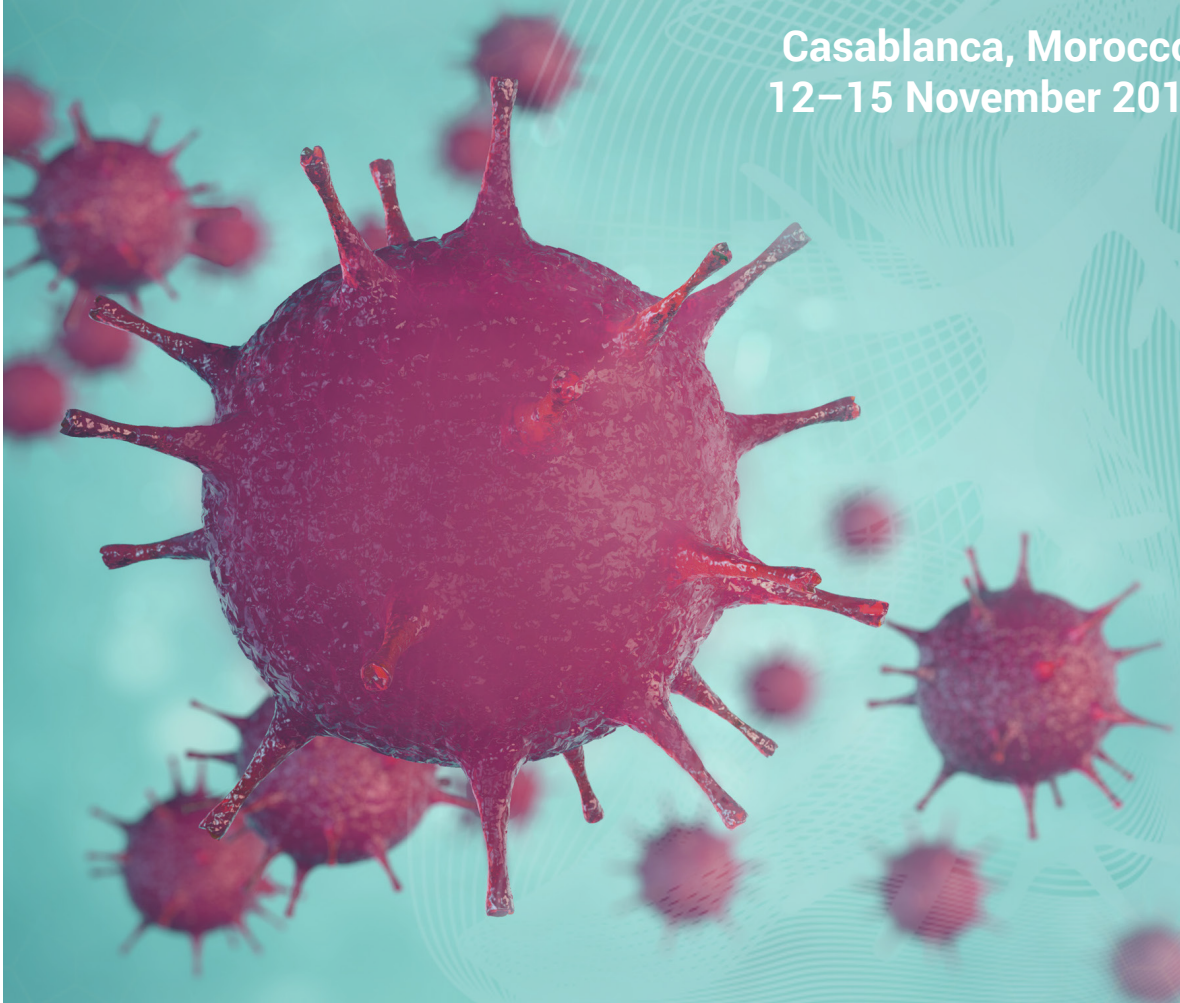
Second Scientific Conference
EMARIS 2019

