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Fourth meeting of the Eastern Mediterranean Acute Respiratory Infection Surveillance (EMARIS) network and first scientific conference on acute respiratory infections in the Eastern Mediterranean Region, 11–14 December, 2017, Amman, Jordan ^{☆,☆☆}

Abdinasir Abubakar^a, Amal Barakat^a, Amira Ahmed^b, Amjad El Kholy^a, Lora Alsawalh^c, Lubna Al Ariqi^a, Mamunur Rahman Malik^{a,*}, Majdouline Obtel^d, Mohammad Sahak^e, Pamela Mrad^f, Soumia Triki^g, Salah Al Awaidy^h, Wasiq Mehmood Khan^a

^a Infectious Hazard Management, Department of Health Emergency, World Health Organization, Eastern Mediterranean Regional Office, Cairo, Egypt

^b World Health Organization Country Office, Egypt

^c World Health Organization Country Office, Jordan

^d Department of Public Health, Faculty of Medicine and Pharmacy, University Mohammed V, Rabat, Morocco

^e World Health Organization Country Office, Afghanistan

^f World Health Organization Country Office, Lebanon

^g World Health Organization Country Office, Morocco

^h Senior Consultant & Medical Epidemiologist, Communicable Diseases Adviser to Health Affairs, Ministry of Health, PO Box 393, PC 113 Muscat, Oman

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ABSTRACT

Influenza causes significant morbidity and mortality worldwide. Owing to its ability to rapidly evolve and spread, the influenza virus is of global public health importance. Information on the burden, seasonality and risk factors of influenza in countries of the World Health Organization Eastern Mediterranean Region is emerging because of collaborative efforts between countries, WHO and its partners over the past 10 years. The fourth meeting of the Eastern Mediterranean Acute Respiratory Infection Surveillance network was held in Amman, Jordan on 11–14 December 2017. The meeting reviewed the progress and achievements reported by the countries in the areas of surveillance of and response to seasonal, zoonotic and pandemic influenza. The first scientific conference on acute respiratory infection in the Eastern Mediterranean Region was held at the same time and 38 abstracts from young researchers across the Region were presented on epidemiological and virological surveillance, outbreak detection and response, influenza at the animal-human interface, use and efficacy of new vaccines to control respiratory diseases and pandemic influenza threats. The meeting identified a number of challenges and ways to improve the quality of the surveillance system for influenza, sustain the system so as to address pandemic threats and use the data generated from the surveillance system to inform decision-making, policies and practices to reduce the burden of influenza-associated illnesses in the Region.

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Introduction

Acute respiratory infections are one of the leading causes of morbidity worldwide and are responsible for an estimated 1.4 million deaths in children under five years of age [1], which represents 18.3% of the total deaths reported in this age group [2]. A substantial proportion of the global burden of acute lower respiratory infections is attributable to influenza and respiratory syncytial virus especially in children and the elderly. However, limited information is available on the burden of acute respiratory infections in the

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* Corresponding author at: Infectious Hazard Management, Department of Health Emergency, World Health Organization Regional Office for the Eastern Mediterranean, Monazamet El Seha El Alamia Street, P.O. Box 7608, Nasr City, Cairo 11371, Egypt.

E-mail address: malikm@who.int (M. Rahman Malik).

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Eastern Mediterranean Region of the World Health Organization (WHO).

The WHO Regional Office for the Eastern Mediterranean has been collaborating with the Influenza Division of International Program of the United States Centers for Disease Control and Prevention (CDC) since 2006 to enhance influenza surveillance in the Region. The goal of this collaboration has been to enable the 22 countries of the Region to collect good quality surveillance data on influenza and influenza-associated illnesses in a timely and reliable manner, use these data to improve understanding of the burden, seasonality and risk factors of influenza in the Region, and use such evidence to introduce control measures such as influenza vaccines to reduce the incidence of severe disease and death attributed to influenza. This successful collaboration has led to substantial improvements in influenza surveillance in the Region and the use of data for public health [3].

