease Detection program, and partners working to control Tuberculosis and HIV/AIDS under KEMRI/CDC conducts comprehensive hospital-based surveillance for multiple respiratory pathogens at Siaya District Hospital, located within the health and demographic surveillance site in Nyanza Province, Kenya. This area has been under systematic surveillance since May 2007.

Study Aims and Objectives:

- Characterize etiologies of hospitalized respiratory illness at Siaya District Hospital.
- Monitor the impact of influenza on hospitalizations and deaths in the context of other respiratory viruses and underlying comorbidities.

Approach: Patients hospitalized with respiratory illness have a nasopharyngeal and oropharyngeal specimen collected. Specimens are tested at the KEMRI/CDC laboratories for influenza A and B, respiratory syncytial virus (RSV), parainfluenza (PIV)— 1, 2 and 3, adenovirus (AdV) and human metapneumovirus (HMPV) by real time RT-PCR. Testing using newly developed Taqman Array Card (TAC) multi-pathogen PCR technologies has recently started to test all specimens simultaneously for seven bacterial and 13 viral pathogens. Comprehensive clinical data are also collected, and asymptomatic controls are being recruited to evaluate the attributable fraction of illness associated with different pathogens.

Timeline: Surveillance is ongoing.

Progress and Findings: From August 2009 to July 2012, we enrolled 5,507 SARI patients and 1,632 ILI patients. Most (SARI=75%, ILI=77%) were children <5 years; median age was 1.6 years and 2.4 years for SARI and ILI patients, respectively. The respiratory viruses most commonly detected in hospitalizations using conventional PCR methods were AdV, PIV-3, RSV, HMPV and influenza A.

The average annual incidence per 1,000 persons of influenza-associated SARI was 4.8(95% CI 3.0–7.6) among children < 2 years; 1.4(95% CI 0.7–2.8) in children aged 2–5 years; and 0.3(95% CI 0.2–0.4) among persons ≥5 years. The incidence of influenza-associated medically attended ILI per 1,000 was 32.6(95% CI 19.2–55.4) among children < 2 years; 19.0(95% CI 11.3–31.8) in children aged 2–5 years; and 3.8(95% CI 2.6–5.7) among persons ≥5 years.

Rates per 1,000 persons of SARI associated with RSV were 10.7(95% CI 7.9–14.6) among children < 2 years; 2.0(95% CI 1.1–3.4) in children aged 2–5 years; and 0.1(95% CI 0.0–0.2) among persons ≥5 years. Rates of ILI associated with RSV were 29.4(95% CI 16.8–51.4) among children < 2 years; 21.6(95% CI 13.3–35.1) in children aged 2–5 years; and 0.8(95% CI 0.3–1.9) among persons ≥5 years. The case fatality proportions were 13/348 (4%) and 14/437 (3%) among SARI patients with laboratory confirmed influenza and RSV, respectively.

Taqman array analyses have found *Streptococcus pneumoniae*, Rhinoviruses, RSV, AdV, Enteroviruses, and Influenza viruses to be most commonly detected in hospitalized patients. Attributable fractions of detected pathogens associated with illness will be calculated with the recruitment of asymptomatic controls during the upcoming year.

Conclusion: Influenza and RSV produce a significant burden of disease in western Kenya. These estimated rates of the inpatient and outpatient burden of influenza in Kenya are higher than published direct estimates from the US. Our estimates of the incidence of hospitalized influenza-associated SARI are also consistent with other studies in western Kenya. Additional work will further estimate the burden of non-medically attended influenza and RSV in this context. During the upcoming year we will also evaluate the burden of multiple respiratory pathogens in the context of underlying HIV and TB.

Related Published Paper: Fuller JA, Summers A, Katz MA et al. Estimation of the National Disease Burden of Influenza-Associated Severe Acute Respiratory Illness in Kenya and Guatemala: A Novel Methodology. *PLoS One*. 2013;8(2):e56882. doi: 10.1371/journal.pone.0056882. Epub 2013 Feb 27.

Surveillance for Hospital-acquired Infections in Kenya

While healthcare-associated infections (HAIs) are an important cause of morbidity and mortality worldwide, the burden of HAIs has not been documented in Kenya. In 2010, the Kenyan Ministry of Health, the Kenya Medical Research Institute (KEMRI) and CDC, initiated surveillance for respiratory in an initiative to build infection control capacity. Surveillance for HAIs is conducted at three public hospitals— a national referral hospital, a provincial general hospital, and a district hospital.

Study Aims and Objectives:

- Monitor respiratory HAI among patients admitted to selected surveillance wards at three hospitals in Kenya.
- Assess the incidence of respiratory HAIs on surveillance wards.

- Describe the epidemiology of incident respiratory HAI on surveillance wards.
- Provide a platform for expanded HAI and anti-microbial resistance surveillance.

Approach: At each site, surveillance officers survey pediatric, adult general, surgical, and specialty wards for HAIs. Patients admitted to the hospital for more than three calendar days who develop new onset of fever or hypothermia ($\geq 38^{\circ}\text{C}$ or $< 35^{\circ}\text{C}$) or who developed new onset of cough or sore throat are considered to have suspected HAI. Suspected HAI cases are assessed for onset of clinical symptoms and signs by questionnaire and medical record review. Nasopharyngeal and oropharyngeal samples are then collected from these patients and sent to the CDC-Kenya laboratory in Nairobi, where they are tested by RT-PCR for influenza A & B, adenovirus, respiratory syncytial virus, human metapneumovirus, and parainfluenza virus 1, 2 and 3. Specimens positive for influenza A are subtyped by real time RT-PCR.

Timeline: Surveillance started in September 2009 and is ongoing.

Progress and Findings: From April 2010–September 2012, of the 379 cases of rHAI; 230 (60.7%) were males and 217 (57.3%) children < 18 years old. The incidence of rHAI was 9.2/10,000 patient-days. Incidence in ICUs (33.0) was significantly higher than in pediatric wards (8.4) and medical wards (7.1) ($p < 0.0001$ for both). Of the 140 cases with specimens tested, 45.7% had at least one virus detected.

Conclusion: This is the first systematically collected surveillance data to estimate the burden of healthcare-associated respiratory illness in East Africa. Our estimates of the incidence of HAIs in Kenya provide baseline estimates that have some consistency with respiratory HAI rates observed elsewhere. Infection control measures should be strengthened in Kenyan hospitals, and this platform will be expanded to monitor the burden of additional HAIs and anti-microbial resistant pathogens.

Observational Seasonal Influenza Vaccine Effectiveness Study

In recent years, surveillance has demonstrated a high burden of influenza throughout Africa. However, influenza vaccine is rarely used on most of the continent. Little is known about the effectiveness of the vaccine in Africa, where HIV, malnutrition, malaria and other comorbidities are prevalent. KEMRI/CDC, with support from the Kenya Ministry of Public Health and Sanitation, is conducting a three-year observational influenza vaccine effectiveness study using the commercially available Southern Hemisphere seasonal vaccine in two sites in Kenya; Lwak— a rural site in western Kenya, and Kibera— an informal urban settlement in Nairobi. The International Emerging Infections Program (IEIP) under KEMRI/CDC currently conducts population-based disease surveillance (PBDS) for severe acute respiratory illness (SARI) and influenza-like illness (ILI) in these two sites.

Study Aims and Objectives: The objectives of the study are to evaluate the following:

- Effectiveness of the vaccine in preventing laboratory-confirmed disease.
- Effectiveness of the vaccine in preventing medically attended ILI and SARI, and symptomatic ILI and SARI reported in the community.
- Acceptability of influenza vaccination among community residents.

Approach: The vaccine is offered on a voluntary basis to children aged 6 months to 10 years enrolled in the IEIP study site. Sanofi Pasteur-France has donated Southern Hemisphere trivalent influenza vaccine for the study. Prior to the vaccination campaign a vaccination awareness campaign was conducted to sensitize the community on the benefits and availability of the influenza vaccine. After vaccination, the study

participants are followed using the routine IEIP surveillance which includes bi-weekly home visits where field workers ask household members questions about recent illnesses and deaths. The study participants also have access to a medical clinic where free care is provided. At the clinic, specimens are collected from patients who have SARI or ILI. Samples are tested at the KEMRI/CDC laboratory using real time RT-PCR for influenza virus.

Timeline: Data from the past three years of influenza surveillance have shown that the influenza season in Kenya peaks from July to October, and therefore most closely mirrors the Southern Hemisphere influenza season. The vaccine is available every year in Kenya beginning in March to coincide with the Southern Hemisphere influenza season. The study has just completed its third and final year.

Progress and Findings: Of the approximately 10,000 eligible children in the two sites, 30%, 36%, and 38% were fully vaccinated in 2010, 2011, and 2012, respectively; 11%, 12%, and 13% were partially vaccinated. During the three 9-month follow-up periods, there were 144, 77, and 102 cases of influenza, respectively, among children aged 6 months–10 years. The median age of cases was 4.8 years and 149 (46%) were female. In the first two years, influenza A predominated (67% of cases in 2010–2011 and in 2011–2012), and influenza A comprised 50% of influenza cases in 2012–2013. In 2010–2011 and 2011–2012, most influenza A cases were influenza A(H1N1)pdm09, while in 2012–2013, influenza A(H3N2) predominated. We included 244 cases and 608 test-negative controls in our evaluation. VE among fully vaccinated children was 44% for the entire study period (95% confidence interval (CI) = 20–61%). Season-specific VE was 51% (95% CI = 16%–71%) during 2010–2011, 48% (95% CI = -16%–77%) during 2011–2012, and 26% (95% CI = -29%–60%) during 2012–2013. We cultured 48/144 specimens in 2010–2011 and 29/77 specimens in 2011–2012; all isolates were considered well-matched to vaccine strains. Strain information for 2012–2013 is not yet available.

Conclusion: During three years in an urban and rural community in Kenya, over one-third of eligible children were fully vaccinated through a campaign offering free trivalent inactivated influenza vaccine. Among children aged 6 months–10 years, fully vaccinated children were ~40% less likely to have an influenza-associated medically attended respiratory illness overall. VE appeared lower in 2012–2013; pending antigenic characterization data may help explain this finding.

Related Published Papers: In Progress.

Determinants of Influenza Vaccine Uptake in Kenya

The overall safety record of trivalent inactivated influenza vaccine in young children is excellent. The challenge with respect to use of the inactivated influenza vaccine in young children is not demonstrating safety and efficacy, but the practicalities of delivering two doses of the vaccine in the first year, followed by annual vaccination. We have undertaken research to evaluate the uptake of seasonal influenza vaccine in children of two Kenyan communities following a seasonal influenza vaccine effectiveness study. We also specifically have investigated the independent roles that mothers and fathers play in the decision to have children vaccinated for influenza.

Study Aims and Objectives:

- To evaluate the social, demographic and geographic determinants of seasonal influenza vaccine uptake in Kenya.
- To evaluate the independent role that fathers and mothers play in the decision to vaccinate children for influenza.

Approach: From 2010–2012 the Kenya Medical Research Institute/Centers for Disease Control and Prevention-Kenya (KEMRI/CDC) and the Kenya Ministry of Public Health and Sanitation implemented an observational seasonal influenza vaccine campaign, offering free vaccine to study residents aged 6 months–10 years old within two existing KEMRI/CDC population-based disease surveillance sites (population=53,000) in Kenya; Lwak, a rural community in western Kenya, and Kibera, an informal urban settlement in Nairobi. During this campaign we evaluated the social, demographic and geographic factors associated with influenza vaccine uptake among eligible children. In 2012, nurses at health facilities administered standardized questionnaires to the parents or caretakers of vaccinated children during the campaign from March–May. We also sampled approximately 500 households at each site and conducted structured interviews of male health care decision-makers/caretakers from July–August. Households were stratified into three categories: fully vaccinated against influenza (all children in the household received the recommended number of doses of influenza vaccine), partially vaccinated (one or more of the children in the household received a dose of vaccine, but not all children received all needed doses), and not vaccinated against influenza (no children in the household received vaccine).

Timeline: March 2010–July 2012.

Progress and Findings: We provided 27,602 doses of vaccine to 17,613 children in the two communities. Of the 1,074 sampled households, 456 (42.5%) were fully vaccinated against influenza, 405 (37.7%) were partially vaccinated and 213 (19.8%) were not vaccinated. Families living >5km from the facilities were significantly less likely to have their children vaccinated (aOR=0.69; 95% CI 0.53–0.90; p=0.006). Over 90% of children were brought by their mothers to the vaccination campaign. Households in which both fathers and mothers were away from home for a duration >3 months at the time of vaccination were less likely to vaccinate their children compared to households in which both parents were in the home during the vaccination campaign (aOR=0.29; 95%CI 0.09–0.88; p=0.03). However households where either the father (aOR=0.81; 95%CI 0.62–1.06; p=.12) or the mother (aOR=1.60; 95%CI 0.68–3.74; p=.28) was away during the vaccination campaign were more likely not to have their children vaccinated than households where both parents were present. Households with fathers who believed that influenza vaccines are important (aOR=5.10; 95%CI 1.63–15.97; p=0.01); mothers who believed that influenza vaccines are important (aOR=11.98; 95%CI 3.97–36.14; p<0.001); and where both parents believed that influenza vaccines are important (aOR=8.35; 95%CI 3.16–22.06; p<0.001) were each more likely to have their children vaccinated when compared to households where both parents did not believe that the vaccines were important. Finally, households where fathers joined in the decision to have children vaccinated were more likely to vaccinate their children than households where the father did not join the vaccination decision (aOR=3.01; 95%CI 1.62–5.62; p<0.001).

Conclusion: Future campaigns will need to consider ways to adapt to vaccination schedules to the needs of working parents, and community mobilization efforts may need to specifically target alternative family members or designated caretakers that may bring children for vaccination if working parents are unavailable. These findings support the notion that future influenza vaccination campaigns in Africa may need to consider opening additional vaccination centers if large portions of the targeted population will have to travel greater than five kilometers for vaccination. Mothers are highly visible parental caretakers at the time of vaccination, as 90% of vaccinated children were brought by their mothers for influenza vaccination in Kenya. However despite the visibility of mothers at the time of a child's vaccination, the fathers' role in vaccine decision-making should not be overlooked. Targeting fathers in sensitization activities during future campaigns may also help to increase vaccination coverage rates.

Related Published Paper: Otieno NA, Nyawanda BO, Audi A et al. Demographic, Socio-economic, and Geographic Determinants of Seasonal Influenza Vaccine Uptake in Rural Western Kenya, 2011. *Vaccine*. 2014 Jan 22. pii: S0264-410X(13)01498-9. doi: 10.1016/j.vaccine.2013.10.089. [Epub ahead of print].

Direct Economic Burden of Medically Attended Influenza in Western Kenya from the Parental Perspective, 2009–2011

The economic costs of influenza in tropical Africa remain under-explored. Calculating the economic burden of influenza is crucial to estimating the costs and benefits of vaccine implementation. We estimated the direct costs of medically-attended influenza disease in Kenya from the parental perspective.

Study Aims and Objectives:

- To estimate the direct economic impact of medical care for influenza on families in Western Kenya.

Approach: We analyzed medical records for 7,388 inpatients and outpatients at Lwak Mission Hospital (LMH) to identify persons with severe acute respiratory illness (SARI) or influenza-like illness (ILI) during January 1, 2009–December 31, 2011. We examined medical chart data for prior outpatient consultations and medications taken for the current illness, routine diagnostic tests, medications administered to patients during the current visit, and length of stay (for hospitalized patients). We determined costs for consultation, routine diagnostic tests, medications, and hospital admission from the medical facility catalogue of prices. Cost estimates for consultations prior to any hospital visit were taken from published literature from western Kenya. Influenza diagnostics are not routine and were not included in direct cost estimates.

Timeline: Medical records reviewed from 2009–2011.

Progress and Findings: The mean (SD) patient cost in Kenyan shillings (KSH) of influenza-associated outpatient ILI, outpatient SARI, and hospitalized SARI in children under age 5 was 1,254(1,129.1–1,378.5), 937(307.6–1,566.9), and 2,609(2,152.2–3,064.8), respectively. The total annual direct economic burden of influenza in children < 5 in Nyanza Province was estimated to be from 68.6 to 133.0 million KSH (US \$847,000–\$1,642,000) for outpatients (ILI and SARI); and 4.8 to 10.3 million KSH (US \$59,000–\$127,000) for inpatients.