WHO-EM/CSR/290/E

REPORT ON THE

Fifth meeting of the Eastern Mediterranean Acute Infection Surveillance (EMARIS) network and the second scientific conference on acute respiratory infections in the Eastern Mediterranean Region

Casablanca, Morocco
12–15 November 2019



World Health Organization
REGIONAL OFFICE FOR THE Eastern Mediterranean

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Better data, better policy, better action

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ACRONYMS AND ABBREVIATIONS

ARI	acute respiratory infection
BSL	biosafety level
CAHO	community animal health outreach
CC	collaborating centre
CDC	US Centers for Disease Control
COM	capability, opportunity and motivation
CVV	candidate vaccine virus
EMARIS	Eastern Mediterranean Acute Respiratory Infection Surveillance Network
EMR	Eastern Mediterranean Region
EQA	external quality assessment
EQAP	WHO External Quality Assessment Project
EV-D68	enterovirus D68
FETP	field epidemiology training programme
GIP	WHO Global Influenza Programme
GISAID	Global Initiative on Sharing All Influenza Data
GISRS	Global Influenza Surveillance and Response System
GOARN	Global Outbreak Alert and Response Network
HAdV	human adenovirus
IHR	International Health Regulations
ILI	influenza-like illnesses
IPC	infection prevention and control
JEE	Joint External Evaluation
LMICs	low- and middle-income countries
MERS-CoV	Middle East respiratory syndrome coronavirus
NAPHS	national action plan for health security
NGS	next-generation sequencing
NIC	national influenza centre
NITAG	national immunization technical advisory group
NPI	non-pharmaceutical intervention
OHZDP	One Health Zoonotic Disease Prioritization Tool
PIP	pandemic influenza preparedness
PISA	Pandemic Influenza Severity Assessment
PIVI	Partnership for Influenza Vaccine Introduction
PPE	personal protective equipment
RSV	respiratory syncytial virus
SARI	severe acute respiratory infections
TIPRA	Tool for Influenza Pandemic Risk Assessment
WHO	World Health Organization

NOTE TO READER

This report aims to capture the key information and themes that emerged from the presentations and discussion rather than providing a strictly chronological account of the meeting.

The scientific proceedings of the conference have been published as a supplement to the *Oman Medical Journal* (Second Scientific Conference for Eastern Mediterranean Acute Respiratory Infections Surveillance (EMARIS): Conference Proceedings. Oman Medical Journal. 2020;35, 1:S02.1–20.).

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EXECUTIVE SUMMARY

In brief

Emerging and re-emerging respiratory pathogens pose a major threat to global public health security. In the WHO Eastern Mediterranean Region, acute respiratory infections (ARIs) are one of the leading causes of illness and death and significantly impact regional health and economic development.

The Eastern Mediterranean Acute Respiratory Infection Surveillance network (EMARIS) was set up in 2006 as a means to enhance surveillance and response capacities for ARIs in the Region, especially influenza. It meets every two years to share best practices in influenza surveillance, track regional progress, address knowledge gaps and identify lessons in public health preparedness and response.

In November 2019, EMARIS met for the fifth time, in Casablanca, Morocco, in conjunction with the second Scientific Conference on Acute Respiratory Infections. Under the theme of "better data, better policy, better action", the conference was designed to support data-driven public health policy-making.

Over four days of presentation and discussion, meeting participants shared their achievements and challenges, presented their best practices and showcased their latest research findings across nine themes: global and regional strategies, surveillance in the Eastern Mediterranean Region, disease burden estimates, leveraging outbreak structures for influenza, Middle East respiratory syndrome coronavirus (MERS-CoV) and other ARIs, influenza vaccination, biosafety and biosecurity, One Health for influenza, and pandemic preparedness.

More than 180 people, including representatives from all 22 countries of the Region, attended the meeting. More than 170 abstracts were submitted by researchers from the Region; 50 were presented at the conference as oral or poster presentations. The broader meeting also included 46 other expert speakers as well as seven panel discussions and four skills-building workshops on pandemic preparedness, outbreak investigation, data quality and epidemiological analysis, and vaccine coverage.