In 2007, a year after a new zoonotic influenza virus, A(H5N1), was detected in Egypt, the Eastern Mediterranean Acute Respiratory Infection Surveillance (EMARIS) network was established to support the ministries of health in Egypt, Jordan and Oman to establish sentinel-based surveillance systems for severe acute respiratory infection. The network was established in partnership with the CDC, US Naval Medical Research Unit No. 3 (NAMRU-3) and the WHO Regional Office. Over the following five years, surveillance efforts expanded to include collaborations with other ministries of health in the Region [4]. Since 2011, the Regional Office has organized meetings of the EMARIS network every two years in order to share best practices for influenza surveillance, track progress, and learn lessons on public health preparedness for pandemic influenza.

The fourth meeting of the EMARIS network was held in Amman, Jordan from 11 to 14 December 2017. At the recommendation of the third meeting [5], the first scientific conference on acute respiratory infection in the Eastern Mediterranean Region was held in conjunction with the fourth EMARIS meeting.

The meeting was attended by representatives from all countries of the Region, the Global Health Development, CDC, WHO headquarters, as well as participants from selected universities and academic institutions and over 40 young researchers who presented abstracts to the conference. This report provides an overview of the outcomes of the meeting and conference.

Influenza surveillance at the global level—lessons from the past and vision for the future: plenary session

WHO coordinates the Global Influenza Surveillance and Response System (GISRS) [6], which plays a vital role in protecting global health against seasonal influenza, pandemic influenza and influenza viruses with pandemic potential. Since its establishment in 1952, the GISRS network has provided early warning of changes in influenza viruses circulating in the global population through timely sharing of influenza viruses and surveillance data. It has also helped mitigate the consequences of pandemic influenza and maintained the efficacy of seasonal influenza vaccines.

Because of this global surveillance, a recent study suggests that seasonal influenza continues to be an acute health burden for young and old people every year around the world resulting in an estimated 291 243–645 832 respiratory deaths (4.0–8.8 per 100 000 individuals) annually [7]. Faced with pandemic threats from highly pathogenic zoonotic infections from different influenza A subtypes, the GISRS continues to be an ideal platform for global collaboration to forestall and respond to public health emergencies [8].

Since 1997, virological data have been shared and monitored on the Internet through FluNet. This was complemented by FluID

in 2009 for reporting epidemiological data. The FluNet and FluID databases support the interpretation of the global influenza situation and also allow a local and regional perspective. In 2016, the Global Influenza Programme of WHO launched a two year pilot project on Respiratory Syncytial Virus (RSV) surveillance using the GISRS platform which was participated by 14 countries across all six WHO Regions. The primary objective of this project was to determine seasonality of RSV estimate the burden of RSV-associated hospitalization and provide evidence for introduction of vaccines through informed public health decisions.

The 2009 H1N1 pandemic demonstrated that WHO and other organizations did not have a robust and standardized method to rapidly assess the national severity of pandemic influenza. In response to the report of the Review Committee on the Functioning of the International Health Regulations (2005) and on Pandemic Influenza (H1N1) 2009 [9], WHO developed the Pandemic Influenza Severity Assessment (PISA) that can assess and measure the severity of every influenza epidemic, whether seasonal or pandemic. In March 2017, the PISA approach was launched officially after piloting between 2014 and 2016.

In 2011, the World Health Assembly adopted the Pandemic Influenza Preparedness (PIP) Framework [10] to put virus sharing and benefit sharing on an equal footing. The PIP Framework for sharing influenza viruses and access to vaccines and other benefits is an international arrangement to improve global pandemic influenza preparedness and response. The Framework establishes a PIP benefit-sharing system that includes an annual partnership contribution to WHO from manufacturers of influenza vaccines, diagnostics and pharmaceuticals that use the GISRS. WHO's global influenza surveillance programme remains critical to: improving global preparedness for influenza; having a better understanding of the influenza burden in high-risk populations; developing tools for rapid assessment of severity; making use of data for vaccine introduction and timing; and monitoring population-based vaccine uptake.

Influenza in the Eastern Mediterranean Region: plenary session

The influenza surveillance and response programme has been strengthened in the Eastern Mediterranean Region since the establishment of the EMARIS network with more countries using influenza surveillance and also using the surveillance data to develop influenza control strategies.

