



Pandemic influenza preparedness (PIP) framework: Progress challenges in improving influenza preparedness response capacities in the Eastern Mediterranean Region, 2014–2017

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ABSTRACT

Influenza viruses with pandemic potential have been detected in humans in the Eastern Mediterranean Region. The Pandemic Influenza Preparedness (PIP) Framework aims to improve the sharing of influenza viruses with pandemic potential and increase access of developing countries to vaccines and other life-saving products during a pandemic. Under the Framework, countries have been supported to enhance their capacities to detect, prepare for and respond to pandemic influenza. In the Eastern Mediterranean Region, seven countries are priority countries for Laboratory and Surveillance (L&S) support: Afghanistan, Djibouti, Egypt, Jordan, Lebanon, Morocco and Yemen. During 2014–2017, US\$ 2.7 million was invested in regional capacity-building and US\$ 4.6 million directly in the priority countries. Countries were supported to strengthen influenza diagnostic capacities to improve detection, enhance influenza surveillance systems including sentinel surveillance for severe acute respiratory infection and influenza-like illness, and increase global sharing of surveillance data and influenza viruses. This paper highlights the progress made in improving influenza preparedness and response capacities in the Region from 2014 to 2017, and the challenges faced. By 2017, 18 of the 22 countries of the Region had laboratory-testing capacity, 19 had functioning sentinel influenza surveillance systems and 22 had trained national rapid response teams. The number of countries correctly identifying all influenza viruses in the WHO external quality assurance panel increased from 9 countries scoring 100% in 2014 to 15 countries in 2017, and the number sharing influenza viruses with WHO collaborating centres increased by 75% (from eight to 14 countries); more than half now share influenza data with regional or global surveillance platforms. Seven countries have estimated influenza disease burden and seven have introduced influenza vaccination for high-risk groups. Challenges included: protracted complex emergencies faced by nine countries which hindered implementation of influenza surveillance in areas with the most needs, high staff turnover, achieving timely virus sharing and limited utilization of influenza data where they are available to inform vaccine policies or establish threshold values to measure the start and severity of influenza seasons.

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Introduction

Influenza viruses with pandemic potential have been detected in humans in the Eastern Mediterranean Region (EMR). This includes influenza A(H1N1)pdm09 virus, and avian influenza A(H5N1) and

A(H9N2) viruses [1]. The circulation of these viruses highlights the importance of pandemic preparedness measures, including strong and sensitive surveillance systems to rapidly detect and respond to new influenza viruses that threaten regional and global health security [1].

The Eastern Mediterranean Regional Office of the World Health Organization (WHO) has made influenza a priority disease and is supporting its 22 countries to strengthen their influenza surveillance capacities. Fifteen countries have National Influenza Centres (NICs) which are designated by the country to undertake influenza laboratory and surveillance activities, and to contribute to Global

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Influenza Surveillance and Response System (GISRS). The aim of influenza surveillance is to provide timely and good quality epidemiological data and viral isolates to monitor trends, detect new strains, assess risk groups for infection and severe outcomes, and support the selection of influenza strains for vaccine production [2]. The Regional Office implements activities in collaboration with countries, the Centers for Disease Control and Prevention and the Naval Medical Research Unit Three. Strengthening laboratory and surveillance (L&S) capacities contributes to pandemic preparedness as outlined in WHO's guidance on pandemic influenza risk management [3], and more broadly, enhances core capacities as required under the International Health Regulations (IHR) (2005) [4].

In the aftermath of the 2009 influenza pandemic and with the ongoing threat of the A(H5N1) virus, WHO together with countries implemented a global approach to pandemic influenza preparedness and response. In May 2011, the World Health Assembly adopted the Pandemic Influenza Preparedness (PIP) Framework [5]. The Framework aims to improve the sharing of influenza viruses with pandemic potential and to increase access of developing countries to vaccines and other life-saving products during a pandemic.

As part of the benefit-sharing established under the Framework, countries are supported to enhance their capacity to detect, prepare for and respond to pandemic influenza. PIP funds are used to improve L&S capacities, estimate burden of disease, strengthen regulatory capacities, plan for pandemic product deployment, and establish risk communication capacities. From 2014 to 2017, PIP funds for these five areas of work were implemented in line with a partnership contribution implementation plan [6]. For L&S capacity-building under the implementation plan, WHO implemented activities globally and in each region to support all countries in pandemic preparedness. Additionally, 43 countries considered in most need of L&S capacity-building support were targeted for country-specific work plans. In the Eastern Mediterranean Region, seven countries were identified: Afghanistan, Djibouti, Egypt, Jordan, Lebanon, Morocco and Yemen.