The mean (SD) patient cost in KSH of influenza-associated outpatient ILI, outpatient SARI, and hospitalized SARI in persons aged 5 and older was 1,155(45.4–2,265.5), 1,997(1,937.9–2,055.5), and 3,036(2,681.3–3,389.9), respectively. The total annual direct economic burden of influenza in persons aged 5 and older in Nyanza Province was estimated to be from 243.8 to 335.4 million KSH (US \$3,010,000–\$4,141,000) for outpatients (ILI and SARI); and 2.8 to 7.0 million KSH (US \$35,000–\$86,000) for inpatients.

The mean direct costs per outpatient visit and hospitalization for influenza of 1,400 and 3,000 KSH are approximately 5% and 11% of average monthly income (28,000 KSH), respectively.

Conclusion: The direct costs of inpatient and outpatient care for influenza-associated illness are considerable. Ongoing work will now estimate the indirect costs of influenza, costs from the governmental perspective, and then the cost-effectiveness of influenza vaccination.

The Role of HIV in the Household Introduction and Transmission of Influenza in an Urban Setting, Nairobi, Kenya, 2008–2011

Little is known about how high HIV seroprevalence affects the transmission dynamics of influenza within household settings in tropical sub-Saharan Africa.

Study Aims and Objectives: We use household and clinic data collected at the IEIP research site in Kibera during 2008 through 2011 to describe

- the association between the HIV status of household members and their risk of introducing influenza to the home, and
- the association between the HIV status of index cases of influenza in the home and the subsequent risk of developing secondary influenza-like illness (ILI) among their household contacts.

Approach: We used respiratory illness data gathered from a population-based household and clinic surveillance system in Kibera urban informal settlement, Nairobi, Kenya to examine the association between the HIV status of household members and their risk of introducing influenza to the home. We also examined the association between the HIV status of laboratory-confirmed influenza index cases in homes and the risk of their household contacts developing influenza-like illness (ILI).

Timeline: Household and clinic data collected from 2009 through 2011.

Progress and Findings: In comparison to persons over age 18, index cases of influenza were more likely to be children aged <2 (aRR 4.78; 95%CI 3.18–7.17), 2–4 (aRR 3.35; 95%CI 2.20–5.09), and 5–17 years (aRR 2.56; 95%CI 1.78–3.67) when adjusted for HIV status and household size. HIV status was not associated with influenza index case status (aRR 1.34; 95%CI 0.68–2.66), when controlling for age group of the household member and household size. However, the risk of developing ILI among household contacts of HIV-positive index cases was more than twice the risk of developing ILI among household contacts of HIV-negative index cases, when adjusted for age group of the household-contacts (aRR 2.36; 95% CI 1.19–4.66).

Conclusion: These results suggest that while children may be most likely to bring influenza into the homes in Kibera, HIV-positive influenza index cases may enhance transmission of influenza within the home. HIV status should be considered in future studies evaluating the risk factors for influenza transmission. HIV control programs also have a possible additional benefit of reducing influenza transmission. Finally prioritizing vaccine availability for clinics treating HIV-positive individuals and encouraging such individuals to be vaccinated may be of possible value not only because HIV-positive individuals are at an elevated risk for severe clinical symptoms and mortality, but also because of the potential to reduce influenza transmission within the home.

Predicting Mortality among Hospitalized Children with Respiratory Illness in Western Kenya, 2009–2012

Pediatric respiratory disease is a major cause of morbidity and mortality in the developing world; 70% of global deaths from respiratory disease in children occur in Africa and South East Asia. In Kenya, approximately 16% of annual deaths in children < five years of age are attributed to acute respiratory infections (ARI). In most health facilities in Kenya, resources are limited; having a better understanding of which children hospitalized with respiratory illness are at greatest risk of severe outcomes could improve patient triage and inform resource allocation. We developed a modified Respiratory Index of Severity in Children (mRISC) scoring system using easy to monitor syndrome-based risk factors for in-hospital mortality in children aged less than five years that were hospitalized with a respiratory illness in Siaya District Hospital (SDH) in Western Kenya.

Study Aims and Objectives:

- To develop a clinical prediction tool with practical utility to rapidly identify children most at risk for fatal outcomes due to respiratory disease in Western Kenya.

Approach: We analyzed data from children <5 years old who were hospitalized with respiratory illness at Siaya District Hospital (SDH) from 2009–2012. We used a multivariable logistic regression model to identify patient characteristics predictive for in-hospital mortality. Model discrimination was evaluated using the concordance statistic. Using bootstrap samples, we re-estimated the coefficients and the optimism of the model. The mRISC score for each child was developed by adding up the points assigned to each factor associated with mortality based on the coefficients in the multivariable model.

Timeline: Influenza and respiratory disease surveillance data from Siaya District Hospital, 2009–2012.

Progress and Findings: We analyzed data from 3,581 children hospitalized with respiratory illness; including 218(6%) who died. Low weight-for-age [adjusted odds ratio (aOR)=2.1; 95% CI 1.3–3.2], very low weight-for-age (aOR=3.8; 95% CI 2.7–5.4), caretaker-reported history of unconsciousness (aOR=2.3; 95% CI 1.6–3.4), inability to drink or breastfeed (aOR=1.8; 95% CI 1.2–2.8), chest wall in-drawing (aOR=2.2; 95% CI 1.5–3.1), and being not fully alert on physical exam (aOR=8.0; 95% CI 5.1–12.6) were independently associated with in-hospital mortality. The positive predictive value for mortality increased with increasing mRISC scores.

Conclusion: This study shows that a clinical prediction tool, similar to the RISC score initially developed in South Africa, may also have practical utility to rapidly identify children most at risk for fatal outcomes due to respiratory disease in Western Kenya. As a complementary tool for use alongside the IMCI guidelines, the mRISC could help improve the clinical management and in-hospital triage of children admitted with respiratory illness.

Related Published Papers: In Progress.

Influenza in Pigs in Kenya

Influenza A H1N1pdm09 (H1N1pdm09) virus is a swine-origin virus that was first detected in humans in April 2009 and has since been detected in multiple animal species in countries across the world. Infections in animals have often been associated with contact with humans infected with the pH1N1 virus. There has been limited surveillance for influenza virus strains circulating in pigs in Kenya. We carried out surveillance in pigs at a local slaughterhouse located near Nairobi to determine prevalence and sero-prevalence of influenza A viruses.

Study Aims and Objectives:

- To determine prevalence and sero-prevalence of influenza A viruses in pigs in Kenya.

Approach: We collected nasal swabs and blood samples from pigs arriving at the slaughterhouse for an interval of 10 days during May of 2010, and then for five subsequent ten day periods in August and December of 2011 and April, August and December of 2012.

Timeline: Samples were collected in slaughterhouses between May 2010 and December 2012.

Progress and Findings: Between May 2010 and December 2012, blood and nasal swab specimens were collected from 978 pigs. In addition, 226 bronchiole swabs were collected. Of 609 pigs for which there was information on their source location, 503 (82%) were from Kiambu County in Central Kenya. The overall mean herd size of source farms was 119 pigs (SD=257) and the median pig herd size was 10 (range 1–500). Of 930/978 sera that were tested, 155 (16.7%) were positive for influenza A antibodies. Influenza A seroprevalence across the six sampling periods was 15.0%, 40.4%, 22.8%, 5.7%, 5.1%, 7.8% with the highest seroprevalence observed in pigs sampled in August 2011 and the lowest among pigs sampled in August 2012. HI assays were undertaken on 129/155 positive sera. Of these, 76 (59%) were reactive to the H1N1pdm09 antigens. Fifty-three (41%) were cross reactive to more than one of the test antigens, or to none of the antigens in the panel, and were termed as inconclusive. For the six sampling periods between May 2010 and April 2012 for which HI has been carried out, H1N1pdm09 was detected in each period and the overall H1N1pdm09 seroprevalence by sampling period ranged from 2.4% and 15.4%. Of 971 nasal swabs tested for influenza A, 5 (0.5%) were positive for influenza A. None of 226 bronchiole swabs tested were positive for influenza. Three virus isolates were obtained from nasal swabs collected in August of 2011 and all subtyped as influenza A H1N1pdm09.

Conclusion: Pigs play a role in the ecology of influenza virus in Kenya and continued surveillance in humans, pigs and other potential reservoirs of influenza viruses may be of value for identifying the risk to humans at the animal-human interface.

A Double-Blind, Randomized, Controlled Trial to Evaluate the Safety, Immunogenicity, and Efficacy of Trivalent Inactivated Influenza Vaccine, High-Dose Trivalent Inactivated Influenza Vaccine, and/or Intradermal Trivalent Inactivated Influenza Vaccine in HIV-Infected and HIV-Uninfected Pregnant Women in a Malaria-Endemic Area of Rural Western Kenya

Immunogenicity of flu vaccine in HIV-infected and HIV-uninfected pregnant women.

Study Aims and Objectives:

- To evaluate the immunogenicity of TIV, hdTIV and idTIV in HIV-infected and uninfected pregnant women.
- To evaluate the level of vaccine-induced influenza antibody transfer to infants of HIV-infected and uninfected pregnant women who receive TIV, hdTIV or idTIV.
- To evaluate the safety of TIV, hdTIV and idTIV in HIV-infected and HIV-uninfected pregnant women and fetus.

Approach: This trial will be conducted as a double-blind, randomized, controlled trial stratified by HIV status in up to 720 (960 if 4 arms) pregnant women in their second and third trimesters and their infants residing in health and demographic surveillance sites (HDSS) around Siaya District Hospital and Lwak Mission Hospital in Nyanza Province, Western Kenya.

Timeline: Trial enrollment will begin in the first quarter of 2014 and will continue for approximately one year.

Lao People's Democratic Republic (Lao PDR)

Feasibility Assessment in Measuring Impact of Seasonal Influenza Status on Birth Outcomes

Capturing pregnant women vaccinated in May–June 2013 and linking with birth outcome measures, with non-vaccinated new mothers' and infants as controls. Also, a 10-year historical review of birthing information in establishing trends and using for historical comparative purposes.

Approach: Collecting information of pregnant women at the time of vaccination and linking with birth outcomes. This work is being carried out at the Maternal and Child Hospital, and collection of birthing information (not practiced in Laos) will be expanded to the north and south of the country.

Timeline: One year.

Progress and Findings: Nine hundred (900) pregnant women have received seasonal influenza vaccine (May–June 2013). To date, 300 vaccinated and 300 (control) unvaccinated women have been interviewed post-delivery and outcome (birth weight measures) obtained. Finally, 10 years of MCH birthing information (~30,000 records) has been entered into a data management program.

LATIN AMERICA

Multi-centric Evaluation of Trivalent Seasonal Influenza Vaccine Effectiveness to Prevent Severe Acute Respiratory Infection among High Risk Groups Targeted for Vaccination (REVELAC-i)

Case test-negative control design.

Study Aims and Objectives:

- Explore the quality of sentinel surveillance data to support vaccine effectiveness estimates.
- Estimate influenza vaccine policies and utilization among target groups.
- Explore influenza and other respiratory vaccine utilization among target groups.
- Estimate trivalent seasonal influenza vaccine effectiveness to prevent severe acute respiratory infection among high risk groups targeted for vaccination.
- Model the impact of influenza vaccine among populations targeted for vaccination.

Approach: During April–December 2012 influenza season, we conducted a pilot test-negative case-control study in 18 influenza sentinel surveillance hospitals in Costa Rica, El Salvador and Panama to assess whether the quality of routinely collected surveillance data was sufficient to conduct a case-control study. The study population included children and elderly who were eligible for vaccination available free of charge. The outcome of interest was severe acute respiratory infections (SARI) associated with laboratory-confirmed influenza. All countries used the regional standard definition for SARI (CDC–PAHO 2006 protocol), consisting of fever and, cough or sore throat, and shortness of breath or difficulty breathing, in the absence of other diagnoses and requiring hospitalization. SARI patients had a respiratory sample (nose and throat swabs or aspirates) collected and tested for the presence of influenza viruses as part of influenza sentinel surveillance. An influenza case was a SARI patient with a positive RT-PCR result for any influenza virus. A control was a SARI patient with a negative RT-PCR result for influenza. For every case, we selected three controls from the same age group and epidemiological week (± 2 weeks).

Timeline: 2012–2014.

Progress and Findings: We identified 915 SARI patients that belonged to target vaccination groups and enrolled 260 influenza cases and 655 controls; 151 cases and 354 controls in Costa Rica, 78 cases and 234 controls in El Salvador and, 31 cases and 67 controls in Panama. Among these, 648 (71%) were children <12 years and 267 (29%) were elderly >60 years. Half (51%) were male patients and 915 (100%) had information on pre-existing medical conditions. The date of sample collection was available for 550 (60%) participants. Most (93%) had information about their 2012 influenza vaccine status. Only 280 (33%) had received an influenza vaccine. Only 86 (10%) had received the 2011 influenza vaccine. Similarly, 345 (38%) were vaccinated against pneumococcal disease. Data collection will continue during the 2014 austral influenza season.

Conclusion: Data collected routinely as part of SARI surveillance included most of the critical variables necessary for estimating vaccine effectiveness but strengthening the data collection and adopting electronic nominal vaccination records are likely to facilitate vaccine effectiveness estimates.

This project is occurring in Argentina, Brazil, Chile, Colombia, Costa Rica, El Salvador, Honduras, Panama, and Paraguay.

Evaluation of Pandemic Influenza Preparedness and Response in Central America

Self-assessment and analysis of surveillance data.

Study Aims and Objectives:

- Measure changes in pandemic preparedness in this region, and identify their related causes, using evaluations conducted between 2008 and 2012.

Approach: Eight Central American countries scored their pandemic preparedness across 12 capabilities in 2008, 2010 and 2012, using a standardized tool developed by CDC. Scores were calculated by country and capability and compared between evaluation years using the Student's t-test and Wilcoxon Rank Sum test, respectively. Virological data reported to WHO were used to assess changes in testing capacity between evaluation years. Linear regression was used to examine associations between scores, donor funding, technical assistance and WHO reporting.

Timeline: 2008–2014.

Progress and Findings: All countries improved their pandemic preparedness between 2008 and 2012 and seven made statistically significant gains ($p < 0.05$). Increases in median scores were observed for all 12 capabilities over the same period and were statistically significant for eight of these ($p < 0.05$): country planning, communications, routine influenza surveillance, national respiratory disease surveillance, outbreak response, resources for containment, community interventions and health sector response. We found a positive association between preparedness scores and cumulative funding between 2006 and 2011 ($R^2 = 0.5$, $p < 0.01$). The number of specimens reported to WHO from participating countries increased significantly from 5,551 (2008) to 18,172 (2012) ($p < 0.01$).

Conclusion: U.S. donor funding and technical assistance provided to the region is likely to have contributed to the improvements in pandemic preparedness we observed.

This project is occurring in Belize, Costa Rica, Dominican Republic, Honduras, Guatemala, El Salvador, and Panama.

Incidence of Influenza and Other Respiratory Viruses and Associated Economic Burden in Central America Cohorts and Population-based Surveillance Platforms

Community-based cohort.

Study Aims and Objectives:

- Estimate the incidence of influenza-like illness by etiology and age group.
- Explore risk factors associated with laboratory-confirmed influenza illness.
- Estimate the cost associated with health seeking for influenza-like illness.

Approach: Patients presenting at three tertiary hospitals (Santa Rosa, Quetzaltenango, and Guatemala City) with symptoms of respiratory disease were invited to undergo screening. Those meeting enrollment criteria and provided written informed consent were asked to provide nasopharyngeal and oropharyngeal swabs and urine samples. Trained staff administered a face-to-face interview to collected patient demographic,

clinical, and risk factor information using a personal digital device (PDA). A chest X-ray and blood culture were obtained. Laboratory confirmation was by real-time reverse transcriptase polymerase chain reaction. Unadjusted annual incidence rates of hospitalized influenza were calculated for Santa Rosa and Quetzaltenango using the denominator population from Guatemala's National Institute for Statistics (INE) data. We calculated age-specific hospitalized influenza incidence of patients hospitalized with influenza and estimated 95% confidence intervals (CI) using the Poisson distribution. Adjustment for health care utilization was based on surveys conducted prior to surveillance system implementation.