Epidemiological surveillance and use of data for estimation of disease burden

Currently, 19 countries of the Region have functional influenza surveillance systems. Data are regularly shared with FluID and EMFLU (Eastern Mediterranean Flu Network)—the online portal for sharing influenza surveillance data. Egypt, Iran, Jordan, Lebanon, Oman and Tunisia have now estimated their influenza disease burden using surveillance data [11]. The seasonality and epidemiology of influenza are now better understood in different influenza transmission zones of the Region. More countries are using the evidence generated to consider introducing and increasing the uptake of seasonal influenza vaccines and other cost-effective interventions to control influenza.

Acute respiratory infections are a major cause of morbidity and mortality in people affected by crises. For example, acute lower respiratory infections accounted for about 10% of visits to outpatient services and 15% of reported deaths in refugee camps in Kenya and Thailand during 2007–2011 [12]. Given that the Region has a large number of internally displaced populations and refugees,

the Regional Office is collaborating with Edinburgh University to develop a manual to estimate the burden of acute respiratory infections in settlements of refugee and internally displaced people. The manual will be helpful not only in estimating the influenza disease burden in such settings but also in planning health service needs in settlements of refugees and internally displaced people.

Virological surveillance and participation in the Global Influenza Surveillance and Response System

There are 16 national influenza centres in 15 countries of the Region. At least 11 of these centres regularly share influenza virological data with the GISRS. Many of them have laboratory capacity for viral isolation, molecular diagnosis through polymerase chain reaction and sequencing. The capacity of these centres, especially the viral sequencing capacity, has been critical for determining genetic changes in the seasonal influenza virus and for identifying new influenza strains or subtypes. An important function of the centres is to share seasonal influenza viruses with the WHO collaborating centres for vaccine strain selection. Between 2010 and 2017, more and more countries from the Region are, now, sharing seasonal influenza viruses with the WHO Collaborating Center for influenza vaccine strain selection.

Use of influenza vaccine in the Region and challenges to increased uptake

The current policies, vaccination coverage and attitudes to influenza vaccination in the Region were assessed through a systematic review of studies published in English between 2006 and 2016 and a survey of ministries of health. Most studies reported low vaccination coverage in the general population and high-risk groups, mainly because of misconceptions about vaccine safety, efficacy and recommendations. Desirable coverage for some at-risk groups, such as healthcare workers and pilgrims, was achieved in few countries. Analysis of the number of vaccine doses distributed in the countries confirmed the low vaccination coverage rates.

Fourteen countries of the Region reported implementation of an influenza vaccine policy and five have included the influenza vaccine in their national immunization programmes. The influenza vaccine policies implemented commonly covered the main risk groups, with some variability between countries. A review of literature published between 2006 and 2016 in the region on influenza vaccine policies, use, recommendations and coverage [13] reveal wide variation in influenza vaccination rates among healthcare workers and other high risk groups within and between the countries from less than 1% in Pakistan to as high as 71.1% in Qatar. Similarly, data on vaccination rates among pregnant women showed wide variation from as low as 0% in a study from Pakistan to about 18% in Saudi Arabia. The annual vaccination rates among other risk groups in most countries in the Region was reported to be below 50%.

Influenza surveillance at the human-animal interface: One Health framework

The Region lies under four of the eight global migratory bird flyways, which makes it important for tracking and monitoring transmission of avian influenza viruses from migratory birds to the resident wild birds, domestic poultry, mammalian species and humans. Highly pathogenic avian influenza A(H5N1) virus has been spreading through the Region since 2006. Transmission of A(H5N1) virus from infected birds to humans has been confirmed mostly in Egypt, but also in Iraq, Djibouti and Pakistan [14]. Recently, several countries of the Region reported the newly emerged A(H5N8)

virus in wild birds and poultry. In addition, A(H9N2) viruses are endemic in several regional countries, and sero-epidemiological studies have found evidence of A(H9N2) antibodies in humans [15,16].

In light of this, and drawing on Egypt's experience with avian influenza A(H5N1) outbreaks, the Regional Office drafted a One Health framework for action to tackle spill overs of animal influenza viruses to humans and to detect early, prevent and control newly emerged zoonotic influenza. A systematic review was also done to gather information on One Health before developing a framework to enhance surveillance and better data collection at the human-animal interface.