During the four years of implementation, US\$ 2.7 million was invested in regional capacity-building through the Regional Office, and US\$ 4.6 million was invested directly in the seven L&S PIP priority countries. Countries were supported to strengthen influenza diagnostic capacities to improve detection, enhance influenza surveillance systems including sentinel surveillance for severe acute respiratory infection (SARI) and influenza-like illness (ILI), and increase global sharing of surveillance data and influenza viruses through GISRS.

This paper highlights the achievements and challenges faced to improve influenza preparedness and response specifically in L&S capacities and influencing influenza disease control policy in the Eastern Mediterranean Region from 2014 to 2017.

Progress in regional laboratory and surveillance capacities

Considerable progress has been made in strengthening L&S capacities to detect, monitor and share influenza viruses across the Region, as well as support the development of policies for influenza prevention and control (Table 1).

Since 2006, four geographically-dispersed countries of the Region (Djibouti, Egypt, Iraq and Pakistan) have identified and confirmed human cases of avian influenza A(H5N1). Egypt is the only country in the region which reported three human cases of influenza A (H9N1) viruses in 2015 and 2016. This highlights the importance of establishing reliable surveillance, laboratory diagnostic and rapid outbreak response capacities.

From 2014 to 2017, the number of countries in the Region with capacity for polymerase chain reaction (PCR) to detect Influenza

A and B and identify different subtypes of influenza A viruses, including seasonal influenza, H5 and H7 increased from 15 to 18. The number of influenza specimens tested and reported to WHO's FluNet/EMFLU from participating influenza laboratories increased significantly from 44,563 (2014) to 74,043 (2017). To monitor the accuracy and reliability of influenza PCR testing, WHO encourages participation in its global External Quality Assessment Programme (EQAP) [8]. The number of countries participating in this programme remained stable from 2014 to 2017. However, by 2017, there was a significant increase in the number of countries correctly identifying all influenza viruses in the EQAP panel from 9 countries scoring 100% in 2014 to 15 countries in 2017. During the same period, 13 countries were visited to assess the laboratory capacities and to provide technical support and hands-on PCR training workshops. The provision of technical expertise through training, mentoring and exchange visits to WHO collaborating centres, as well as the provision and maintenance of essential equipment and reagents, has contributed to this achievement. Improved laboratory diagnostic capacities enable detection of influenza viruses with pandemic potential, and can bolster virus sharing with GISRS for further characterization and risk assessment. This is in line with the objectives of the PIP Framework to strengthen protection against pandemic influenza by improving and strengthening GISRS.

To investigate and rapidly respond to influenza and other disease events, WHO promotes the establishment of multisectoral rapid response teams at national and subnational levels. Rapid response teams bring together the different skills and sectors (human and animal in particular) needed to appropriately characterize and control an outbreak, including emergency coordination, epidemiological investigations, data management, infection prevention and control, laboratory diagnosis, social mobilization, risk communication and logistics. In 2014, none of the countries of the Region had central or periphery rapid response teams. By 2017, all 22 countries of the Region, including all PIP priority countries, had rapid response teams established and trained at the central level. Of the 22 countries, 15 (68%) had also established multisectoral rapid response teams at the subnational level to facilitate rapid localized response to disease events. This success has advanced IHR (2005) core capacities and will benefit the response to influenza during seasonal epidemics and future pandemics.

Strong influenza surveillance is essential for effective pandemic detection, monitoring and response. Surveillance is used to assess the patterns of disease including seasonality, risk groups and other epidemiological factors. The information guides response strategies during a pandemic including for case management, risk communication and vaccination. In line with the partnership contribution implementation plan [6], the Regional Office promoted the establishment of sentinel surveillance systems that collect, analyse and report data on ILI and SARI. By the end of 2017, 27% more countries in the Region had functioning ILI or SARI surveillance systems including five countries with protracted complex emergencies. Among the seven L&S PIP priority countries, six countries have established ILI or SARI surveillance systems (Table 1). Only Djibouti did not achieve this milestone by the end of 2017.

As a collateral benefit, ILI and SARI surveillance systems serve as a platform for other respiratory disease surveillance including for respiratory syncytial virus (RSV) and Middle East respiratory syndrome (MERS) coronavirus [9,10]. In the Region, Egypt is participating in the global RSV surveillance project with data collection from their existing SARI sentinel surveillance sites [11]. The well-established SARI/ILI sentinel surveillance system in Jordan and Egypt contributed to the detection of MERS and H5N1 cases during 2014–2017.