Timeline: 2008–2014.

Progress and Findings: During May 2008–July 2012, we identified 446 hospitalized influenza patients, 362 (81%) had influenza A and 84 (18%) had influenza B. The median age of case-patients was 2.4 years (interquartile range: 0.7–32.3). Median length of hospitalization was five days (range: 0–77). Eighty (17.9%) were admitted to the ICU, 28 (6.2%) died; overall, 88 (19.7%) experienced either ICU admission or death. Children aged <6 months comprised 19% of cases, 22% of those admitted to the ICU, and 7% of the deaths. Other deaths occurred in 11 (6%) children aged 7–60 months, 6 (6%) persons aged 5–50 years, and 9 (11%) patients aged >50 years. Women of child-bearing age comprised 6% of cases (2 admitted to ICU; 1 death). The annual incidence of hospitalized laboratory-confirmed influenza in Santa Rosa and Quetzaltenango was 19.7/100,000 overall and 85.4/100,000 for children aged <5 years. In general, Santa Rosa department had higher incidence of hospitalizations with influenza for those aged <25 years. Quetzaltenango department had higher rates for all older age groups except for those aged >65 years. Costa Rica data analyses are ongoing.

Conclusion: Influenza is an important cause of hospitalization in Guatemala, especially among children aged <5 years, who comprised 59% of all hospitalizations for influenza.

This project is occurring in Costa Rica and Guatemala.

Estimating the Incidence of Influenza-associated Hospitalizations and In-hospital Decedents

Leveraging influenza-like illness and severe acute respiratory infection sentinel site data to assess burden through multiplier and linear regression models.

Study Aims and Objectives:

- Assess burden of severe influenza illness among health seekers.

Approach: We quantified the number of persons nationally hospitalized with severe acute respiratory infection (SARI) (or their ICD-10 code proxies J9–18) and who died in the hospital. We calculated the proportion of nose and throat specimens that nationally tested positive for influenza through immunofluorescence or reverse transcription polymerase chain reaction. To estimate how many case-patients would have tested positive for influenza if all had been sampled, we multiplied the number of SARI cases by the proportion testing positive for influenza each month. In Argentina, we also used Serfling regression models to estimate the excess case-patients during influenza periods. We divided the influenza-associated number of severe acute respiratory infections by the national or sentinel site census to estimate influenza-associated rates. We corrected for health utilization (e.g. El Salvador, Honduras, and Panama) when appropriate.

Timeline: 2008–2014.

Progress and Findings: We identified 29,870 SARI case-patients during 2009–2012. Twenty percent (3,352) of 16,597 case-patients with respiratory specimens tested positive for influenza. We estimated that 6,634 (95% confidence interval [CI] 5,134–8,163) influenza hospitalizations and 787 (95% CI 468–1,125) deaths occurred during the study period. These represented 1.4 influenza-associated hospitalizations per 1,000 person-years (py) and four influenza-associated deaths per 100,000py. Deaths occurred primarily among persons aged >60 years where influenza-associated mortality was a mean of 29/100,000py vs. 1/100,000py among younger persons ($p=0.01$).

Conclusion: There was a significant influenza-associated hospitalization and mortality rates particularly among persons aged ≥ 60 years.

Related Published Papers:

Azziz-Baumgartner E, Cabrera AM, Chang L et al. Mortality, severe acute respiratory infection, and influenza like-illness associated with Influenza A(H1N1)pdm09 in Argentina, 2009. PLoS ONE 2012 Available at <http://dx.plos.org/10.1371/journal.pone.0047540>.

Clara A, Armero J, Rodriguez D, et al. Influenza-associated severe pneumonia rates in children younger than 5 years in El Salvador, 2008–2010. Bulletin of the World Health Organization 2012;90:756–763. doi: 10.2471/BLT.11.098202.

This project is occurring in Argentina, Belize, Colombia, Costa Rica, El Salvador, Honduras, Guatemala, Panama, Paraguay, and Peru.

Influenza-associated Mortality in the PAHO Region

Linear modeling of influenza-associated mortality rates by age group.

Study Aims and Objectives:

- Estimate the incidence of influenza-associated mortality rates.

Approach: We identified hospitalized persons and deaths in persons diagnosed with pneumonia and influenza (P&I, ICD-10 codes J10–J18) and respiratory and circulatory illness (R&C, codes I00–I99 and J00–J99). We defined the influenza season as the months when the proportion of samples that tested positive for influenza exceeded the annual median. We used hospitalizations and deaths during the influenza off-season to estimate, using linear regression, and the number of excess deaths that occurred during the influenza season. To explore whether excess mortality varied by sex and age group, we used Poisson regression of the influenza-associated rates.

Timeline: Used 2001–2013 surveillance data.

Progress and Findings: Influenza-associated mortality rates were similar to those reported in countries with published rates. For example, in Argentina, during 2002–2009, 2,411 P&I and 8,527 R&C mean excess deaths occurred annually from May–October. If all of these excess deaths were associated with influenza, the influenza-associated mortality rate was 6/100,000 person-years (95% CI 4–8/100,000 person-years for P&I and 21/100,000 person-years (95% CI 12–31/100,000 person-years) for R&C. During 2005–2008, we identified an average of 7,868 P&I excess hospitalizations and 22,994 R&C hospitalizations per year, resulting in an influenza-associated hospitalization rate of 2/10,000 person-years (95% CI 1–3/10,000 person-years) for P&I and 6/10,000 person-years (95% CI 3–8/10,000 person-years) for R&C.

Conclusion: Our findings suggest that annual rates of influenza-associated hospitalizations and were substantial particularly among older adults.

Related Published Paper: Marinho de Souza MF, Widdowson MA, Alencar AP et al. Trends in mortality from respiratory disease in Latin America since 1998 and the impact of the 2009 influenza pandemic. Bull World Health Organ 2013;91:525–532. DOI: <http://dx.doi.org/10.2471/BLT.12.116871>.

This project is occurring in Argentina, Brazil, and other PAHO member countries.

Costs of Severe Acute Respiratory Infections and Influenza-associated Hospitalizations in Central America

Investigators identify severe acute respiratory infection case-patients and use questionnaires and administrative data to estimate direct and costs associated with illness.

Study Aims and Objectives:

- Estimate the direct, indirect, and provider costs associated with severe acute respiratory infection and hospitalized influenza-illness.

Approach: We retrospectively estimated the costs of hospital treatment among a random sample of severe acute respiratory case-patients (operationalized as those diagnosed with ICD–10 codes J9–18 admitted during 2009–2011 and treated in teaching hospitals. The average costs were expressed in 2011 international dollars (I\$). Costs were determined through the review of administrative records and billing data. In a second phase of the project, investigators sought to obtain the costs associated specifically with laboratory-confirmed influenza case-patient hospitalization.

Timeline: 2009–2013.

Progress and Findings: We reviewed 671 medical records: 337 in Guatemala, 184 in Honduras, and 150 in Nicaragua. The average cost per SARI hospitalization was I\$1,435. On average, cost at general hospitalization among children was I\$725 in Guatemala (95% CI I\$548–903), I\$1,142 in Nicaragua (95% CI I\$953–1,332) and I\$1,143 in Honduras (95% CI I\$991–1,296). In adults, the average cost at general hospitalization was I\$2,942 in Guatemala (95% CI I\$2,500–3,383) vs. I\$1,969 in Honduras (95% CI I\$1,554–2,383). Data analyses in Costa Rica and El Salvador are ongoing.

Conclusion: Influenza hospitalization is an important financial burden of health care systems in Central America.

This project is occurring in Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, and Panama.

Panama and El Salvador Children's Oseltamivir Study (PECOS)

Randomized controlled trial.

Study Aims and Objectives: The primary objective of this study is to evaluate the efficacy of oseltamivir phosphate treatment initiated at the time of hospital admission to reduce disease severity among children aged <10 years hospitalized with influenza-associated respiratory illness. Additional objectives are to: 1) evaluate the tolerability of oseltamivir phosphate treatment, 2) evaluate the effect of oseltamivir treatment on viral clearance and development of oseltamivir-resistant influenza virus during and after treatment in children hospitalized with influenza, 3) estimate the direct and indirect costs of all-cause respiratory illness

and influenza-associated respiratory illness requiring hospitalization, and 4) evaluate the effect of empiric oseltamivir treatment during the influenza season on these costs.

Approach: This study is a multi-site randomized, double-blinded, placebo-controlled clinical trial conducted at five tertiary care hospitals in Panama and El Salvador. Children hospitalized <7 days after symptom onset with cough or sore throat plus tachypnea were eligible. Participants were randomized 1:1 to receive empiric standard dose oseltamivir suspension or placebo twice daily for 10 doses, and then had respiratory specimens tested for influenza viruses. During hospitalizations, participants underwent standardized twice daily physical exams to assess key clinical outcomes which included duration of increased work of breathing and duration of hypoxia. Participants' guardians were interviewed about costs associated with the illness episode at the time of hospital discharge and again 7–9 days after hospital discharge.

Timeline: 2012–2014.

Progress and Findings: During September–October 2012 and April–August 2013, 551 participants were enrolled and randomized, of whom 327 (59%) were male and 292 (53%) were aged <1 year. Twenty-six (5%) of participants had laboratory-confirmed influenza.

This project is occurring in El Salvador and Panama.



← PECOS investigators from CDC, the Universidad del Valle de Guatemala (UVG), and Hospital del Niño (HDN) and study monitors at a meeting to discuss study progress in Panama City, Panama. From left to right, Jorge Jara (UVG), Salvador Rivera (UVG), Fatimah Dawood (CDC), Patricia Durango (UVG), Angie Donado (HDN), Ilenia Forero (HDN), Mariana Rodríguez (HDN), Dora Estripeaut (HDN), Onix de Suman (HDN),



← Dr. Cesar Ortiz draws up study medication for a newly enrolled PECOS participant at Hospital San Juan de Dios de Santa Ana, Santa Ana, El Salvador.



↑ Dr. Leonidas Benavides administers a questionnaire about costs of hospitalization to a parent of a PECOS participant at Hospital Materno Infantil José Domingo de Obaldía, David, Panama.

Timing of Influenza Activity, Predominant Strains, and Match to Available Vaccine Formulations in the Americas

Analyses of virology surveillance data in the Americas.

Study Aims and Objectives:

- Describe the timing of influenza activity in tropical countries before and after the pandemic.
- Assess which antigenic characteristics seemed predominant annually during the past decade.
- Determine which vaccine formulations were best matched to identified strains.
- Explore ecological associations between the timing of influenza activity and climate parameters.

Approach: We obtained the monthly number of samples which tested positive for influenza from the World Health Organization. We defined epidemics as months when the proportion of samples that tested positive for influenza exceeded the annual median. We also obtained antigenic characterization data from the CDC. We defined influenza strains as predominant during each season if they comprised the largest proportion of positive samples.

Timeline: Used data from 2002–2013.

Progress and Findings: South America reported 690,015, Central America 58,542, and North America 3,773,340 samples to the World Health Organization. Southern influenza seasons started on average in May and Central America seasons in June. South America submitted 2,625, Central America 1,225, and North America 21,333 samples for antigenic characterization. Preliminary findings suggest that southern strains were predominant in five (71%) of seven subsequent Central American and six (67%) of nine North American seasons. Central American strains most often matched the southern hemisphere vaccine formulation (57% of years).

Conclusion: Strains identified in South America typically became predominant in subsequent Central and North America seasons. Central America should consider vaccinating with the southern hemisphere formulation.

This project is occurring in Belize, Costa Rica, Honduras, Guatemala, El Salvador, and Panama.

Demographics and Clinical Characteristics of Influenza A(H1N1)pdm09 Deaths

Analysis of surveillance data.

Study Aims and Objectives:

- Explored the demographics and clinical characteristics persons who died with influenza A (H1N1) pdm09 infection during 2009–2010.

Approach: We identified influenza-associated deaths by hospital-based surveillance of severe acute respiratory infection (SARI) in Argentina and seven Central America countries (Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, Panama and Dominican Republic). A case of influenza-associated death was defined as a person with SARI (defined as sudden onset of temperature $>38^{\circ}\text{C}$, cough or sore-throat, and shortness of breath or difficulty breathing requiring hospitalization) who tested positive for influenza A (H1N1)pdm09 by real time polymerase chain reaction in the two weeks prior to death. We then abstracted decedents' demographic and clinical information from medical records and described these characteristics through proportions using Chi square, T-test and ANOVA as appropriate.

Timeline: 2009–2013.

Progress and Findings: Our case-series suggest that decedents in the Latin America were similar to those described by other case-series throughout the world. For example, during May 2009 to June 2010 Central America staff identified 186 cases with influenza A (H1N1)pdm09 decedents. The median age was 31 years and 48% were aged 15–44 years. One-hundred and three (55%) were female of which, 21 (20%) were pregnant, and seven (7%) were postpartum. Among 113 cases (61%) that had a pre-existing medical condition, 27 (24%) had obesity, 23 (20%) had diabetes, 21 (19%) had asthma, 15 (13%) had other chronic metabolic diseases, 11 (10%) had chronic obstructive pulmonary disease, 11 (10%) had seizure disorder, and seven (6%) had cerebral palsy. Sixty-nine percent of cases received treatment with oseltamivir, but only 9% received it within the first 48 hours of symptoms onset.

Conclusion: The pandemic affected the young and those with pre-existing medical conditions. Most patients belatedly sought health care after oseltamivir could provide much benefit. Based on these results, it may be useful to review the indications in targets groups and availability of oseltamivir in the country.

Related Published Paper: Balanzat AM, Hertlein C, Apezteguia C et al (2012) An Analysis of 332 Fatalities Infected with Pandemic 2009 Influenza A (H1N1) in Argentina. PLoS ONE 7(4): e33670. DOI: 10.1371/journal.pone.0033670.

This project is occurring in Argentina, Costa Rica, Dominican Republic, Honduras, Guatemala, El Salvador, Nicaragua, and Panama.

MADAGASCAR

Viral Etiology of SARI in Madagascar

In order to describe epidemiology and etiology of various viruses known to be responsible for SARI cases, we selected two hospitals in the SARI surveillance system in Madagascar. Samples were analyzed at the NIC for influenza detection and characterization, but also for the detection of other respiratory viruses, using a multiplex real-time PCR implemented at the NIC.

Study Aims and Objectives:

- Describe epidemiology of SARI cases.
- Study viral etiology of SARI cases.
- Identify risk factors for hospitalization.
- Estimate economic burden of SARI for Malagasy population.

Approach: Based on the SARI surveillance system implemented in 17 hospitals in Madagascar, we selected two hospitals for an active SARI surveillance (Antananarivo and Moramanga). Every hospitalized patient with clinical features of SARI syndromes is included in the study. Respiratory specimens are tested for a panel of 14 viruses developed at the NIC. Genetic studies are conducted to characterize Malagasy strains and see if there is a correlation between genotype and severity of the disease.

Timeline: This study began in November 2010 ended in August 2013.

Progress and Findings: From November 2010 to August 2013, 930 SARI cases were recruited, including 32 cases of aggravation and 37 deaths. Most patients included were less than five years old (>75%). NIC tested all samples of SARI cases for 14 respiratory viruses (influenza A and B; respiratory syncytial virus; human Coronaviruses HKU1, OC43, NL63 and 229E; human Metapneumovirus; human Rhinovirus; Parainfluenza virus type 1, 2 and 3; Adenovirus; Bocavirus). Among them 25.4% (236/930) were negative for all respiratory viruses tested. RSV was the most common virus detected with 37.3% of positivity rate, followed by influenza A (18.6%), HRV (13.7%) and adenovirus (8.3%).

Conclusion: The part of viral infection in SARI hospitalized patients is important. Some viruses may have a role in the severity of disease, particularly in the younger (<5 years old).