Surveillance of respiratory syncytial virus

Respiratory syncytial viruses cause about 33 million episodes of acute lower respiratory infections in children under five years worldwide, with about 10% requiring hospital admission and up to 199 000 dying from the infection every year [17,18]. Studies have been conducted in several countries to better understand the burden and epidemiology of respiratory syncytial virus in the Region and its importance as a cause of acute lower respiratory infections in children under five years [19–21]. The countries used the existing surveillance platform for severe acute respiratory infections and identified the highest number of influenza-positive cases in children between 6 and 12 months of age whereas the highest number of cases positive for respiratory syncytial virus were in children between 2 and 6 months [22]. These studies also identified seasonality and undertook molecular characterization of the genotype of circulating respiratory syncytial virus.

Influenza surveillance: challenges for the Eastern Mediterranean Region

The progress in influenza surveillance and response in the Region has been hampered by the fragility of the health systems as a result of protracted humanitarian crises and civil war. From the viewpoint of influenza surveillance programme of WHO Eastern Mediterranean Region, a number of issues were highlighted in the plenary discussions as challenges which hampers to improvement of influenza surveillance and response system in the Region. A summary of these challenges identified in the plenary discussions are shown in **Box 1**. Because of the constant evolution of influenza viruses, and the limitations in knowledge and control measures, two essential elements of surveillance and response to influenza are collecting good quality data year round and testing samples using a systematic sampling strategy. Timely sharing and reporting of data are also critical in order to achieve optimal disease control.

Pandemic influenza threats: recognition, prevention and response

The year 2018 marks the 100th anniversary of the greatest influenza pandemic in history, the 1918 “Spanish flu”. Since then, three influenza pandemics have occurred (1957, 1968 and 2009), and future pandemics appear inevitable. However, no pandemic has ever been correctly predicted before it began its spread within the human population.

In recent years, new respiratory infections of zoonotic origin, including avian influenza and Middle East respiratory virus coronavirus (MERS-CoV), have emerged which could not have been predicted and this demonstrates the gaps in knowledge in predicting pandemic threat. As we cannot predict influenza pandemics and new infectious disease threats such as MERS, effective respiratory disease surveillance for early warning, together with strong preparedness measures, are essential. The foundation for this exists

Box 1: Challenges to improving and sustaining the influenza surveillance system in the Eastern Mediterranean Region

- The influenza surveillance system does not operate all year round. Until the influenza season in the Region is well defined, data collection, sampling and testing of the influenza virus should be conducted all year.
- Clinicians are often unaware of the need to use consistent and systematic surveillance case definitions for severe acute respiratory infection/influenza-like illness (SARI/ILI) and to enrol only cases meeting the case definitions.
- The virological and epidemiological components are often not integrated into the SARI/ILI surveillance system and are not part of the national routine disease surveillance and reporting system (often the SARI/ILI surveillance system is considered a stand-alone vertical system which is fund-driven).
- There is a tendency to collect too many non-essential data which can overwhelm the system. Efforts should be directed to collecting minimum essential data from sentinel sites in accordance with the nationally defined objectives of the SARI/ILI surveillance system.
- Public funding to sustain and maintain the SARI/ILI surveillance system is often lacking and relies on donor funding.
- SARI/ILI surveillance data are not used enough to provide alerts and epidemic thresholds and assess the severity of influenza in a given influenza season. This leads to either late detection or no detection at all of a seasonal surge or an influenza outbreak.
- Countries do not have a consistent or systematic sampling strategy for collecting clinical samples from SARI and ILI cases and testing for influenza virus. As a result, influenza cases and the disease burden associated with influenza are underestimated in many countries.
- A lag time often exists between data collection and influenza testing, or influenza testing and sharing of the test results for public reporting, as well as sharing influenza virus specimens for vaccine strain selection. This results in poor understanding of the types of influenza virus circulating in real time and also increases the probability of vaccine mismatch specific to the Region.
- A standard protocol is lacking, including a validated algorithm for testing and diagnosis of respiratory syncytial virus and other respiratory viruses using multiplex respiratory assays where specimens are tested both for influenza and non-influenza respiratory viruses. The absence or inadequacy of appropriate diagnostic facilities to define the viral etiology of severe pneumonia is a problem and means that many acute lower respiratory infections are undiagnosed and hence that viral pneumonia incidence rates are underestimated.
- Annual projections of the requirements for reagents and consumable laboratory supplies for the detection and diagnosis of seasonal influenza and other respiratory viruses based on a well-defined sampling strategy are often lacking. This can lead to stock outs in the middle of a busy influenza season.
- Countries often do not use the data generated locally from their surveillance systems to define control policies and practices that can reduce the influenza disease burden in the general population.
- Countries do not use the surveillance data to better understand the economic burden of influenza and often undervalue the role of control policies such as use of vaccines to reduce healthcare-associated severe influenza illness.
- In countries where control policies exist and are implemented, such as the use of seasonal influenza vaccines, surveillance data are not used to monitor the effectiveness of these policies and interventions.