Special awards to recognize the most innovative abstracts and the best oral and poster presentations were given to Farag Elmoubasher from Qatar, Hind Bouguerra from Tunisia and Fatimah Alghawi from Saudi Arabia, respectively.

Influenza capacities in the Eastern Mediterranean Region

At both global and regional levels, the world's collective capacity to detect influenza has improved significantly over the past half-century. The backbone of this capacity is the Global Influenza Surveillance and Response System (GISRS); and the Eastern Mediterranean Region's contribution to this critical network is growing steadily. Today 19 of the Region's 22 countries have functioning surveillance systems, and the other three are not far behind. There is good data coverage at national and regional levels and growing laboratory capacity for generating robust epidemiological and virological data and reporting it to GISRS.

The Region also has its own data-sharing platform, EMFLU, which produces weekly and monthly bulletins and receives regular data from 18 countries across the Region. Every year, countries in the Region test and report 84 668 influenza specimens to EMFLU, contributing around 20–25% of all influenza detections that are used in the biannual global vaccine composition meetings.

The Eastern Mediterranean Region's capacities in influenza prevention and control are also increasing, with a growing number of influenza policies in place, more rapid response teams present in the Region and increasing use of seasonal vaccines in several nations. Five countries have used their surveillance data to estimate the burden of influenza, and a further seven are in progress. Several countries have also carried out cross-sectional studies on influenza vaccine hesitancy, acceptance and demand among health care workers.

Challenges to tacking influenza in the Eastern Mediterranean Region

EMARIS participants highlighted the challenges they face in undertaking influenza surveillance, implementing prevention and control activities and preparing for the next pandemic. Key challenges cited include:

- Complex operational contexts and increasing fragility: more than half of the countries of the Region are dealing with ongoing conflict, which poses significant operational challenges.
- Limited animal surveillance: animal surveillance is critical in the Region where human–animal interaction is high, yet remains weak in many countries.
- Limited use and uptake of vaccines: vaccine coverage in the Region remains low. Vaccine hesitancy is partly to blame; but so too are political barriers, industry constraints and technical challenges.
- Inconsistent data sharing: the timeliness and quality of data shared varies across the Region.
- Limited cross-sectoral involvement: influenza requires a One Health approach but cross-sectoral collaboration in many countries remains informal at best.
- Lack of preparedness planning: only six countries in the Region have a publicly available pandemic influenza preparedness plan; and only two have been published or revised since WHO's new guidance was released in 2013.

Priorities for action

Across the four days of EMARIS 2019, meeting participants considered what countries can do to strengthen influenza detection, prevention and control in the Eastern Mediterranean Region. A broad range of recommendations emerged from their deliberations. These were:

To Member States

1. Support early detection by strengthening human and animal epidemiological and virological surveillance, filling related knowledge gaps strategically, and building laboratory capacity to support the Global Influenza Surveillance and Response System (GISRS).

2. Enhance and expand influenza prevention by improving seasonal vaccination programmes and investing in non-pharmaceutical preventive measures.

3. Prepare for pandemic influenza through updating and testing national preparedness plans, including the development of national pandemic vaccine deployment plans.

4. Strengthen the national evidence base to improve understanding of influenza seasonality, estimate burden of influenza in more countries, scale up severity assessments and, ultimately, translate research outcomes into policy.

5. Search for synergies across diseases by using the influenza infrastructure to strengthen other respiratory disease surveillance capacities and integrating influenza into national disease surveillance systems.

6. Work together to align efforts by building partnerships in research and practice, fostering regional collaboration, aligning plans with global strategies and promoting greater data sharing.

7. Promote the One Health approach through building political will for animal health, prioritizing zoonotic disease threats collaboratively and developing mechanisms for integration.

8. Boost awareness and influenza seasonal vaccine uptake by tailoring and targeting messages to key groups, engaging new partners in communication and harnessing behaviour change theory.

9. Engage and mobilize communities by involving them in prevention, detection and control of influenza as equal partners, and engage marginalized groups and political leaders.