Seasonal Pattern of Influenza in Antananarivo, Madagascar, from 2002 to 2012

In settings where seasonal fluctuations in climate factors are limited, it has been proposed that non-environmental factors can dictate the seasonality of influenza, perhaps via population fluxes with regions that experience seasonal outbreaks. Madagascar is a particularly interesting case study because it is an island comprising a range of climatic zones, which presumably experiences relatively limited external virus seeding relative to the African continent. In this study, we aim to disentangle the contribution of environmental forcing and population travel on influenza transmission in Madagascar. We assess the association between influenza activity and local climate in Antananarivo (Madagascar's capital) and compare influenza activity patterns in countries in close proximity or with high connectivity to Madagascar.

Study Aims and Objectives:

- Describe influenza activities in Antananarivo, Madagascar, from 2002 to 2012.
- Describe the travel patterns in Madagascar from 2002 to 2012.
- Study temporal comparison with influenza circulation from other countries.
- Assess climatology effects on influenza detection in Antananarivo, Madagascar, from 2002 to 2012.

Approach: Influenza virus activity was based on laboratory testing of respiratory specimens contributed by Influenza Surveillance Sentinel Network participating to ILI surveillance in Antananarivo, Madagascar. We compiled the weekly numbers of influenza A/H3, A/H1, A/H1pdm and B positive specimens for the period 2002 to 2012. We obtained similar data from WHO FluNet to study viral activity patterns in countries in the Sub-Saharan African region and those contributing most foreign travelers to Madagascar (France, Germany). Weekly climate indicators were compiled for the study period.

Spearman cross-correlation and hierarchical clustering were used to assess statistical association between time series.

Timeline: We analyzed influenza detection in Antananarivo from 2002 to 2012 and compared it to the patterns of travels, to other countries detection and to climatologic factors during the same period.

Progress and Findings: Viral detection in Antananarivo did not reveal a clear seasonal pattern. Overall, the pattern of circulation of seasonal strains in this locality led viral activity in the Northern Hemisphere winter (in particular, France), and presented poor temporal matching with viral activity in other countries from the African continent. Influenza detection was not associated with any climatologic signal in Antananarivo.

Conclusion: Our analyses indicate that the timing of circulation of influenza strains in Antananarivo is not driven by influenza circulation from countries which contribute the most to volume of travelers to Madagascar, nor does it fall in months with most intense incoming travelers to the island. Therefore, the intriguingly irregular circulation of influenza in Madagascar may obey unidentified internal factors that are highly stochastic, rather than “echo” patterns from more connected places.

Related Published Paper: Influenza Seasonality in Madagascar: The Mysterious African Free-runner. (Article in preparation).

Outcome Risk Factors during Respiratory Infections in a Pediatric Ward in Antananarivo, Madagascar 2010–2012

Acute respiratory infections are a leading cause of infectious disease-related morbidity, hospitalization, and mortality among children worldwide, particularly in developing countries. In these low-income countries, most patients with acute respiratory infection (ARI), mild or severe, are still treated empirically. The aim of the study was to evaluate the risk factors in relation with the evolution and the outcome of respiratory illnesses in patients under 5 years old.

Study Aims and Objectives:

- Evaluate the risk factors in relation with the evolution and the outcome of respiratory illnesses in patients aged under 5 years old.

Approach: In the context of SARI surveillance implemented in Madagascar, we collected demographic, socio-economic, clinical, epidemiological data and samples for laboratory analysis from patients less than five years suffering from respiratory infections and hospitalized in a pediatric ward in Antananarivo. Deaths, clinical aggravation, hospitalization time more than 10 days were considered as worse outcomes. The impact of the co-infections has been also studied using multivariate analysis.

Timeline: We conducted a prospective study in a pediatric ward in Antananarivo from November 2010 to July 2012.

Progress and Findings: From November 2010 to July 2012, a total of 290 patients were enrolled. Co-infection was found in 192 patients (70%). The co-infections were more frequent in children under 36 months, with statically difference for the groups [19–24 months] (OR: 8.0). Sixty nine percent (230/290) of patients fully recovered without complication during hospitalization; 60 children had a worsening during hospitalization. Nine patients (3%) died. Risk factors significantly associated with worse evolution during hospitalization were admission for age group less than 6 months (OR= 5.3), comorbidities (OR= 4.6) and low household incomes (OR= 4.1).

Conclusion: Numerous respiratory infection hospitalized cases were due to viral and bacterial pathogens also found in community setting. Some of these etiologies could be prevented by vaccine (e.g. influenza, pneumococcus, haemophilus) to reduce the burden of respiratory diseases on childhood morbidity and mortality in low income countries.

Related Published Paper: Rajatonirina S, Razanajatovo NH, Ratsima E et al. Outcome risk factors during respiratory infections in a paediatric ward in Antananarivo, Madagascar 2010–2012. PLoS One. 2013 Sep 12;8(9):e72839. doi: 10.1371/journal.pone.0072839. eCollection 2013.

MALAWI

Enhanced Surveillance for Influenza in an African Population with a High Burden of HIV, Malaria and Malnutrition

Hospital-based surveillance for respiratory illness at Queen Elizabeth's Central Hospital.

Study Aims and Objectives:

- Provide robust surveillance for Severe Acute Respiratory Infection (SARI) in the context of HIV, malaria and malnutrition amongst adults, pregnant women, and children presenting to Queen Elizabeth Central Hospital, Blantyre, Malawi. Surveillance will include viral and bacterial respiratory pathogens and assess implications of co-infection.
- Assess the severity (attendee hospitalisation rate, high-dependency care admission rate) and outcome (hospital attendee mortality) of laboratory proven influenza and examine the influence of HIV, malnutrition and malaria on influenza presentation and outcome.
- Document the frequency of secondary invasive bacterial infections in adults and children with influenza-associated SARI and examine the influence of HIV, malnutrition and malaria.
- Evaluate the utility of the TAC diagnostic platform on samples from SARI patients and non-SARI controls.

Approach: All patients presenting to pediatric and adult admission and emergency units are screened for fever and respiratory symptoms. Each day the first four subjects meeting the SARI case definition are enrolled in the pediatric unit and four are enrolled from the adult unit. During the pandemic period up to 10 children/adults meeting the case definition were sampled. Nasal aspirates are collected for influenza testing by rRT-PCR.

Timeline: Initiated in 2011.

Progress and Findings: Over 1,500 case-patients were enrolled in SARI surveillance in 2011. Influenza was in circulation from January to September 2011 with peak percent positive in March and April. Adults with SARI were more likely to be HIV-infected than adults with ILI ($p < 0.01$).

Conclusion: Influenza contributed substantially to the burden of acute respiratory illness among children and adults seeking hospital care in Malawi.

Related Published Papers: In preparation.

A photo of the Queen Elizabeth Central Hospital in Blantyre, Malawi. It is the largest hospital in Malawi. ➔



The Association between Malaria, Influenza and Lower Respiratory Tract Infection in Malawian Infants

This work will aim to assess the contribution of influenza virus infection to pneumonia and severe malaria in Malawian children <1 year of age presenting to a large Central Hospital in Malawi. Specifically we will investigate whether influenza infection is associated with an increased risk of having World Health Organization (WHO) defined radiological pneumonia (WHO-RP) and non-WHO defined radiological pneumonia in hospitalized Malawian infants with clinical LRTI.

Study Aims and Objectives:

- Determine the proportion of infants with WHO defined radiological pneumonia (WHO-RP) and non-WHO defined radiological pneumonia (Other-RP) who are co-infected with influenza.
- Determine the proportion of clinical pneumonia co-infected with influenza.
- Determine the proportion of severe hypoxaemic pneumonia co-infected with influenza.
- Determine the prevalence of antibodies to seasonal and pandemic influenza virus amongst infants presenting with pneumonia, with and without concurrent influenza infection.
- Determine the potential modifying effect of malaria on the association between influenza virus and pneumonia.

Approach: Infants meeting the WHO-RP and clinical pneumonia case definitions will have nasal aspirates collected for influenza virus testing by rRT-PCR.

Timeline: Under IRB review, anticipated start date October 2013.

Progress and Findings: Under IRB review.

The Prevalence of Serum Antibodies to Seasonal and Pandemic Influenza Virus in Pregnant Women and their Infants

Assess the prevalence of serum antibodies to influenza in pregnant women in the third trimester and transplacental transfer to their infants in a population with a high burden of HIV, malaria and malnutrition.

Study Aims and Objectives:

- Determine the prevalence of influenza antibodies amongst mothers and their new born infants
- Assess the influence of maternal HIV and placental malaria on influenza antibody transfer.

Approach: Women will be consented and enrolled in this study when they present at the labor ward for delivery. A peripheral blood sample will be obtained from the mother to document the presence of circulating influenza antibodies and this will be compared to antibody titers found in a cord blood sample from the infant. The potential impact of HIV and/or placental malaria on antibody titers will be assessed controlling for gestational age of the infant estimated by Ballard exam.

Timeline: Subject recruitment began in June 2013.

Progress and Findings: Nearly 200 women have been enrolled to date, another 100 will be enrolled.

The Influence of Influenza and HIV on Clinical Severity and Outcomes of Respiratory Illness in Adults

This work will include a case control study of adult inpatient SARI subjects and outpatient ILI subjects to assess the influence of HIV infection and influenza on clinical severity in hospital-attended cases of respiratory illness. It will also assess the role of influenza, other bacterial and respiratory pathogens, HIV and other clinical factors on outcomes of in-patient pneumonia cases.

Study Aims and Objectives:

- Assess the impact of HIV on clinical severity of influenza infections.
- Assess the role of influenza and other pathogens on outcomes of pneumonia hospitalizations.

Approach: Additional clinical data are abstracted from HIV-infected SARI case-patients. Patients are also followed-up at home four weeks post-discharge to assess outcomes.

Timeline: Initiated in 2013, enrollment ongoing.

Progress and Findings: Pending.

Nosocomial Transmission of Influenza and RSV in a High-dependency Unit for Infants <6 Months of Age

This work will evaluate new onset respiratory illness in infants <6 months of age hospitalized three or more days in the high-dependency nursery at Queen Elizabeth's Hospital, a large referral hospital in Blantyre.

Study Aims and Objectives:

- Determine the frequency of nosocomial influenza and RSV acquisition in the high-dependency nursery.
- Determine whether physical location in the unit, respiratory symptoms in mothers, or other factors affect nosocomial transmission of influenza and RSV.

Approach: Caregivers of infants admitted to the high-dependency nursery will be asked to participate in the study. Infants <6 months old with new onset respiratory illness hospitalized three or more days in the high-dependency nursery will be considered possible cases of nosocomial transmission. Nasal aspirates will be obtained from enrolled infants on admission, at three days, at seven days and then weekly until hospital discharge.

Timeline: Study began enrollment in September 2012.

Progress and Findings: There has been little influenza circulation in the community this year and therefore little nosocomial transmission of influenza. However, several cases of RSV have been detected.

Conclusion: Pending.

NICARAGUA

Nicaraguan Influenza Birth Cohort Study

Birth Cohort Study.

Study Aims and Objectives: Estimate influenza-associated illness rates among young children.

Approach: We plan to enroll infants into the study for three years, with 250 infants recruited each year and followed until two years of age, for a total sample size of 750 infants. Approximately 21 newborns, aged four weeks or less, are enrolled in the study each month to maintain the age structure. Families of infants are contacted on a weekly basis by study personnel, and data on daily symptoms are collected using diary cards. Children are provided with all primary medical care through the study, and 189 variables are collected at each medical visit. All participants presenting with fever or reported fever are tested for influenza by RT-PCR. Respiratory samples are collected at the participant's home in the event that the family does not bring the infant in to the health center for a consultation. Yearly blood samples are collected beginning at 6 months of age to enable detection of asymptomatic influenza infections and to evaluate nutritional status. Socio-economic, household risk factor, and breastfeeding data are collected at enrollment and on a yearly basis.

Timeline: 2011–2013.

Progress and Findings: As of August 15, 2013, 528 infants have been enrolled, with a median age at enrollment of 14 days. At enrollment, a majority of infants were breastfed (95.3%); however, only 48.9% were exclusively breastfed. The participants attended more than 6,222 medical visits at the study health center. Among the 528 infants who participated in the study, the incidence of influenza was 33.9 cases per 100 child-years (95% CI: 29.0, 39.6). A majority of influenza infections occurred in infants aged 6 months and older. A total of 142 participants were transferred to the hospital. Forty-seven percent of the transfers to the hospital were for respiratory illness; one infant was transferred for bronchial hyperactivity and 52 for pneumonia. Three infants died of pneumonia.

Conclusion: Infants in Nicaragua experience a high incidence of influenza with a majority of cases occurring in infants aged 6 months and older.

NEW ZEALAND

Southern Hemisphere Influenza and Vaccine Effectiveness Research and Surveillance Study (SHIVERS)

In September 2011, the Institute of Environmental Science and Research (ESR) in New Zealand was awarded a five-year research cooperative agreement with CDC, to conduct a five-year study in the southern hemisphere on influenza and other respiratory diseases; their burden, epidemiology, transmission, risk factors, and the effectiveness of vaccination.

Study Aims and Objectives: The SHIVERS study has nine objectives.

- Determine the incidence and prevalence of severe acute respiratory infections.
- Assess influenza vaccine effectiveness.

- Study the interaction between influenza virus and other pathogens.
- Ascertain the causes of respiratory mortality.
- Determine the incidence and prevalence of non-severe respiratory illness.
- Conduct an influenza seroprevalence study.
- Determine influenza risk factors.
- Study the immune response to influenza.
- Determine the health care and societal economic burden and vaccine cost-effectiveness of influenza.

Approach: A multi-centre and multi-disciplinary collaboration between ESR, Auckland District Health Boards (ADHB), Counties Manukau District Health Board (CMDHB), University of Otago, University of Auckland, the WHO Collaborating Centre at St. Jude Children's Hospital in Memphis, USA, and the U.S. Centers for Disease Control and Prevention, to set up hospital and general practitioner-based surveillance in the Auckland area.

Timeline: Hospital-based surveillance for SARI was established in year one. Year two of the study focused on establishing influenza surveillance through primary health care providers and developing robust estimates of vaccine effectiveness.

Progress and Findings: Since 30 April 2012, four hospitals serving ADHB and CMDHB have enrolled and tested 2,550 SARI cases, of which 453 (18%) tested positive for influenza. Infants under one year experienced the highest rate of influenza hospitalization (412/100,000) followed by persons 80 years and older (223/100,000). Rates among Pacific People and Maori were 136 and 70/100,000 respectively compared to 38/100,000 among those of European descent.

Conclusion: The SHIVERS study is expected to answer many questions related to the epidemiology of influenza in a southern hemisphere setting at a time when influenza is not circulating in the northern hemisphere through enhanced real-time surveillance in hospitals and primary health care providers

PERU

Influenza Seasonality, Incidence and Economic Burden in Four Ecologically Diverse Regions of Peru

Population-based surveillance.

Study Aims and Objectives:

- Describe the variation in incidence rates, health seeking behavior, and seasonal pattern of influenza illness in four different regions of Peru.
- Estimate the direct and indirect costs of influenza episodes according to the health care utilization per episode from June 2009 to December 2010 in Peru.
- Explore between influenza illness, pre-existing conditions, and vaccine use.

Approach: Since 2009 NAMRU-6 has conducted active community-based household surveillance in four ecologically distinct regions of Peru: coastal desert (Lima), dry forest (Tumbes), highlands (Cuzco) and

rainforest (Puerto Maldonado). Approximately 7,200 people in 1,500 randomly selected households are visited three times per week. Nasopharyngeal swabs are collected from persons with influenza-like illness (ILI) and tested for influenza virus by RT-PCR.

Timeline: January 2009–September 2014.

Progress and Findings: After 15,583 person-years (PY) of follow-up (the overall influenza incidence was approximately 102/1,000 PY (95% CI: 97–107). Of these, 46/1,000 PY (95% CI 43–50) sought care, 0.8/1,000 PY (95% CI: 0.5–1.4) required hospitalization, and one died. Overall, the highest total cost was observed in the hospitalized category, US\$263 (median 171; IQR 145) and the lowest in the self-treated category, US\$19 (median 13; IQR 21). Overall, 92% of study participants took some medication for their ILI, of which 13% were prescribed by a physician.