To improve surveillance for influenza, the following actions are needed.

- Sustain the existing platform for influenza surveillance in order to detect and monitor threats from new and emerging respiratory viruses.
- Make available good quality data and a common stock of diagnostic kits and reagents.
- Involve academia and the private sector, and ensure continued coordination, information sharing and joint actions at the human-animal interface.
- Estimate the economic burden of influenza.
- Develop key guiding measures for pandemic influenza.
- Develop long-term plans for the use of seasonal influenza vaccines, at least among high-risk groups.

in the influenza surveillance systems. Building on these systems will require an enhanced capability to collect and coordinate data across national borders and identify the pathogens in real time (or near real time), and agreement on triggers for appropriate response activities.

Given that pandemic influenzas appear to have a zoonotic origin, cross-species surveillance (a One Health approach) is essential. The number of reported novel influenza A virus infections in humans has increased over 30-fold in the past 20 years [23]. This is due, in part, to the ever increasing and well connected human population and the global expansion of domestic poultry and pig populations. Many subtypes of novel influenza A viruses have emerged from these animal reservoirs to cause zoonotic infections.

As an influenza pandemic is an unpredictable but recurring event that can have serious consequences on human health and economic security worldwide, advanced planning and preparedness are critical to help mitigate the effect of a pandemic. The lessons from the 2009 influenza A(H1N1) pandemic emphasized the need for risk-based and integrated approaches in pan-

demically preparedness and harmonized national and international preparedness and response efforts. Countries should consider reviewing and/or updating national influenza preparedness and response plans. The global health security agenda and the revised International Health Regulations (2005) provide mechanisms to enhance and implement consistent standards for surveillance and preparedness.

First scientific conference on acute respiratory infection in the Region

The conference with the theme “Better understanding, better preparedness, and better response” provided a forum for young health researchers and health professionals in the public, semi-public and private sectors throughout the Region to present their research findings on influenza surveillance, laboratory detection, outbreak detection and response, acute respiratory infection, collaboration at the animal-human interface, vaccination for influenza and pneumonia, and pandemic preparedness and response. A total of 38 abstracts were presented, 24 orally and 14 as posters.

Box 2: Key action points discussed during the panel discussions

Sustainable actions to improve the quality of data collection and analysis

- The existing platform for influenza surveillance should be enhanced and sustained for detection and monitoring of threats from circulation of seasonal, pandemic and zoonotic influenza viruses with epidemic potential.
- Emphasis should be placed on: improving the quality of data collection and systematic analysis; promoting timely and complete public reporting of data; and enhancing prompt virus sharing to avoid vaccine mismatch.
- The quality of the influenza surveillance system should be evaluated regularly using a standardized approach in order to improve data quality, analysis and influenza sampling.
- An electronic-based system should be promoted for data entry and storage to improve real-time data analysis and data quality,

Better use of influenza surveillance data for public health decisions-making

- Surveillance data should be used regularly to assess the severity of seasonal, epidemic and pandemic influenza; data should always be linked to its use in public health actions, especially to develop policies for influenza control.
- Greater collaboration should be established between the ministries of health, academia and the private sector so as to translate research findings into optimal strategies, policies and practices for influenza control.
- Surveillance data should also be used to monitor the effectiveness of control programmes or interventions in reducing deaths and disabilities from influenza and influenza-associated illness. Collaboration between scientific communities, academia and the public sector on the use of such data for informed decision-making would contribute to capacity building.

Sustaining influenza virological surveillance: actions needed by the countries

- National influenza centres should build and maintain sequencing capacity for both seasonal influenza and other non-influenza respiratory viruses.
- Greater use should be made of the FluNet and EMFLU platforms for timely influenza data reporting.
- National influenza centres should share the influenza virus specimens with the WHO collaborating centres promptly to avoid vaccine mismatch.