10. Be flexible and pragmatic by adapting systems to evolving situations and tailoring solutions to local contexts.

To WHO

11. Continue to support countries in building capacities to strengthen influenza systems and structures for influenza prevention, detection and control.

12. Facilitate research for policy by promoting and supporting national influenza burden estimations and other studies to build the relevant national evidence base for meaningful policies.

13. Incorporate country priorities into regional and global guidance and strategies.

14. Facilitate knowledge exchange and collaboration through forums and opportunities for exchanging experience and expertise across the Region, including for other respiratory diseases beyond influenza.

15. Continue to promote the One Health approach through capacity-building and the development of standard operating procedures and other guidance documents.

PART 1. INTRODUCTION

1. INFLUENZA: A GLOBAL AND REGIONAL THREAT

Emerging and re-emerging respiratory pathogens pose a major threat to global public health security; every year seasonal influenza alone affects an estimated one billion people, causing up to 650 000 deaths worldwide. An influenza pandemic could be even more fatal, depending on when and where it emerges and how severe the disease is. The 2009 pandemic of A(H1N1) spread to more than 214 countries in less than nine weeks, killing up to 395 000 people. But the previous pandemic in 1968 was even more deadly, killing an estimated one to three million people.

Influenza pandemics are predictably unpredictable. But the World Bank estimates that even a moderate pandemic would cost up to US$ 570 billion, or 0.7% of global income, every year. And WHO cites a global influenza pandemic as one of the world's top 10 threats to global health in 2019.

Just as with many diseases, influenza hits poor and vulnerable groups the hardest. It is among the most fatal illnesses in low- and middle-income countries (LMICs); and it is typically more deadly in very young or elderly people, as well as pregnant women and people with underlying conditions.

In the WHO's Eastern Mediterranean Region, ARIs are one of the leading causes of illness and death and significantly impact regional health and economic development. Across all countries in the Region, influenza is the biggest cause of morbidity and mortality associated with ARIs, although other respiratory viruses, such as respiratory syncytial virus (RSV) and rhinovirus, are also important, as are emerging respiratory viruses, including the Middle East respiratory syndrome coronavirus (MERS-CoV).

Characteristics of influenza seasons in the Region vary from country to country, and year to year. Both influenza A and B are present in the Region. Over the past two years, influenza B has been more deadly in some countries, such as Yemen, while the opposite has been true in other countries, like Tunisia. Subtypes similarly vary across countries; A(H1N1)pdm09 was the most prevalent virus in 2018/2019 across the Region as a whole (see Figs. 1a and 1b), although in some countries, including Morocco and Oman, A(H3) has dominated the latest season. Across all countries, young children and the elderly are particularly adversely affected (especially during winter), as well as those living with chronic disease and those living in cold climates.

The Region is also home to many emerging strains of influenza in animals that have pandemic potential.

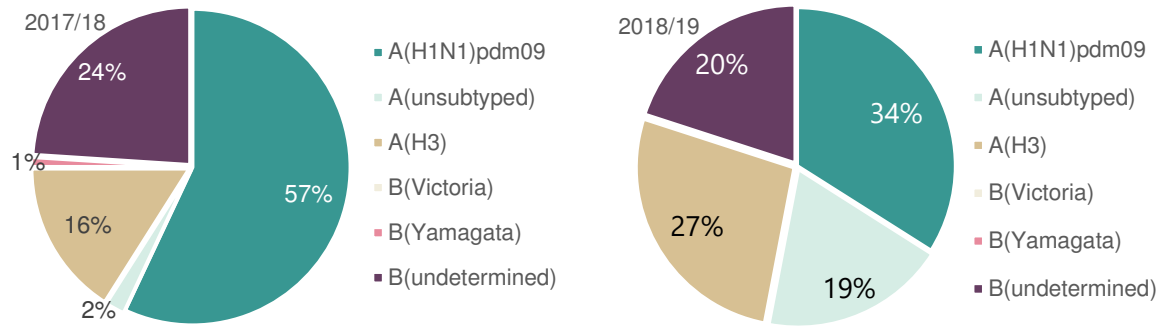

Fig. 1a. Circulating strains of influenza in the Eastern Mediterranean Region in 2018/2019