Conclusion:

- Laboratory confirmed influenza illness burden in Peru is considerable particularly in children less than 11 years of age.
- Influenza poses a significant economic burden to the ill person and their households.
- Prescription drugs, including antibiotics, are frequently taken by persons with ILI.

Intra-household Backyard Influenza Cross-species Transmission Dynamics in Semi-rural Communities in Peru

Population-based surveillance.

Study Aims and Objectives:

- To assess the prevalence of antibody to pandemic H1N1 influenza virus (pH1N1) and to detect active infection in swine from community backyard farms in Tumbes, Peru, before, during, and after the pandemic.

Approach: We conducted surveillance for influenza among backyard swine in Tumbes, Peru, from 2009 to 2011. Sera, tracheal swabs, and lung samples were collected in March 2009 (pre-pandemic), October 2009 (human pandemic peak), April 2010 and October 2011 (post pandemic). The hemagglutination inhibition test to detect antibodies against pH1N1 virus was performed on sera. Tracheal swabs and lung tissue were cultured in SPF embryonated chicken eggs and positive specimens tested and sequenced by rRT-PCR.

Timeline: January 2009–September 2013.

Progress and Findings: We collected 1,303 sera samples, 923 tracheal swabs, and 962 lung samples. None of the 310 animals sampled during pre-pandemic period were positive by PCR or HI. Antibody prevalence to pH1N1 during the pandemic was 8% (27/321), with virus isolation from three tracheal swabs (1%) and one lung sample (< 1%). Samples from the two post-pandemic periods showed an antibody prevalence of 24% (79/328) and 1% (4/343), respectively. No virus was isolated from the post-pandemic period. Characterization of pH1N1 isolates in pigs confirmed a close phylogenetic relationship with human isolates circulating at the time in Tumbes.

Conclusion:

- Infection with pH1N1 in backyard swine occurred frequently during and after the pandemic period in Tumbes.

- Continuous surveillance at different production levels (i.e. pig farms and slaughterhouses) is necessary in order to monitor zoonotic and interspecies transmission of pH1N1 and swine influenza viruses in Peru.

Related Published Paper: Manuscript currently under development: Cross-species transmission of pandemic influenza (pH1N1) virus from humans to backyard pig farms in semirural communities in Tumbes, Peru.

Influenza Virus Surveillance in Swine Populations of Peru

Population-based surveillance.

Study Aims and Objectives:

- To determine the different strains of influenza (swine, avian and human) circulating swine raised in the Department of Lima and surrounding areas of the central coast of Peru.

Approach: Surveillance was conducted at a central slaughterhouse in Lima in which animals are brought from Lima and the surrounding region. Upon arrival at the facility, animals were inspected for health status and kept in groups according to the seller for a maximum of 14 hours. Blood and nasal and tracheal swab specimens were collected at the time of slaughter. Serum was tested for IgG antibody to influenza A virus by ELISA (IDEXX Laboratories, Maine, USA) and the swab samples by rRT-PCR using the CDC Flu A assay to detect universal influenza A virus. PCR positive samples were further analyzed with subtype-specific primers.

Timeline: January 2009–September 2013.

Progress and Findings: From December 2011 to May 2012, 963 adult pigs were sampled, with a prevalence of IgG antibody of 60% (573/958) and 4% (42/963) of animals positive by PCR. Subtype identifications from the 42 PCR positive animals were 25 (60%) pandemic H1N1, 8 (19%) H3, 6 (14%) seasonal H1, and 4 (10%) unsubtypeable, on which sequencing is presently underway. H1 pandemic/H3 co-infection was noted in 3 (7%) samples.

Conclusion: Pigs in the study area are frequently infected with influenza A viruses, primarily human subtypes, providing ample opportunity for coinfections and reassortment.

Related Published Paper: Manuscript currently under development: Influenza A Virus in Swine in Peru.

SENEGAL

Safety, Immunogenicity, and Effectiveness of Influenza Vaccines among Children in Senegal

These research activities encompass three separate but related clinical trials to evaluate the safety and immunogenicity of inactivated, adjuvanted, and live-attenuated influenza vaccines, as well as the effectiveness of live-attenuated and inactivated vaccines among children in Senegal.

Study Aims and Objectives:

- Evaluate the direct and indirect effectiveness of inactivated influenza vaccine (IIV) in reducing influenza among vaccinated children and their communities, as compared to inactivated polio vaccine (IPV).

- Evaluate age-specific post-vaccination immune responses to IIV among a subset of vaccinated children.
- Estimate the immunogenicity of MF59-adjuvanted IIV by age group, and compare these findings with immunogenicity of unadjuvanted IIV.
- Estimate the efficacy of live-attenuated influenza vaccine (LAIV) in reducing influenza among LAIV-vaccinated children, as compared to those receiving placebo.
- Describe the safety profiles of IIV, MF59-adjuvanted IIV, and LAIV in this population.

Approach: This research is conducted through a partnership with PATH, the Institut de Recherche pour le Développement (IRD), and Institute Pasteur Dakar. Study One is a Phase IV village-randomized trial to evaluate of the direct and indirect effectiveness of IIV. In this study, ~3,500 children aged 6 months to 10 years received either IIV or IPV control, with a small subset of vaccinated children providing additional immunogenicity and safety data following vaccination. Study Two is a Phase 2b trial to evaluate the immunogenicity of MF59-adjuvanted IIV. For Study Two, ~300 children 6 months through 5 years of age were randomized to receive either MF59-adjuvanted IIV, IIV, or placebo, and followed for up to four months for safety outcomes. Study Three, a Phase III trial to evaluate the efficacy of LAIV, randomized ~1,700 healthy children 2 years through 5 years of age to receive LAIV or intranasal placebo. Laboratory-confirmed influenza outcomes among vaccinated children (for Study One and Study Three) and consenting unvaccinated persons (for Study One only) are collected by a combined approach of active and passive influenza surveillance by routine visits to study households and village health posts.

Timeline: August 2008–July 2014.

Progress and Findings: Three vaccination rounds with IIV and IPV control took place each spring from 2009 to 2011, with full vaccination of between 7,600 and 9,500 eligible children annually. Surveillance activities for IIV direct and indirect effectiveness (Study One) continued until the end of 2012. During this time, over 20,000 febrile respiratory episodes were identified and tested for influenza, with influenza A(H1N1)pdm first detected in February 2010. Vaccination activities for Study Two and Study Three were carried out in spring 2013, with follow-up and laboratory testing ongoing.

Conclusion: Influenza viruses are a major cause of febrile respiratory illness in this population. Preliminary year one findings of IIV effectiveness indicate that although vaccine was not matched to the drifted influenza A(H3N2) virus that circulated widely in the population, significant reduction in laboratory-confirmed influenza was still measured among vaccinated children. Moreover, significant benefit was measured at the level of the entire community, including unvaccinated children too young to receive vaccine and unvaccinated adults.

SOUTH AFRICA

Prospective Cohort Study of Influenza Viral Shedding in HIV Infected and Uninfected Adults

This study aims to assist with the description of influenza viral shedding in a high HIV prevalence setting. The results will assist with policy recommendations on the use of antiviral drugs in HIV infected and other persons at risk for severe illness or increased transmission due to prolonged shedding.

Study Aims and Objectives:

- To determine the time period (range and median) in days that HIV-infected and -uninfected adults continue to shed influenza virus after influenza symptom onset using quantitative reverse transcriptase (RT)-PCR and viral culture.
- To compare the intensity of influenza virus shedding (viral load) amongst HIV-infected and – uninfected adults.
- To correlate the duration of influenza virus shedding detected by RT-PCR and viral culture with influenza signs and symptoms.
- To determine amongst HIV-infected adults whether individuals with more severe immunosuppression (based on CD4 count) shed influenza virus for longer and with greater intensity than individuals with higher CD4 counts.
- To assess factors that may affect influenza virus shedding dynamics.

Approach: Patients who are enrolled into the influenza-like illness surveillance programme at public health clinics are tested for influenza by rapid test and enrolled into the shedding study if they test positive for influenza. Respiratory samples are taken for qualitative and quantitative viral testing. Patients are then followed up at regular interval until 28 days post presentation. Respiratory samples are collected at each visit. HIV status is also determined at enrollment to ensure enrolment of HIV-infected and HIV-uninfected patients.

Timeline: The influenza shedding study started in the 2012 influenza season and is ongoing through the 2013 season.

Progress and Findings: Thirty seven patients have been enrolled. Eleven patients completed follow up in the 2012 influenza season. The median age of patients was 13 years (range 3–38 years) and 73% (8/11) were male. One patient was later hospitalized with severe acute respiratory illness. Eight patients had A(H3N2) and three had influenza B. One child had prolonged viral shedding of A(H3N2) of 14 days duration.

Conclusion: With the small number of patients who have complete data, it is difficult to draw conclusions.

Household Transmission Study of Influenza Virus from HIV-infected and—uninfected Index Cases, South Africa

Understanding the transmission dynamics of influenza virus in settings with high HIV-prevalence is important to be able to properly advise and implement appropriate public health measures for influenza control. In this study, we aim to characterize the transmission dynamics of influenza virus from HIV-infected and— uninfected index cases to household contacts.

Study Aims and Objectives:

- To determine the secondary infection risk and associated risk factors in household contacts of HIV-infected and -uninfected index cases in South Africa.

Approach: Participants will be recruited from the ongoing influenza-like illness (ILI) surveillance program. Potential participants with ILI will be screened at primary health care facilities in Pietermaritzburg and Klerksdorp. Patients meeting the enrollment criteria of a positive rapid influenza test and agreement to HIV testing will be enrolled as index cases following informed consent. A home visit will then be scheduled

to enroll household contacts of those with a positive rapid influenza test for follow-up. Household contacts will be offered HIV testing at the initial visit. Nasopharyngeal swabs and questionnaires will be administered at follow-up visits to household contacts.

Timeline: Patients will be enrolled through the 2013 and 2014 influenza seasons.

Progress and Findings: Thirty-two index patients and 66 household members have been enrolled.

Conclusion: This study will add to the burden and risk factor influenza data that will inform vaccine programmes and resource allocation at policy level.

Estimating the Economic Burden of Respiratory Illness Associated with Influenza and Respiratory Syncytial Virus in South Africa

This study aims to describe the patient and hospital/clinic costs associated with influenza-like illness and severe influenza-related severe acute respiratory illness (SARI) in order to inform policy on influenza prevention (vaccine), influenza treatment (antiviral) and resource allocation. The study enrolls patients enrolled into the SARI surveillance programme and collects data on the cost of hospitalization including direct costs (e.g., medication, procedures) and indirect cost (e.g., staff, administration) related to admission. The patients cost in terms of transport, payment for medical care and loss of income are collected by interview.

Study Aims and Objectives:

- To estimate the annual cost of hospitalized severe acute respiratory illness and outpatient influenza-like illness (ILI) of any aetiology in South Africa.
- To estimate the annual cost of hospitalized severe acute respiratory illness and outpatient influenza-like illness (ILI) associated with influenza in South Africa.
- To estimate the annual cost of hospitalized severe acute respiratory illness and outpatient influenza-like illness (ILI) associated with respiratory syncytial virus in South Africa.

Approach: Patients are enrolled in age groups each week at all SARI and ILI surveillance sites. Data on hospital/clinical costs will be sourced from each hospital/clinic and from published health care costs which are available at district level. Hospital day bed costs and length of hospital stay will provide the base for the costing model. Additional costs of procedures, laboratory costs and medication will be added to the costing model for each patient. Initially a model will be built for all cause SARI and then costs for pathogen specific admissions will be constructed.

Timeline: Enrollment started in March 2013 and will continue through March 2014.

Progress and Findings: The target sample size of 144 patients is nearly completed, however there are challenges in recruiting certain age groups (young adults and the elderly) so enrollment will continue through 2013. Site visits to collect hospital cost will start in September 2013, with the aim to start data analysis early in 2014.

Conclusion: Costing of influenza will inform policy on resource allocation and is an important component of a national influenza policy.

Development of a Severe Respiratory Disease Clinical Score— South Africa

Respiratory diseases are a common cause of morbidity and mortality worldwide. In South Africa, respiratory diseases are the second most common cause of death. Health care providers often use pneumonia severity prediction tools to quickly identify patients at highest risk of severe outcomes, such as death or Intensive Care Unit (ICU) stay, early in their presentation. Such tools help to identify which patients may require additional interventions and can help distribute scarce health care resources. Although many pneumonia severity prediction tools exist, most have been developed and tested in North America and Europe in populations that may differ from those in South Africa. The ability of existing tools to accurately predict severity in patients with severe respiratory disease in South Africa is unknown.

Study Aims and Objectives:

- To validate existing pneumonia severity prediction tools in inpatient adult populations (≥ 18 years) at three sites in South Africa.
- To develop a new respiratory severity prediction tool for adults including HIV-specific variables, such as CD4 count, and compare its performance to existing severity scores.

Approach: We will use data collected as part of ongoing surveillance for severe acute respiratory illness (SARI). All adult patients enrolled in SARI will be included in the analysis population. Patients from June 2010–June 2012 will be included. Some variables important in forming a respiratory illness severity prediction tool which are not included in the SARI database will be abstracted from patient charts.

Timeline: Complete by July 2014.

Progress and Findings: Data extraction is completed. Data analysis is to begin soon.

Conclusion: The goal of this study is to help health care providers accurately triage patients at greatest risk of severe outcomes of respiratory illness in settings which may have limited resources and a high prevalence of HIV or tuberculosis.

Surveillance for Outpatient Influenza-Like Illness and Asymptomatic Respiratory Virus Colonization in South Africa

We make use of the structure provided by the public health care influenza-like illness surveillance platform to enroll patients asymptomatic for respiratory illness.

Study Aims and Objectives:

- To describe the burden and aetiology of outpatient ILI in children and adults in selected sites in South Africa, in HIV-infected and HIV-uninfected populations.
- To determine the prevalence of selected respiratory viruses in a subset of asymptomatic children and adults, i.e., colonization, in selected sites in South Africa.
- To determine the relative contribution of selected respiratory pathogens to severe respiratory disease in a setting with a high prevalence of HIV by comparing to individuals with ILI or who are asymptomatic.
- To determine risk factors for development of severe disease due to influenza and other respiratory viruses by comparing asymptomatic illness to mild and severe disease.

- To identify the strains of influenza and the genotypes of rhinovirus, enterovirus, adenovirus, and respiratory syncytial virus responsible for asymptomatic and mild respiratory infections among humans.
- To characterize and determine cytokine profiles associated with asymptomatic and mild respiratory syncytial virus, rhinovirus, and other respiratory viruses, among individuals with and without HIV co-infection.

Approach: Patient attending primary health clinic for non-respiratory ailments with no respiratory symptoms in the preceding 14 days are systematically enrolled by age group and HIV status. Meaning that patients enrolled represent all age groups and are equally enrolled by HIV status. Respiratory samples in the form of nasal pharyngeal aspirates or throat swabs are collected and tested at NICD for 13 respiratory viruses and for *Streptococcus pneumoniae*, *Bordetella pertussis*, *Haemophilus influenzae* type B, atypical bacterial causes of pneumonia (*Legionella* species, *Chlamydia pneumoniae* and *Mycoplasma pneumoniae*).

Timeline: Started enrolling in March 2013 and enrollment is ongoing.

Progress and Findings: Up to June 2013, 544 healthy controls have been enrolled. As compared to healthy controls patient with influenza were eight times for likely to have ILI (Adjusted relative risk ratio (aRRR) 8.2 (95% confidence interval CI 4.3–15.7) and three times more likely to have SARI (aRRR 3.4 95%CI 1.8–6.7). Similarly patient with RSV (ILI:aRRR 1.8(95% CI1.1–2.8 and SARI aRRR2.5 (95% CI 1.6–3.8)) and hMPV (ILI: aRRR10.9 (95% CI 2.6–45.2) and SARI 6.2(95%CI 3.0–45) were associated with ILI and SARI. Although rhinovirus (ILI: aRRR 1.6 (95%CI 1.2–2.1) and SARI (aRRR1.4 95% CI 1.1–1.9) was associated with ILI and SARI the measure of effect was small and so the clinical significance is marginal. Comparing clinical factors associated with SARI as compared to ILI, HIV infection (odds ratio (OR) 2.2 (95% CI 1.1–4.5) and extremes of age (age<5 years OR 3.9; 95% CI:1.7–9.0) and age 65 years and older, OR 9.7 (95% CI 2.3–41.7) were associated with severe infection.