Increasing the use and uptake of seasonal influenza vaccines in the Eastern Mediterranean Region

- Vaccination against seasonal influenza should be recognized as part of pandemic influenza preparedness. In countries with low vaccine uptake and in general, a case should be developed for economic investment in seasonal influenza vaccination highlighting the saving in healthcare cost that can be made as a result of the substantial decrease in influenza incidence through yearly vaccination.
- Best practices for introducing and managing seasonal influenza vaccination through national immunization programme should be shared with the countries so they can develop appropriate policies and practices to increase the use and uptake of seasonal influenza vaccines.
- In countries where the uptake of seasonal influenza vaccine is low or fragmented in the general population, seasonal influenza vaccination in high-risk groups should be considered an incremental gain. Of the high-risk groups, healthcare workers should be targeted for voluntary or mandatory vaccination backed up with policies and strong advocacy and awareness campaigns on the introduction of the vaccination and monitoring of coverage and uptake.
- Increasing the uptake and monitoring the vaccination coverage will still be a challenge. Coverage of seasonal influenza vaccines should be monitored periodically using population-based data and measures taken to correct any problems.
- Countries will need policies to support the introduction of seasonal influenza vaccines based on local evidence and analysis of their influenza burden and the likely effect of vaccination.
- Studies should be conducted on the use of and barriers to access to seasonal influenza vaccines in the general population and high-risk groups.

One Health for influenza surveillance: actions needed to improve detection and response

- Detection of and response to zoonotic influenza with epidemic potential can be improved by enhancing surveillance at the human-animal interface including periodic information sharing and joint risk assessment between the animal and human health sectors.
- The public health response to zoonotic influenza will rely on joint surveillance, investigation and laboratory detection under the One Health framework

Using the influenza platform for surveillance of respiratory syncytial virus and other emerging respiratory virus threats

- Surveillance for respiratory syncytial virus should be piloted using the same sentinel-based surveillance platforms used for severe acute respiratory infection.
- National influenza centres should build capacities to detect non-influenza respiratory viruses, especially for molecular detection of respiratory syncytial virus and sequencing of genotypes.
- Should vaccines against respiratory syncytial virus become available, surveillance data should be regularly analysed to better understand the burden, epidemiology and seasonality of respiratory syncytial virus.

Accelerating progress against pandemic threats: actions needed by the countries to prevent, detect and respond

- The surveillance platform for severe acute respiratory infection should be enhanced and sustained to detect any new influenza or other respiratory viruses with epidemic potential in real time.
- Essential capacities for managing the risk and effect of pandemic influenza need to be linked with the core capacities required to manage broader health security threats in the country.
- Planning for pandemic influenza preparedness should be considered in the context of strengthening the core capacity of the International Health Regulations and should be a part of national action plan for health security.
- The national pandemic influenza preparedness plan should be updated and reviewed using WHO's planning guidance and checklists. The plan should be tested periodically using desktop or other simulation exercises.

Sustaining better use of surveillance data for public health decision-making: panel discussion

Seven panel discussions were held on a broad range of topics. Panellists comprised ministry of health officials managing the influenza programme in their countries, academia, scientists and WHO staff who discussed ways to sustain the influenza programmes, the value of improving the system to better manage other health security threats, and how to improve the use of surveillance data for influenza control strategies and monitor the effectiveness of control intervention (Box 2).

Conclusions

Each year, influenza illness causes a substantial disease and economic burden throughout the world. This is being increasingly recognized even in tropical and subtropical areas like the WHO Eastern Mediterranean Region. Improving influenza surveillance is the key to better understanding the effect of influenza epidemics and pandemics and the measures used to limit or prevent them. The emergence of MERS-CoV in the Region in 2012 is a reminder that new respiratory viruses will continue to appear and are risks to national, regional and global health security. The continued circulation of MERS-CoV and avian influenza highlight the need to further improve the surveillance system for severe acute respiratory infection in order to track, detect, identify and monitor viruses which continue to evolve and change.

A vision for the future would be to sustain the quality and effectiveness of epidemiological and virological surveillance systems for influenza in the Region, including timely sharing of data for public reporting and better use of surveillance data. Establishing such an evidence base is necessary to make informed policy decisions to improve preparedness for and response to influenza epidemics or pandemics.

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