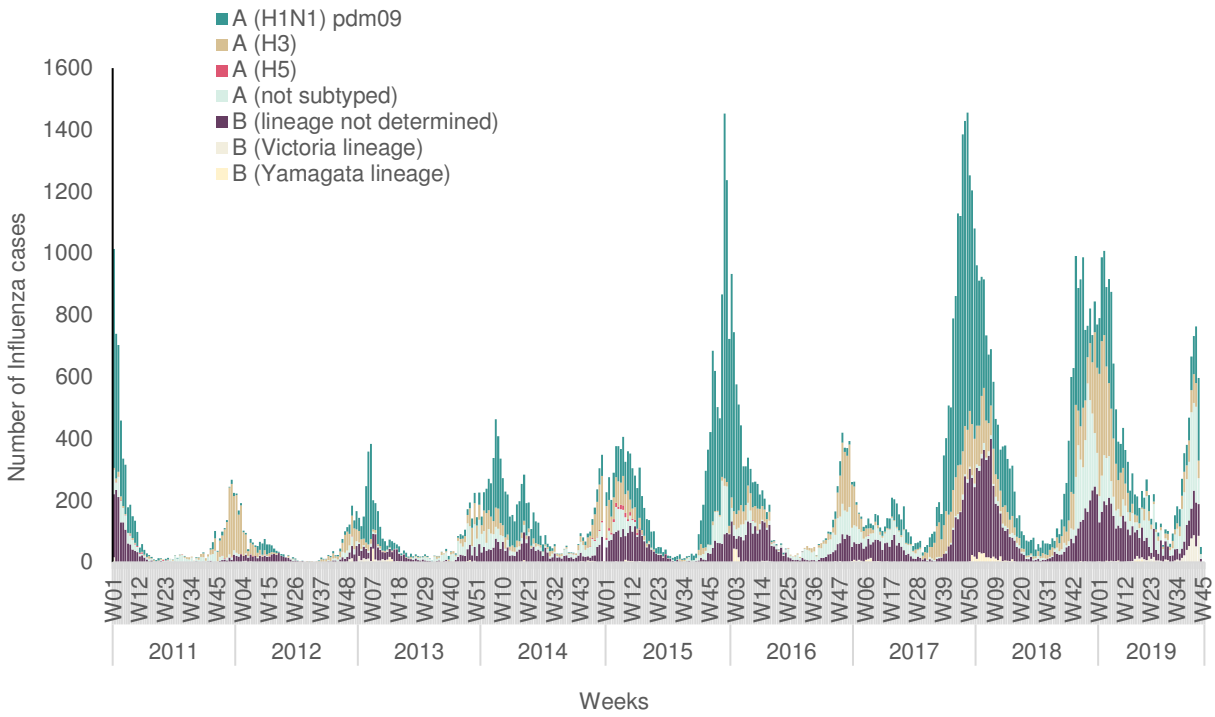

Fig. 1b. Weekly positive influenza cases by subtype, 2011–2019

Source of data: FluNet and EMFLU.

2. EMARIS

The Eastern Mediterranean Acute Respiratory Infection Surveillance (EMARIS) network was set up in 2006 to enhance surveillance and response capacities for ARIs in the Eastern Mediterranean Region, especially influenza. The network, which is made up of national and international policy-makers, researchers and scientists, doctors and clinicians, and other stakeholders in the Region, meets every two years to share best practices in influenza surveillance, track regional progress, and draw lessons on public health preparedness and response. In 2017, to enable a review of interesting and relevant research on ARIs in the Region to take place during its meetings, EMARIS integrated the first Scientific Conference on Acute Respiratory Infections for young researchers into its agenda. A review of this last meeting can be found at: https://emarisconference.com/review-of-2017/.