Conclusion: This study will allow us to describe the respiratory viruses associated with ILI and SARI in a high HIV prevalence setting.

Human Infections with Avian Influenza H7N1 and H5N2 Strains during Outbreaks in Ostriches

Several avian influenza outbreaks have been reported in ostriches over the last 10 years in South Africa, the most recent in the Western Cape being highly pathogenic Influenza A H5N2 in 2004 and 2011, low pathogenic (LPAI) H7N1 in 2012 and H7N7 in 2013. No evidence exist of H5N2 and H7N1 strains causing severe disease in humans although a serosurvey in 2004 documented serological evidence of H5N2 infection in 3 of 129 highly -exposed persons. Recent emergence of LPAI H7N9 causing severe disease in humans in China and the continued threat of highly pathogenic (HPAI) H5N1 in Asia and other areas raise the question as to the risk of infection and possible symptoms due to other LPAI H7 or HPAI H5 strains in humans.

Study Aims and Objectives:

- To conduct a serosurvey of at-risk persons during the 2011 and 2012 outbreaks and track positive cases retrospectively to identify symptoms.

Approach: In August 2011 and August 2012, sera were collected from 207 and 66 people respectively with a history of direct contact with ostriches infected with AI H5N2 (2011) or H7N1 (2012) either through handling or slaughtering of infected birds. Sera were also collected from 38 state veterinarians from across the country at an annual congress in 2012 a proportion that had been involved in the AI outbreaks.

Questionnaires including demographic, occupational characteristics and clinical illness history data were administered during the 2011 outbreak while an abbreviated questionnaire and retrospective follow up of seropositive people occurred in 2012. Hemagglutination inhibition assays (HAI) reference antigens as well as outbreak- specific inactivated were run at the National Influenza Centre, NICD against H5 and H7 AI and human influenza specific control antisera and serum samples from study participants.

Timeline: The serosurvey was conducted at two time points. Neutralization confirmation is expected by November 2013.

Progress and Findings: Of 207 veterinarians, ostrich farmers, farm workers and abattoir workers exposed to avian influenza H5N2, and 66 exposed to H7N1 in the 2011 and 2012 outbreaks three people with HAI antibody titers greater than 1:40 to influenza H5N2 and one person with H7N1 antibodies were identified. For H5N2 this included a veterinarian who was actively involved in post-mortem investigations of ostriches, a farm worker and an abattoir worker. The H7N1 positive person was an abattoir worker. Reported symptoms included conjunctivitis and influenza-like illness for two of the H5N2-seropositive cases, whilst the third H5N2 seropositive case and the single H7N1 seropositive case reported no symptoms.

Conclusion: A low risk exists for human infection with Influenza A H5N2 (1.4%) and H7N1 (1.6%) during outbreaks amongst ostriches suggesting a need for increased biosecurity and surveillance of humans in contact with ostriches during avian influenza outbreaks, even if the strains are LPAI or birds are asymptomatic.

Pneumocystis jirovecii (PCP), tuberculosis (TB), *Streptococcus pneumoniae*, *Bordetella pertussis*, *Haemophilus influenzae* type B and Atypical Bacterial Causes of Pneumonia (*Legionella* species, *Chlamydia pneumoniae* and *Mycoplasma pneumoniae*) in Hospitalized Patients with Severe Acute Respiratory Infections (SARI)

This study makes use of the SARI programme structure to take additional samples from patients admitted with a longer duration of symptoms (14 days) and suspected TB. In addition to the upper respiratory tract samples taken as part of SARI, an induced sputum sample is collected.

Study Aims and Objectives:

- To estimate the incidence of and proportion of patients with PCP, TB, *Streptococcus pneumoniae*, *Bordetella pertussis*, *Haemophilus influenzae* type B and atypical bacterial causes of pneumonia (*Legionella* species, *Chlamydia pneumoniae* and *Mycoplasma pneumoniae* in HIV-infected and HIV-uninfected patients admitted with severe acute respiratory illness (SARI).
- To estimate the extent of respiratory virus co-infection with these cause of pneumonia and describe how these viral co-infection relate to patient morbidity and outcome.

Approach: Samples collected as part of the SARI surveillance will be tested for the additional pathogens. A modified case definition to include a longer duration of symptoms and a physician diagnosis of suspected TB will be used to enroll patients at two sites. Additional specimens will be collected to enhance detection of PCP and TB; these include induced sputum and oropharyngeal mouth rinse. TB samples will be tested by Gene Xpert and followed up by culture. PCP samples are to be tested by PCR.

Timeline: Recruitment started in 2012 and continues through 2013.

Progress and Findings: From June 2013 to date the following tests have been conducted. At total of 1,469 oral washes have been tested for PCP and 5% (74) were positive, 810 induced sputa samples were tested and 11% (88) were positive for PCP. Of the 2,085 nasopharyngeal samples that were tested 7% (146) were positive for PCP DNA. To date 1,231/1,984 (61%) of enrolled patients have been tested for TB and 22% (271) were positive for TB. The detection rate for atypical bacteria was higher on induced sputa (N=728): with a 1% (9) detection rate for *Mycoplasma pneumoniae*, 0.3% (2) for *Chlamydia pneumonia* and 3% (19) for *Legionella* species.

Conclusion: PCP and TB infection is commonly associated with SARI in our setting. Validation of testing methods for PCP is not complete but it appears induced sputa has a higher detection rate for PCP. Although the detection rate for atypical bacteria is low these pathogens are more commonly detected in the 15–45 age group, the age group with the highest HIV prevalence.

Health care Utilization Surveys— Soweto, Gauteng Province, and Klerksdorp, Northwest Province

Understanding patterns of health care utilization in South Africa for common illnesses and conditions such as respiratory disease including influenza and febrile illness such as enteric fever is important to be able to interpret sentinel surveillance data and estimate the true disease burden at the community level. In this study, we aim to characterize the health care utilization behaviors related to influenza-like illness, pneumonia, diarrhea, meningitis, febrile illness and death in a peri-urban site by conducting a cross-sectional survey.

Study Aims and Objectives:

- Estimate the catchment population, the proportion of people who seek medical care at sentinel surveillance sites for ILI, pneumonia and febrile illness, and characterize the health care utilization behaviors related to these illnesses; the catchment population will be used as denominator for incidence calculations and to adjust for residents not seeking care.
- Characterize health care utilization behaviors related to other conditions such as diarrhea, meningitis, and chronic respiratory illness.

Approach: We conducted a cross-sectional survey of representative samples of households throughout the catchment area of the Klerksdorp-Tshepong hospital complex and Chris Hani Baragwanath Academic Hospital and their surrounding regions. Sampled households were visited and administer a questionnaire on demographics and socio-economic factors, medical conditions, ILI in the last 30 days, pneumonia in the past year, diarrhea in the last 14 days, meningitis in the past year, and deaths in the last year. In addition, we collected GPS (global positioning system) coordinates of the interviewed household. For each disease syndrome, we collected information on the type of health care services sought and the services obtained.

Timeline: The survey is complete; analysis is ongoing.

Progress and Findings: Eighty six percent of target households were enrolled (1,426/1,653) in Klerksdorp and 71% (970/2,396) in Soweto. More than 50% of households had a monthly income of less than USD \$200. Most people were able to identify the symptoms of influenza-like illness, however the majority thought that influenza is caused by cold weather. A little more than half the respondents knew that there is a vaccine for influenza (821/1,426, 58% in Klerksdorp and 598/970, 62% in Soweto). The majority of respondents (1,202/1,426, 84% in Klerksdorp and 728/970, 75% in Soweto) said they would access a vaccine at a public health care clinic.

Conclusion: Early results suggest that people in the population access health care at primary health care clinics and public hospitals. This will allow us to estimate the population served by the hospital and facilitate models to estimate incidence of influenza and other respiratory illness in the community.

THAILAND

Randomized Controlled Trial of the Immunogenicity of Intramuscular versus Intradermal Trivalent Inactivated Split Virion Influenza Vaccine in HIV-infected Men who have Sex with Men in Bangkok, Thailand

This study will assess the efficacy of a new intradermal formulation of the trivalent inactivated influenza vaccine (TIV) compared to standard intramuscular TIV in HIV-infected men who have sex with men (MSM) in Bangkok, Thailand.

Study Aims and Objectives:

Primary Objective

- To assess humoral antibody responses to intramuscular versus intradermal TIV in HIV-infected MSM prior to vaccination and at one month, six months, and 12 months post vaccination. We will further characterize humoral antibody responses by low versus high CD4 cell count.

Secondary Objectives

- In a subset of participants, we will characterize cell-mediated immune responses to intramuscular versus intradermal TIV in HIV-infected MSM prior to vaccination and at one week, one month and six months post-vaccination. We will further characterize cell-mediated immune responses by low versus high CD4 cell count.

Approach: Randomized controlled trial.

Timeline: November 2011–September 2013.

Progress and Findings: We enrolled and vaccinated 480 participants (400 were HIV positive and 80 were HIV negative). Of the 480, 476 (99%) returned for the one month visit and 461 (96%) for the six month visit. The 12 month visits will be complete in September 2013. Investigators remain blinded and are drafting the analytic plan.

Conclusion: None yet.

Pediatric Respiratory Infections Cohort Evaluation (PRICE)

This is a longitudinal study to follow healthy and high-risk children aged 0–36 months for two years. At medically-attended respiratory events, swabs were tested for influenza and RSV by PCR; direct and indirect costs and outcomes were recorded.

Study Aims and Objectives:

Primary Objectives

- To measure the rate of influenza acquisition and duration influenza illness in a cohort of healthy children and children with underlying disease.

- To evaluate the difference in the rate of influenza acquisition and duration of influenza illness between healthy children and children with underlying disease.

Secondary Objectives

- To repeat the first two primary objectives for RSV.
- To assess and compare disease severity between healthy children and children with underlying disease.
- To assess the medical costs (direct and indirect) associated with influenza and RSV infections and the difference in costs between healthy children and children with underlying disease.
- To evaluate the predictive value of markers of nutritional and inflammatory markers particular Vitamin D with the incidence, duration and severity of influenza and RSV infections, as well as how these differ between healthy children and children with underlying disease.
- To investigate the relationship between environmental tobacco smoke exposure and occurrence of lower respiratory track disease and influenza and RSV infections.

Approach: Prospective, observational cohort study.

Timeline: Enrollment started August 2011, participants followed for two years.

Progress and Findings: We enrolled 466 high-risk and 619 healthy children. We will enroll until we get 500 high-risk children. Preliminary analysis is underway.

Conclusion:

- Compared to high-risk children, healthy children had higher incidences of influenza and RSV-associated ARI and incurred similar costs for outpatient influenza and RSV and hospitalized influenza.
- Influenza-associated ARI prevention should target both healthy and high-risk young children.

Influenza Vaccine Knowledge, Attitudes, and Practices in Pregnant Women and Their Providers in Thailand: A Vaccination Program Evaluation

To evaluate Thailand's current influenza vaccination program and develop additional strategies to address barriers to influenza vaccination, we conducted a knowledge, attitudes, and practices (KAP) survey of pregnant women and their health care providers to identify barriers to influenza vaccination and characterize perceptions of influenza and influenza vaccination during pregnancy.

Study Aims and Objectives:

Primary Objective

- To ascertain knowledge, attitudes, and practices related to influenza vaccination of pregnant women, including barriers to vaccination, among both pregnant women and their health care providers in Thailand.



A research nurse at Queen Sirikit National Institute of Child Health interviews a mother and child as part of prospective study on influenza in young children in Bangkok, Thailand.

Secondary Objective

- To identify predictors of willingness to receive influenza vaccine during pregnancy among pregnant women.

Approach: Survey.

Timeline: December 2012–June 2013.

Progress and Findings:

- Pregnant women: 967 (90%) of 1,072 pregnant women surveyed completed the questionnaire.
- Physicians: 643 (57%) of 1,134 completed the questionnaire.
- Analysis is ongoing.

Conclusion:

- Over half of Thai pregnant women were willing to get an influenza vaccine; however, influenza vaccine uptake was low.
- Subsidizing vaccine and encouraging health care providers of pregnant women to support influenza vaccination recommendations may be effective strategies to improve influenza vaccine uptake in Thai pregnant women.
- To improve influenza vaccination coverage among pregnant women, strategies are needed to increase vaccine availability and free vaccine services in ANCs in Thailand.
- Efforts to increase health care provider awareness of Ministry of Public Health recommendations for influenza vaccination are warranted and additional targeted outreach to physicians providing care to pregnant women should be considered.

Influenza Associated Mortality in Thailand, 2006–2011

We analyzed weekly mortality and viral data from 2006–2011 to estimate deaths attributable to influenza in Thailand.

Study Aims and Objectives:

- Estimate influenza-associated deaths in Thailand.

Approach: Negative binomial regression model.

Timeline: November 2012–June 2013.

Progress and Findings: Analysis ongoing.

Conclusion: Influenza-associated mortality in Thailand is much greater than previously appreciated.

UNITED STATES OF AMERICA (ATLANTA, GA)

Severe Acute Respiratory Infection (SARI) among Children less than Five Years of Age: Use of TAC Multiple Pathogen Detection Platform in International Influenza Program Sites (TAC-KID)

The TAC-KID study is a prospective case-control study aimed at understanding the etiology of severe respiratory disease among hospitalized children less than five years of age in four countries. The study will enroll case children less than five years of age who are hospitalized meeting the WHO case definition for severe acute respiratory infections and control children who visiting outpatient clinics but not experiencing an infectious illness over a 12-month period. Epidemiologic data including demographics, risk factors, clinical course of illness, treatment, and vaccination history will be obtained. Both nasopharyngeal and oropharyngeal swabs will be collected from case and control children and will be tested using the TaqMan array technology. The Taqman® Array Card (TAC, Life Technologies, Carlsbad, CA), is a multiple pathogen detection tool that uses a solid-phase quantitative polymerase chain reaction assay technology. This platform allows for the rapid simultaneous detection of multiple pathogens (approximately 34) from up to six individual clinical specimens in a single TaqMan array card and requires a relatively low volume for testing.

Study Aims and Objectives:

- To estimate the prevalence of selected viral and bacterial respiratory pathogens among children less than five years of age hospitalized with SARI (first hospitalization for SARI episode) in four countries during a 12 month period.
- To estimate the prevalence of selected viral and bacterial pathogens among children without respiratory illness in four countries over a 12 month period.
- To determine the proportion of SARI cases caused by select pathogens by comparing the prevalence of select viral and bacterial respiratory pathogens among children with SARI and children without SARI.
- To describe the seasonality and compare the etiology of SARI among children less than five years of age at four international sites (Peru, Malawi, South Africa, and India).
- To identify risk factors for severe acute respiratory infection by etiology and compare by site among children less than five years of age. To describe clinical episodes attributable to specific etiologies and understand asymptomatic carriage.

Approach: To establish severe acute respiratory infection surveillance at sites to enroll children into the TAC-KID study and to obtain non-infectious controls from clinics at the same facilities.

Timeline: Study will be conducted for 12 months at each of the four sites, August 2013–December 2014.

Progress and Findings: Study was initiated in India in August 2013 and is expected to begin in all other sites by November 2013.

This project is occurring in India, Malawi, Peru and South Africa.



A surveillance team member at Edendale Hospital in Pietermaritzburg, South Africa interacts with a patient's mom to complete the severe acute respiratory infection and TAC-KID study questionnaire.



The TAC-KID project officer at Kalawati Hospital in New Delhi, India is asking the mother of a child admitted to the hospital a screening questionnaire to determine enrollment eligibility while other mothers in this busy hospital ward look on.