Through increased influenza monitoring activities, the 15 NICs and other influenza laboratories in the Region have contributed positively to GISRS. In the four-year period, the number of countries

routinely sharing seasonal influenza viruses with WHO collaborating centres increased by 75% (from eight to 14 countries). Among L&S PIP priority countries, the number increased from two to five by the end of 2017. The number of positive influenza specimens shared with WHO collaborating centers increased from 174 in 2012 to 706 in 2017. Egypt, which is one of the PIP beneficiary countries shared positive isolates of human cases of influenza A (H5N1) viruses with the WHO Collaborating Center in Atlanta. Sharing seasonal influenza viruses is an important proxy of the capacity to share influenza viruses with pandemic potential, and it maintains the linkages between GISRS institutions including NICs and WHO collaborating centres. Seasonal influenza virus sharing from the Region also increases the representativeness of viruses available to inform the yearly composition of influenza vaccines.

For effective monitoring of influenza, WHO encourages regional and global data sharing. The Regional Office established a regional platform, Eastern Mediterranean Flu (EMFLU) Network, in 2016. By the end of 2017, 14 countries were consistently sharing their influenza data through this regional platform which assists in the analysis of trends, spread, intensity and impact of influenza. More countries in the Region are sharing their data globally through WHO's virological data platform, FluNet, and epidemiological data

platform, FluID (Table 1). For FluNet, the number of countries sharing their virological data increased from 11 in 2014 to 13 in 2017, and from four to six countries in the case of FluID during the same period.

Furthermore, efforts were exerted to improve the monitoring and networking capacities in the Region, and WHO supported the establishment of the Eastern Mediterranean Acute Respiratory Infection Surveillance (EMARIS) network. EMARIS is a network of countries in the Region working together to strengthen and enhance influenza surveillance, improve the use of surveillance data for developing control programmes, and promote research on influenza and other respiratory viruses. Two EMARIS meetings were organized in 2015 and 2017 to discuss and share surveillance and research findings for improving pandemic preparedness [12–14].

Influencing influenza disease control policy

Estimating influenza disease burden is one of the priority areas of work under the four-year implementation plan [6]. Burden of disease data are used by countries to develop evidence-based policies including for pandemic influenza response. WHO guidance pro-

Table 1
Influenza capacity achievements in countries of the World Health Organization (WHO) Eastern Mediterranean Region from 2014 to 2017.^a

Indicator ^b	Number of countries			
	2014		2017	
	All countries (N = 22)	L&S PIP priority countries subset (n = 7)	All countries (N = 22)	L&S PIP priority countries subset (n = 7)
(1) Rapid response team established and trained at:				75
– Central level and	0	0	22	7
– Periphery level	0	0	15	5
(2) Presence of at least one WHO recognised national influenza centre	15	6	15	6
(3) Capacity to detect new influenza viruses using polymerase chain reaction	15	5	18	6
(4) Capacity to characterize influenza virus by sequencing	6	1	7	2
(5) Participated yearly and scored 100% in the WHO External Quality Assessment Programme	Participated: 14	5	Participated: 15	6
	Scored 100%: 9		Scored 100%: 15	
(6) Routinely shared influenza viruses with WHO collaborating centres at least once a year in the past two years	8	2	14	5
(7) Functioning ILI or SARI surveillance system for influenza	15	3	19	6
(8) Consistently ^c reported virological data to WHO FluNet during the influenza season	11	4	13	5
(9) Consistently ^c reported epidemiological data during the influenza season to:				62
– EMFLU	NA ^d	NA ^d	14	6
– WHO FluID	4	1	6	2
(10) Completion of influenza disease burden estimates using surveillance or other data ^e	1	0	7	4
(11) Seasonal influenza vaccination introduced in high-risk populations	0	0	7	3

EMFLU: Eastern Mediterranean Flu Network, ILI: influenza-like illness, NA: not applicable, PIP: Pandemic Influenza Preparedness, SARI: severe acute respiratory infection.

^a Data source: For indicators 1, 3, 4, 7, 10 and 11, WHO surveyed Ministry of Health influenza focal points yearly to confirm the presence or absence of the capacity. For indicators 2, 5, 6, 8 and 9, WHO databased maintained at regional or headquarter level were used.