Since the network was established, a range of initiatives have combined to strengthen the Region's capacity to detect, prepare and respond to both seasonal and pandemic influenza. As the availability of surveillance data continues to increase, countries across the Region have started to use their data to improve decision-making to prevent, detect and control ARIs.

3. ABOUT THE MEETING

In November 2019, the Infectious Hazard Management technical unit of the WHO Regional Office for the Eastern Mediterranean convened the fifth meeting of the EMARIS network, in Casablanca, Morocco. Centred on the theme of "better data, better policy, better action", the meeting was designed to support the growing focus on data-driven public health policy-making.

The meeting was held alongside the second Scientific Conference on Acute Respiratory Infections. During the combined meeting, participants shared their achievements and challenges, presented evidence and best practices and showcased their latest research findings on influenza and other respiratory viruses.

Over four days of presentation and discussion, the meeting specifically aimed to:

- review the achievements and challenges countries face in strengthening surveillance and response capacities for seasonal and pandemic influenza in the Region;
- share evidence and best practices emerging from the Region on using influenza surveillance data for severity assessments and on outbreak detection;
- discuss how surveillance data on influenza and other respiratory diseases can be translated into setting policies and programmes for influenza prevention and control;
- document and showcase new scientific achievements and operational research findings for prevention, detection and response to seasonal, novel and other emerging respiratory viruses;
- and enhance young researchers' knowledge and skills on selected technical and topical areas befitting the theme of the conference.

Presentations and discussions were split across nine themes, covering topics such as detecting respiratory infections, estimating influenza burdens, preventative action and outbreak response (see Fig. 2). The agenda also included 50 oral and poster presentations on the latest research findings as well as 46 expert presentations and four skills-building workshops.

Fig. 2. EMARIS 2019 in numbers

PART 2. SUMMARY OF DISCUSSIONS

1. GLOBAL AND REGIONAL INFLUENZA STRATEGIES, CAPACITIES AND CHALLENGES

1.1 International frameworks

Individual countries may or may not have their own strategies for tackling seasonal and/or pandemic influenza. At a global and regional level, the recently launched Global Influenza Strategy sets the framework for driving and shaping a coherent approach to tackling influenza in the Eastern Mediterranean Region.

WHO Global Influenza Strategy

In March 2019, WHO launched the Global Influenza Strategy 2019–2030, aimed at protecting people in all countries from the threat of influenza. The strategy provides a common framework for WHO, countries and partners to jointly enhance global and national pandemic preparedness, combat the ongoing threat of zoonotic influenza, and improve seasonal influenza prevention and control.

With strong links to major existing global health strategies, including the WHO Thirteenth General Programme of Work, the International Health Regulations (IHR) (2005) and the Public Health Research Agenda for Influenza, the new strategy places a large focus on two key areas of activity:

- the development of better global tools, such as vaccines, antivirals and treatments; and
- stronger country capacities, which are integrated within national health security planning.

The first key area of activity focuses on promoting research and innovation to address unmet needs. This includes developing improved, novel and universal vaccines as well as more effective treatments. It also includes establishing better detection methods and improving the collective understanding of both the virus and host response, to better predict virus evolution, forecast spread and improve vaccine selection.

The second key area includes strengthening global surveillance and data use (for example, by improving countries' understanding of severity, continuing to enhance the global influenza surveillance and response system and coordinating across sectors) as well as expanding national seasonal influenza prevention and control policies and programmes, and improving countries' pandemic preparedness by developing, updating and testing pandemic preparedness plans.

Regional strategic framework

At a regional level, the WHO Regional Office for the Eastern Mediterranean has translated the WHO Global Influenza Strategy to the regional context, developing a strategic framework for the prevention and control of emerging and epidemic-prone infectious diseases in the Eastern Mediterranean Region, 2019–2023 (see Fig. 3).