Global Seasonal Influenza Mortality Estimation

The World Health Organization (WHO) estimates that 250,000–500,000 seasonal influenza deaths occur globally each year. However, this estimate does not account for differences between countries in influenza virus circulation, population structure, underlying health status of populations, and access to life-saving interventions or care. Our goal is to develop a model to estimate global mortality due to seasonal influenza that attempts to account for differences in population age structure, risk of influenza-associated death, and variation in mortality between influenza seasons.

Study Aims and Objectives:

- To estimate global mortality due to seasonal influenza using excess mortality data by country and region.
- To obtain estimates of respiratory and circulatory excess mortality by year and age group from a set of diverse countries to calculate base respiratory and circulatory excess mortality rate estimates.
- To apply these estimates to populations of countries where such estimates cannot be obtained.
- To develop a method to account for variation between countries in risk of influenza-associated death due to respiratory illness and use this method to adjust the base respiratory mortality rate as needed to calculate influenza-associated respiratory deaths for each country and/or region.
- To develop a method to account for variation between countries in risk of influenza-associated deaths due to circulatory etiologies to apply to the base circulatory mortality rate to calculate influenza-associated circulatory deaths for each country and/or region.

Approach: We will use vital records and viral surveillance data from a diverse group of countries from different regions of the world to create a base influenza mortality rate estimate and develop methods to extrapolate the base estimate to other countries around the world that lack such data. After building our base estimate(s), we will develop an extrapolation approach to account for variation in risk of influenza-associated deaths across countries to develop a robust, globally representative estimate of annual seasonal influenza mortality.

Timeline: Study is ongoing.

Progress and Findings: We have established collaborations with approximately 25 countries around the world to participate in this work. We have both analyzed individual country data and received mortality estimates from countries to incorporate into our model to estimate global seasonal influenza mortality. We have established a collaboration with the World Health Organization Global Burden of Disease group to develop adjustment factors for respiratory and circulatory mortality.

Global Respiratory Influenza Proportional Positive (GRIPP)

Many countries worldwide now conduct hospital-based surveillance for influenza. Yet these data are rarely used to determine absolute burden. This study aims to collect the influenza percent positive among children and adults hospitalized for respiratory disease to get to a global disease burden estimate using published estimates of lower respiratory tract disease.

Study Aims and Objectives:

- To estimate global burden of pediatric hospitalizations due to seasonal influenza using percent positive by country and region for both pandemic and seasonal influenza.
- To estimate global burden of adult hospitalizations due to seasonal influenza using percent positive by country and region for both pandemic and seasonal influenza.
- To understand the percent of all respiratory hospitalizations positive for influenza before and after the pandemic of 2009.

Approach: We extract data from published papers and use and viral hospitalized surveillance data from a diverse group of countries from different regions of the world. We then conduct a meta-analysis to come up with a best point estimate of the percent positive by age and region and if pandemic year or not. We then apply this percent positive to the envelope of adult and [pediatric hospitalization globally.

Timeline: Study is ongoing.

Progress and Findings: We have completed the study for children and are now completing the final data extraction and analysis for adults.

VIETNAM

SARI and ILI in the North of Vietnam: Burden, Economic Impact, and Health Care Utilization

The study consists of two components: a hospital-based study of severe acute respiratory infection (SARI) patients to estimate the burden of SARI at three hospitals in Thai Binh province (North Vietnam), and a community-based household survey on health care utilization among people who experienced influenza-like illness (ILI) and SARI.

Study Aims and Objectives:

- To determine the burden of influenza-related SARI in hospitalized patients in one district hospital and in two provincial hospitals in Thai Binh province.

- To describe clinical, virological and epidemiological characteristics of influenza-related hospitalized SARI cases.
- To describe health care utilization of SARI hospitalized patients admitted to hospitals.
- To describe the economic impacts to patients of influenza-related SARI.
- To determine the incidence of self-reported ILI/SARI and the health seeking behaviors of people in the community when they have self-reported ILI/SARI.

Approach: A descriptive study has been conducted to describe epidemiological, virological and clinical features at the district and provincial hospital levels in Thai Binh province, North Vietnam. Adults and children with SARI admitted to Kien Xuong District Hospital, to Thai Binh Pediatric Hospital and to Thai Binh Provincial Hospital have been enrolled into the study. Epidemiological, virological, clinical, economic, and health-seeking information from these patients are collected to estimate the disease burden of seasonal influenza virus in hospitalized SARI in the province. In addition, health-care utilization information regarding ILI/SARI episodes was obtained from a household survey in Thai Binh city (urban area) and in Kien Xuong district (rural area).

Timeline: The hospital SARI surveillance began January 2013 and will last for 24 months. The household survey was conducted in May–June 2013.

Progress and Findings: Within the household health utilization survey (HUS), a total of 2,100 households were visited, including 630 households (2,094 members) from Thai Binh city and 1,470 households (4,666 members) from Kien Xuong district. Of the 6,760 total household members, 704 (10.4%) self-reported ILI and SARI and were individually interviewed for their health seeking behavior. There was a significant difference of reported SARI and ILI prevalence between the urban and rural areas ($p < 0.05$), and the majority of sick people sought some health care services from the public sector. Under the burden of SARI component of the study, as of 10 August 2013, 704 SARI patients are enrolled from the three participating. Of 682 SARI samples tested, 117 (17%) were positive for influenza, of which 89 (76%) were influenza A/H1N1pdm09, 15 (13%) were influenza A/H3, 10 (8%) were influenza B, 2 (2%) were co-infected with influenza A/H1N1pdm09 and influenza B, and 1 (1%) was influenza A/H3 and influenza B co-infection.

Conclusion: Preliminary analyses indicate a significant difference in the prevalence of self-reported ILI/SARI between Thai Binh city and Kien Xuong district. Most sick people sought health care, often from the public sector. Interim results from the burden of disease component show that influenza viruses contribute to the burden of acute respiratory disease in hospitals in Vietnam. Full analysis of the entire 24 month time period is pending.

Animal-Human Interface Longitudinal Study to Identify Influenza Viruses Infecting Humans and Animals over Time in Vietnam

The study proposes to determine the level of influenza virus, and to identify potential risk factors for developing influenza, in people, pigs, and poultry over time, through 12 months of follow-up of influenza-like illness (ILI) in selected households in the rural areas of Vietnam. If any people or animals are confirmed with influenza infection by RT-PCR test of swab samples, other people and animals in the same household will be tested to determine if any of them also have or had influenza. In addition, baseline samples from people, pigs, and poultry will be taken at the beginning and end of the study to assess the types, prevalence, and burden of influenza viruses in these species in the areas.

Study Aims and Objectives:

- To identify and characterize over time and place, the circulating influenza viruses in people, pigs, and poultry living in close proximity in Vietnam.
- To determine the variables associated with cross-species influenza virus transmission events over time.
- To determine the phylogenetic relationships and genomic characteristics of human and animal influenza virus isolates over time in Vietnam.
- To correlate influenza virus strains from this study with strains identified through existing influenza surveillance systems in Vietnam.

Approach: The study has been initiated in Binh Minh commune, Kien Xung district, Thai Binh province (North Vietnam) and Lac Tan commune, Tan Tru district, Long An province (South Vietnam), with participating households that raise both pigs and poultry. Baseline blood samples were collected from humans, swine and poultry of study households at the beginning and in 12 months later. During the 12 months syndromic surveillance, all enrolled households are observed for ILI events through frequent visits. Once a person or animal in one of the households develops an ILI, humans in the same household will have throat swabs and blood samples taken and tested for influenza by RT-PCR, as part of the ILI virologic and serologic surveillance. If tests are positive, humans and animals in the same household will be followed for two weeks and will have blood samples and throat swabs taken to detect influenza infection. An epidemiological surveillance will be also run in parallel with the other surveillance components, where epidemiological and environmental information are collected from baseline, ILI cases, and their households, to identify the risk factors for influenza virus transmission and other variables relating to the animal-human interface.

Timeline: The first baseline serological sampling was conducted in February 2013, followed by 12 months of surveillance. The second baseline sampling will be done at the end of the follow-up study.

Progress and Findings: In Thai Binh province, 150 households (409 participants) and in Long An province, 119 households (444 participants) were enrolled for the syndromic and ILI virologic and serologic surveillance. During the syndromic surveillance, a total of 79 ILI human cases, 20 ILI pig cases and 11 ILI poultry cases were identified in both study sites. Swab and blood samples have been collected from these cases for influenza testing. Of the human ILI tested samples, 12 (15%) were positive for influenza, of which 10 (83%) were influenza A(H1N1)pdm09 and 2 (17%) were influenza B. None of the animal ILI tested samples were positive for influenza. Among the households with human ILI cases, three asymptomatic pigs with influenza A were identified in the same household where a human case of influenza A(H1N1)pdm previously identified.

Conclusion: Preliminary findings suggest that multiple strains of seasonal influenza viruses circulate in humans, creating the potential for transmission of virus among human and animal populations in rural communities of Vietnam.

Animal Human Interface Studies: Pilot Extension South Project W Influenza Viruses Infecting Humans and Animals in Vietnam

This study proposed to determine the level of influenza virus, and to identify potential risk factors for developing influenza, in people, pigs, and poultry in a rural Mekong River Delta area of southern Vietnam. Through a syndromic surveillance, study investigators determined if any people, pigs, or poultry in the household have flu-like symptoms, and subsequently sampled and tested for influenza. Other people and

animals in the household were investigated to determine if any of them also have or had influenza. In addition, the investigators took baseline blood samples from people, pigs, and poultry to assess the types, prevalence, and burden of influenza viruses in these species.

Study Aims and Objectives:

- To identify the co-circulation of animal and human influenza viruses in selected rural communities.
- To determine the dynamics of animal-human interface transmission of influenza viruses in selected rural communities.
- To determine the phylogenetic relationships and genomic characteristics of virus isolates.

Approach: The study was conducted in households that raise both pigs and poultry in Lac Tan commune, Tan Tru district, Long An province (south Vietnam). In between two baseline serologic samplings, the syndromic and ILI virologic and serologic surveillance was implemented, with frequent visits (once every two days) to the enrolled participants' households for ILI event monitoring. Any person or animal in one of the households that developed an ILI will have throat/nasal swabs and blood samples taken and tested for influenza by RT-PCR. If tests were positive, humans and animals in the same household were followed up for two weeks and had blood samples and swabs taken to detect influenza infection. In addition, baseline samples were collected from all species from the study households at the beginning and end of the study.

Timeline: The field study was implemented from February to May 2013.

Progress and Findings: A serological sampling was conducted in eligible study households in Lac Tan commune at the beginning of the study (February 2013) and three months later (May 2013). In the first baseline sampling, blood specimens were collected from 444 human participants, 301 pigs and 1,396 poultry from 119 households. In the second baseline sampling, 409/444 people participated, and 207 pigs and 1,511 poultry from the same study households were sampled. During three months of syndromic surveillance, seven human ILI cases were identified, with swab and blood samples collected for influenza testing. One of seven specimens (14%) was positive for influenza B. No ILI cases were identified among the animal population, or from the subjects living in the same households with the human ILI cases. Epidemiological and environmental information was collected from the ILI cases to identify the risk factors for influenza virus transmission and other variables relating to the animal-human interface. Data analyses are ongoing.

Conclusion: Preliminary conclusions suggest that in a rural community over a short period of time, events of ILI are minimal, limiting potential for exchange of influenza viruses between animals and humans, when living in close proximity.

Animal Human Interface Study: Serological and Genetic Analyses of Influenza Virus Isolates Collected from Humans and Animals in Vietnam

Using virus isolates collected from previous AHI studies (Pilot Extension North, Pilot Extension South, and Longitudinal) in Vietnam, serological analyses will be performed to identify influenza virus types and phylogenetic analyses of virus isolates, including virus clade identification, characterization of select virus isolate genes, and full genome sequencing of select influenza virus isolates. This data will assist in the determination of potential evolutionary patterns and species characteristics of influenza virus isolates in people, pigs, and poultry living in close proximity in select rural communities in Vietnam.

Study Aims and Objectives:

- To perform serologic analyses of human and animal virus isolate samples to detect antibodies to influenza virus infection;
- To determine the genomic characteristics and phylogenetic relationships of human and animal influenza virus isolates over time in Vietnam;
- To characterize over time and place, the evolution of circulating influenza viruses in people, pigs, and poultry living in close proximity in Vietnam.

Approach: Serological tests for the measurement of influenza A-specific antibody include the hemagglutination inhibition (HI) test and the microneutralization (MN) assay. Of these, the MN assay is the recommended test for the measurement of highly pathogenic avian influenza specific antibody. Isolates will be further characterized by genomic sequencing, bioinformatics, and phylogenetic analyses. The eight genes, HA, NA, PB1, PB1, PA, NS, M and NP of the influenza virus will be sequenced. Animal serum samples will be screened by ELISA assay and reconfirmed by HI test for different antigens.

Timeline: February 2013–February 2014.

Progress and Findings: Serum samples were collected from a total of 1,262 people, 703 pigs and 1,511 poultry from study sites in Thai Binh (North Vietnam) and Long An (South Vietnam) in the AHI Pilot Extension South and AHI Longitudinal studies. HI tests have been completed on 30% of the collected human serum samples, and MI assay is being performed for confirmatory results. Approximate 1,000 animal serum samples are being tested by ELISA and HI against the antigens of influenza A (H1N1pdm; H3; H5 – clade 1, clade 2.3.4, and clade 2.3.2.1; H7; and H9).

Conclusion: Study in progress.

Co-Evolution of Human and Animal Influenza A Viruses in Vietnam

This study is to better understand the co-evolution of influenza viruses in animals and humans in Vietnam, including HPAI A(H5N1) viruses, to better understand their potential threats to human and animal health. A principal focus will be to better understand how influenza viruses transmit across species, and their pandemic potential, by evaluating novel human and animal influenza viruses, and comparing identical subtypes of influenza viruses in humans and animals, both geographically and temporally.

Study Aims and Objectives:

- To understand the phylogenetic evolution and co-evolution of human and animal influenza viruses, especially as related to adaption mechanisms of A(H5N1) influenza virus from animals to humans by conducting molecular virology analysis.
- To identify amino acid changes that may be critical for acquisition of high virulence and reduced susceptibility to antiviral drugs, by conducting bio-informatic analysis of the virus isolates.

Approach: Human and avian influenza isolates that are matched by time of and location of collection were selected for phylogenetic characterization. For human H5N1 isolates, at least two poultry H5N1 isolates were selected and then matched with the human isolate. The poultry virus isolates that were closer both temporally and geographically to a human isolate were prioritized for selection. Standard methods for phylogenetic characterization of human and avian influenza viruses, including RNA extraction, PCR analysis, antigenic characterization, nucleotide sequencing and phylogenetic analysis, were performed.

Bioinformatics were used as means for detecting amino acid changes related to mutations associated with replication, virulence, susceptibility to antivirals, and vaccine match. Viruses were monitored especially for evidence of emerging genotypes arising from mutations or re-assortment that could pose an increased risk for animal-to-human transmission and for epidemic or pandemic spread.

Timeline: The analyses were performed in January–August 2013.

Progress and Findings: Avian influenza A(H5N1) isolates from 30 human samples and 59 avian samples were sequenced for all genes using Sanger sequencing (ABI 3130). Phylogenetic trees were analyzed.

Conclusion: Genotypes Z and V strains have a continued predominance of the A(H5N1) virus in Vietnam. All of the human viruses isolated between 2003 and 2012 belonged to clades 1 and 2.3.4, while animal viruses clustered into clades 1, 2.3.2, and 2.3.4. Mutations related to resistant or reduced susceptibility or resistance to oseltamivir were found in some isolates in 2005–2008.

Related Published Paper: ISIRV Conference in Hanoi, Vietnam in October 2012, poster “Co-evolution of human and animal of Highly Pathogenic Avian Influenza A/H5N1 in Vietnam”.

Cross-sectional Study of Influenza in Humans and Swine at Slaughterhouses in Select Areas in Vietnam

A repeated cross-sectional study at swine slaughterhouses will be conducted in nine select provinces in Vietnam to determine the prevalence and sub-types of influenza A viruses. At three month intervals over a 12-month period, live pigs at slaughterhouses will have collected blood and nasal swab specimens for evidence of influenza virus. Pigs identified as previously exposed to influenza virus will be traced back to their sources, and potentially identified for additional studies. Slaughterhouse workers and matched human controls will be also sampled, once every six months occurring at the same time as the animal sampling. The sampled slaughterhouse workers and human control subjects will be interviewed through structured questionnaires to identify potential risk factors for the exposure to and transmission of influenza viruses at slaughterhouses.