^b The indicators were selected from PIP framework indicators and used in WHO reports [7].

^c Consistently means that a country reports most of the weeks during the influenza season(s).

^d 2014 data are not available as the regional platform 'EMFLU' was established in 2016.

^e Of all countries in the Region, four countries estimated disease burden by calculating incidence rates, and three described burden in terms of the proportion of disease caused by influenza from total admissions/health-care facility visits. Of L&S PIP priority countries, two estimated disease burden by calculating incidence rates, and two described burden in terms of the proportion of disease caused by influenza from total admissions/health-care facility visits.

vides efficient methods to estimate the burden of disease using surveillance data [15]. By the end of 2017, nearly one-third of countries (seven out of 22) in the Region had estimated their disease burden including three L&S PIP priority countries. Five countries have already published their findings (Egypt, Iran (Islamic Republic of), Lebanon, Oman and Tunis) [16–20], while the manuscripts from Jordan and Morocco are under peer-review. National disease burden estimates can now be used by countries to inform pandemic influenza policy such as for risk-group identification and response measures required. The national estimates have also been used to develop updated global burden estimates. These are important achievements given the comparatively recent expansion of influenza surveillance systems in the Region to generate the necessary data for burden estimation.

Regional prioritization of influenza disease control, capacity-building and advocacy efforts by WHO in 2014–2017 have contributed to the introduction of seasonal influenza vaccines [21]. In 2014, none of the countries of the Region had a vaccination policy. By the end of 2017, seven countries, including three L&S PIP priority countries, had introduced seasonal influenza vaccination for high-risk populations. WHO provided technical support to these countries and facilitated information-sharing through EMARIS and other meetings to support countries in these vaccine introduction decisions [22].

Challenges and the way forward

The achievements in improving L&S capacities as well as influencing influenza disease control policy from 2014 to 2017 have been considerable. The commitment of countries of the Region and the systematic approach to capacity-building among WHO and other partners have led to great success. The contribution of PIP funds to these improvements has been important to catalyse activities and sustain the momentum required to strengthen influenza disease control and pandemic preparedness [23].

Challenges were encountered during the four years. Several countries in the Region are yet to share influenza surveillance data with regional or global WHO platforms, or to share viruses, including influenza viruses with pandemic potential, in a timely manner with WHO collaborating centres. Timely information and virus sharing are critical to rapidly detect changes in the virological, clinical or epidemiological patterns associated with influenza and to quickly implement seasonal or pandemic risk management measures. WHO continues to work with countries to address these gaps through meetings, technical support and by encouraging countries without NICs to designate a national laboratory so that there is dedicated participation in GISRS and global information- and virus-sharing. In 2017, WHO also published practical guidance for countries on sharing influenza viruses [24,25]. The WHO Regional and Country Offices will continue to advocate for the application of the guidance especially as the sharing of influenza viruses with pandemic potential constitutes a key component of the PIP Framework.

Despite the availability of influenza surveillance data, many countries in the Region have not calculated the baseline or threshold values to measure the start and severity of influenza seasons. Having baseline or threshold values for influenza will help countries to determine the level of disease activity that would signal the start or end of a season or provide an alert to an unusually severe or atypical season [26]. The establishment of EMFLU for data management and the ongoing surveillance capacity-strengthening efforts by WHO and other partners will help countries to better utilize surveillance data. Many countries do not have a seasonal influenza vaccine policy. In future, PIP funds will be used to support countries to utilize disease burden data to inform vaccination policies and strategies [27].

For laboratory capacities, a number of countries experienced stock-outs of influenza testing kits which hindered timely processing of specimens and monitoring of trends. WHO is encouraging countries to preposition additional testing kits before the start of the influenza season and to establish reliable procurement practices.

Broader challenges to implementation were also encountered. Nine of the 22 countries in the Region faced protracted complex emergencies which hindered implementation of influenza surveillance in areas with the most needs. In addition, despite regular capacity-building and training for health workers, high staff turnover, reassignment of trained staff to other responsibilities, and multitasking of trained staff may affect the sustainability of the work. WHO works closely with countries to address immediate needs as health system initiatives facilitate longer term solutions.

Despite the challenges, strengthening pandemic preparedness remains a key regional priority. Moving forward, PIP funds will continue to be used to strengthen GISRS, underlying L&S capacities, and to support the utilization of surveillance and burden data for decision-making. These are directions for future implementation and are necessary components of better pandemic influenza preparedness.

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