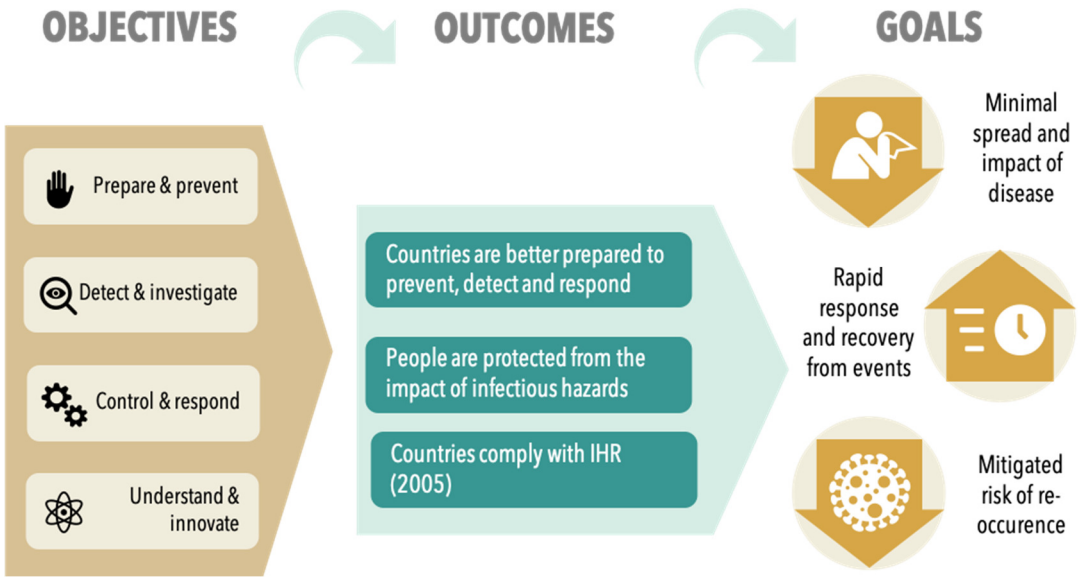

Fig. 3. The strategic framework for the prevention and control of emerging and epidemic-prone infectious diseases in the Eastern Mediterranean Region, 2019–2023

Acknowledging the multiple threats facing the Region, the framework aims to ensure that countries are better prepared to prevent, detect and respond to a range of infectious hazards and are better protected from their impacts. It will do this through a range of activities aimed at fulling four strategic objectives, as outlined in Fig. 3.

1.2 Capacities for tackling influenza

The influenza virus is constantly evolving so effective prevention and control relies on access to the most recent information. Because a new strain can emerge anywhere in the world, at any time, constant surveillance and worldwide coordination are essential to catch and contain it quickly.

"GISRS is a global asset…that has been the mainstay of influenza surveillance and control for 67 years."

At both global and regional levels, the world's collective capacity to detect influenza is growing as surveillance improves. The backbone of this capacity is the network of national influenza centres, WHO collaborating centres, essential regulatory laboratories and H5 reference laboratories called the Global Influenza Surveillance and Response System (GISRS). GISRS provides continuous seasonal and zoonotic influenza surveillance and virus sharing across the world. Made up of 153 institutions in 114 countries, GISRS tests up to four million specimens each year to identify new strains of influenza with pandemic potential as and when they emerge. GISRS also provides the backdrop for the free exchange of epidemiological data (through FluID), virological data (through FluNet) and sequencing data (through the Global Initiative on Sharing All Influenza Data, GISAID). Established in 2008, GISAID now contains HA sequencing data for more than 270 000 viruses from 198 countries.

Twice a year, WHO convenes a global group of experts to analyse the latest genetic and antigenic data generated by GISRS, and issue recommendations on the composition of the influenza vaccines for the next influenza season. These recommendations are used by national regulatory agencies and pharmaceutical companies to develop, produce and license influenza vaccines.