Study Aims and Objectives:

- To estimate the prevalence of influenza A virus infection in pigs and in humans who are currently working at the slaughterhouses and slaughter points, and in matched human controls living in the same areas.
- To determine the potential exposure of the swine slaughter workers to influenza viruses, and to assess the potential transmission that may have occurred between humans and pigs.
- To identify risk factors of influenza virus exposure and transmission at slaughterhouses and slaughter points in three main regions of Vietnam.

Approach: The study will be conducted in nine provinces in Vietnam, including Bac Ninh, Hai Phong, Nam Dinh (North), Quang Tri, Thua Thien Hue, Quang Nam (Central), Binh Duong, Tien Giang and Vinh Long (South). A cross-sectional sampling of humans and pigs will be conducted in the selected slaughterhouses, once every three months over a 12 month period. During each round of animal sample collection, 10 live pigs in each slaughterhouse will be sampled for blood and nasal swab specimens. At the second and fourth (six months later) rounds of animal sample collection, two workers from each slaughterhouse and two matched control subjects living in the same area of the slaughterhouse will have throat swabs

and blood taken. The collected specimens will be tested for influenza A by RT-PCR (for swabs) and hemagglutinin inhibition (for sera). Trace-back information from slaughterhouse owners regarding the sources and quantity of pigs present for slaughter will be conducted. Risk factors for potential exposure and transmission of influenza viruses are obtained from structured questionnaire interviews of slaughterhouse workers and the controls.

Timeline: Field study is proposed to start in September 2013 and end in September 2014 with animal sampling in every three months. The first human sampling will be conducted in December 2013, in concurrence with the second animal sampling.

Progress and Findings: To prepare for the field activities, three training seminars were organized in North, Central, and South Vietnam for 65 animal health field staff and 37 human health field staff. The training seminars introduced the study and the implementation plan for discussion, and provided guidance for data collection as well as sample collection, storage and transportation.

Conclusion: Study in progress.

PARTNERSHIP FOR INFLUENZA VACCINE INTRODUCTION (PIVI)

Partnership for Influenza Vaccine Introduction (PIVI)

Background

In April 2012, Walgreens Co. donated 375,000 doses of inactivated trivalent seasonal influenza vaccine directly to the Lao People's Democratic Republic (Lao PDR), in a unique public-private partnership, one of the first of its kind. WHO WPRO and CDC's Influenza Division collaborated with the Lao PDR Ministry of Health (MoH) to support operational costs and provide technical assistance. This pilot project, dubbed the "Lao PDR Influenza Vaccine Donation Project", successfully vaccinated populations at high risk for seasonal influenza (pregnant women, persons 50+ years of age, persons with chronic diseases) and health care workers for the first time in Lao PDR. This pilot program was recognized by CDC Director Dr. Thomas Frieden in September 2012 with the 2011 CDC Director's Award for Innovation; the program also received the CDC Excellence in International Partnering Award, and has been highlighted by WHO as a promising global vaccine strategy.

The pilot project expanded in 2013 to support influenza vaccination of pregnant women in Nicaragua while continuing collaboration with Lao PDR. Existing partners including Lao PDR MoH, WHO Country Office, Walgreens Co. and United Parcel Service (UPS) were joined by new program partners including Nicaragua Ministry of Health, the Pan-American Health Organization, bioCSL, Becton Dickinson and Company (BD), and U.S. Department of Defense. The Task Force for Global Health also joined the project in 2013. In the Fall of 2013, the Task Force for Global Health and CDC formally launched the Partnership for Influenza Vaccine Introduction (PIVI) with support from the Bill & Melinda Gates Foundation.

The Partnership for Influenza Vaccine Introduction

The Partnership's mission is to help low- and middle-income countries reduce morbidity and mortality from influenza and enhance their pandemic preparedness through introduction of vaccine and expansion of existing vaccination programs. The Partnership plays a pivotal role by supplying donated influenza vaccine and supplies to countries that lack those resources but which are otherwise ready to establish or expand their influenza vaccination programs. Country program evaluation and sustainability planning are identified as important program components.

On December 3–4, 2013, the Task Force for Global Health's Center for Vaccine Equity convened a meeting in Atlanta, Georgia to formally launch the Partnership by bringing together the founding partners, engaging new partners, and providing a forum for the 2014 participating countries to work with technical experts from CDC and other organizations to develop their program plans for the coming year. Partnership Co-chairs Dr. Alan R. Hinman, Director for Programs, Center for Vaccine Equity at the Task Force for Global Health and Dr. Joseph Bresee, Chief, Epidemiology and Prevention Branch, Influenza Division welcomed more than 60 participants from across the globe to the two-day meeting to develop future plans and direction for the PIVI program.

Objectives of PIVI

- Reduce morbidity and mortality from seasonal influenza by protecting at-risk populations, particularly those prioritized by WHO/Strategic Advisory Group of Experts (SAGE) on Immunization, such as pregnant women.
- Evaluate the programmatic aspects of seasonal influenza vaccine implementation.
- Demonstrate that the introduction of seasonal influenza vaccine can be both feasible and accepted and can strengthen future public-private partnerships for the introduction of new vaccines into the Expanded Programme on Immunization (EPI).

Principles

- Vaccine donation should not interfere with current influenza vaccine program growth and should serve as a catalyst for sustainable vaccine program.
- There must be demonstrated commitment from MoH's, and WHO Country offices.
- The country must have existing influenza surveillance systems in place and/or a National Influenza Center.
- Vaccine target groups should be based on local data and be informed by WHO SAGE recommendations.
- An evaluation plan must be developed to assess the vaccine program's introduction and impact.
- A sustainability plan should be developed by the country to develop a sustainable source of seasonal influenza vaccine among priority groups.
- The program should be coordinated with WHO's Global Action Plan for Influenza Vaccines and other partners.

Partnership Deliverables

- Increases in vaccine coverage in vaccine target groups in partner countries.
- Successful integration of influenza vaccine in partner countries' current immunization programs.
- Reduction in influenza-associated health outcomes in immunized populations in partner countries.
- High acceptability of influenza vaccine among stakeholders in partner countries.
- Sustainability of respiratory disease surveillance, laboratory capacity and rapid response capabilities that have been developed in response to pandemic preparedness priorities.
- Data to support evidence-based decision making related to influenza vaccination of potential target populations .

Future Plans

The program targets the most vulnerable populations as designated by WHO SAGE influenza vaccine recommendations, with an emphasis on maternal immunization. The program seeks to meet country partners' target requirements from Partnership-supply resources. PIVI plans to engage new country partners on an annual basis. PIVI's expansion will be governed by the level of vaccine and other donations and the successful transitioning of existing partner countries to sustainable programs. Enabling factors include collaboration with WHO Global Action Plan for Influenza Vaccines (GAP-II), incorporation into CDC

Influenza Division's International Strategic Plan as a key component, HHS/BARDA's flu vaccine development program, and Global Alliance for Vaccines and Immunization (GAVI)'s future consideration of support for flu vaccine in GAVI-eligible countries. Constraints include vaccine supply limitations; regulatory time frames for approval of new vaccines; predictability of donations; timing of flu season in partner countries and selection of vaccines; provision of immunization supplies; and logistics and transport of vaccines and supplies.

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U.S. Deputy Chief of Mission at the U.S. Embassy in Vientiane, Laos, administering Vitamin A tablets.



Nurse administering influenza vaccine.

SUSTAINABILITY

Sustainability

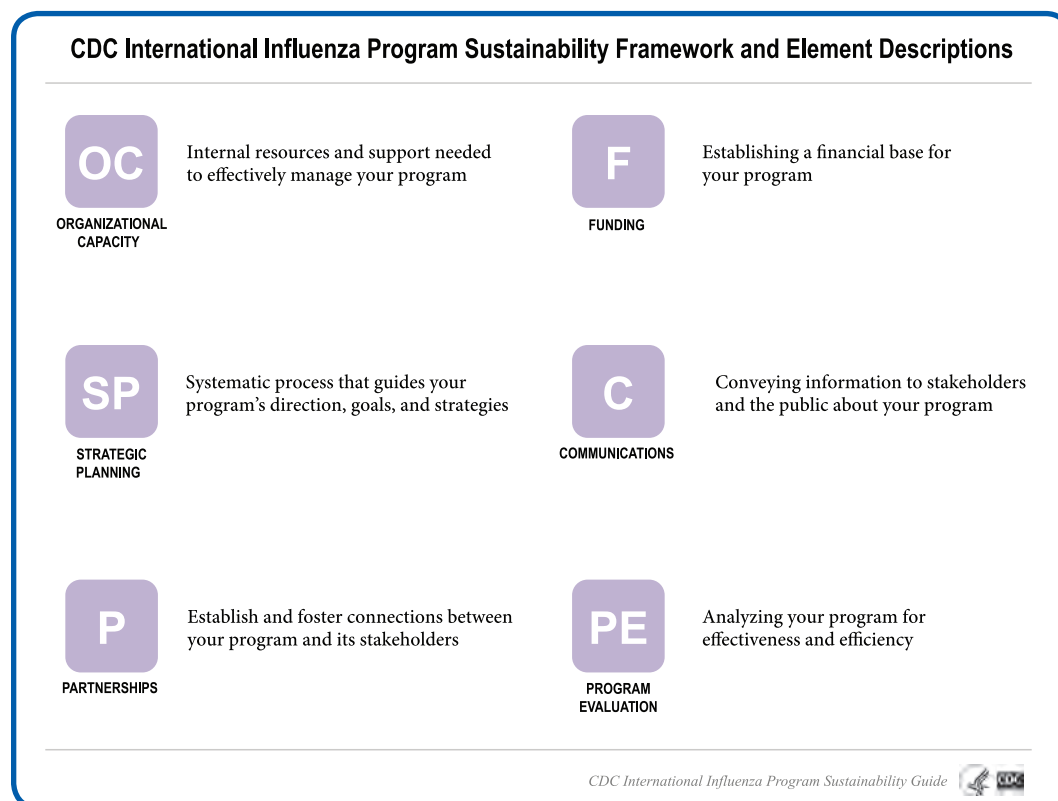
Sustainability can be defined as a country's ongoing maintenance and support of a routine virologic and epidemiologic influenza surveillance system including the capacity to financially maintain the system or a portion of the system.

When countries transition from the capacity-building phase to the sustainability phase, they are asked to develop and implement a plan for influenza surveillance initiated or enhanced during the capacity-building phase. The plan should be reviewed annually or as changes occur.

Developing such a sustainability plan is a critical part of the transition to a sustainable system. A written plan can provide overarching guidance for your initiative. A plan can help an organization:

- Sustain systems using government funds.
- Obtain input and agreement from key stakeholders (i.e. MOH, WHO, etc.).
- Make the best use of human capital, funding and other resources to achieve your objectives.
- Develop strategies for long-term success.

To assist grantees with their plans, CDC's Influenza Division developed the International Influenza Program Sustainability Guide and Framework (Guide). The Guide consists of six elements: Program Capacity, Strategic Planning, Partnerships, Funding, Communications, and Program Evaluation. These elements provide the framework for sustainability planning and implementation.



Sustainability Framework and Element Descriptions for CDC's International Influenza Program.

Some expectations of sustainability include:

- Country ownership and investing in country-led plans (Global Health Initiative).
- Aligning goals with national priorities.
- Developing and implementing sustainability plans with a detailed budget to fully assume responsibilities and funding for robust and timely routine surveillance systems for seasonal, novel and pandemic influenza.
- Ensuring systems have the ability for rapid detection of and response to potential pandemic influenza as well as for monitoring the occurrence and assessing the impact of seasonal influenza in the country.
- Maintaining or making progress towards having an active World Health Organization (WHO) National Influenza Center (NIC) laboratory and contribute regularly to the Global Influenza Surveillance and Response System (GISRS).

Sustainability should be discussed continuously and plans updated as things change so countries can develop surveillance networks that will continue after USG funding ends and provide the necessary data to accurately identify and track potential public health issues.



ACRONYMS & REFERENCES

Acronyms

2009 H1N1	2009 Pandemic Influenza A (H1N1)
AFR	WHO African Region
AFRO	WHO Regional Office for Africa
AI	Avian Influenza
AHI	Animal-Human Interface
AMR	WHO Region of the Americas
APHL	Association of Public Health Laboratories
ARI	Acute Respiratory Illness
BEP	Biosecurity Engagement Program
BSL	Biosafety level
CARPHA	Caribbean Public Health Agency
CDC	Centers for Disease Control and Prevention
CDC-CAP	CDC Central America and Panama
CoAg	Cooperative Agreement
DFA	Direct Immunofluorescence
DOD	Department of Defense
DVM	Doctor of Veterinary Medicine
ECDC	European Centers for Disease Control
EMR	WHO Eastern Mediterranean Region
EMRO	WHO Regional Office of the Eastern Mediterranean
EOC	Emergency Operations Center
EPT	Emerging Pandemic Threats
EQAP	WHO External Quality Assessment Project
EUR	WHO European Region
EURO	WHO Regional Office for Europe
FAO	Food and Agriculture Organization

FDA	United States Food and Drug Administration
FETP	Field Epidemiology Training Program
FELTP	Field Epidemiology and Laboratory Training Program
FY	Fiscal Year
FMOH	Federal Ministry of Health
GDD	Global Disease Detection
GDP	Gross Domestic Product
GIP	WHO Global Influenza Program
GISRS	WHO Global Influenza Surveillance and Response System
HA	Hemagglutinin (a protein on the surface of the influenza virus)
HAI (or HI)	Hemagglutination Inhibition Assay
HAI	Health care-associated Infection
HHS	United States Department of Health and Human Services
HPAI	High Pathogenic Avian Influenza
IATA	International Air Transport Association
ICEID	International Conference on Emerging Infectious Disease
ID	Influenza Division
IDSR	Integrated Disease Surveillance and Response
IHR	International Health Regulations
IFA	Immunofluorescence, Indirect Antibody Staining
IEIP	International Emerging Infections Program
ILI	Influenza-like Illness
IRR	Influenza Reagent Resource
LPAI	Low Pathogenic Avian Influenza
MD	Medical Doctor
MDCK	Madin-Darby Canine Kidney Cells
MOH	Ministry of Health
MPA	Master of Public Administration

MPH	Master of Public Health
MSc	Master of Science
NA	Neuraminidase (a protein on the surface of the influenza virus)
NAI	Neuraminidase Inhibitors
NAMRU	United States Naval Medical Research Unit
NCIRD	National Center for Immunization and Respiratory Diseases
NGO	Non-Government Organization
NI	Neuraminidase Inhibition Assay
NIC	National Influenza Center
NP	Nasopharyngeal swab
OIE	World Organisation for Animal Health (Office International des Épizooties)
OP	Oropharyngeal swab
PAHO	Pan American Health Organization
PATH	Program Appropriate Technology in Health
PCR	Polymerase Chain Reaction
PPE	Personal Protective Equipment
QA	Quality Assurance
QC	Quality Control
QMS	Quality Management System
RRT	Rapid Response Team
RSV	Respiratory Syncytial Virus
RT-PCR	Reverse Transcriptase Polymerase Chain Reaction
SADC	South African Development Community
SARI	Severe Acute Respiratory Infection
SARS	Severe Acute Respiratory Syndrome
SEAR	WHO South-East Asia Region
SEARO	WHO Regional Office for South-East Asia
SOP	Standard Operating Procedure

SPC	Secretariat of the Pacific Community
TB	Tuberculosis
TLDA	TaqMan Low Density Array
UNICEF	United Nations Children's Fund
USAID	United States Agency for International Development
USB	Universal Serial Bus
USDA	United States Department of Agriculture
VTM	Viral Transport Media
WPRO	WHO Regional Office for the Western Pacific
WPR	WHO Western Pacific Region
WHO	World Health Organization
WHO CC	World Health Organization Collaborating Center for Reference and Research on Influenza

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