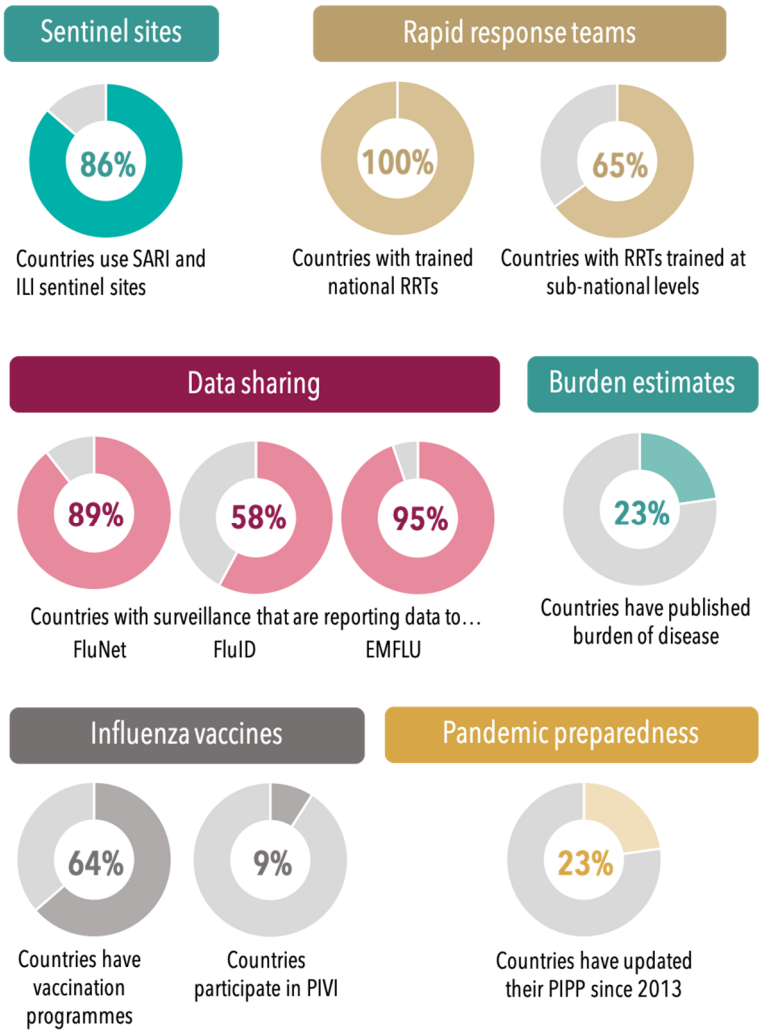

Fig. 4. Main components, and current status, of influenza programmes in the Eastern Mediterranean Region

Number of countries in the Eastern Mediterranean Region = 22; number of countries that have surveillance = 19.

In the Eastern Mediterranean Region, capacities to monitor influenza and contribute to GISRS have increased significantly in recent years. Today, 19 out of the Region's 22 countries have functioning surveillance systems using sentinel sites for influenza-like illnesses (ILI) and severe acute respiratory infections (SARI); the remaining three countries are not far behind. There is good data coverage at national and regional levels and growing laboratory capacity for generating robust epidemiological and virological data (see Fig. 4).

Data-sharing is similarly improving: the Eastern Mediterranean Region has its own data-sharing platform, EMFLU, which produces weekly and monthly bulletins and receives regular data from 18 countries across the Region. The number of specimens tested and reported from the Region has nearly tripled since 2011; and the number of viruses shared has more than quadrupled in the same time. Today, the Region tests and reports 84 668 influenza specimens to EMFLU every year; it contributes around 20–25% of all influenza detections that are used in the biannual vaccine composition meetings.

Other capacities in the Eastern Mediterranean Region are similarly increasing, with growing use of seasonal vaccines and an increasing number of laboratories able to use RT-PCR, cell

culture and gene sequencing technologies. Research and data analysis are ongoing, particularly in estimating disease burden and understanding vaccine use.

Vaccination coverage across the Region remains low, even in countries with vaccination programmes in place. And influenza preparedness planning is similarly weak, with nearly half of the countries in the Region having no publicly-available preparedness plan for pandemic influenza.

1.3 Challenges to tackling influenza

Despite progress in influenza detection, prevention and control in the Eastern Mediterranean Region and beyond, many challenges remain. Some of the most significant, as identified by participants at the EMARIS meeting, are listed below.

Complex operational contexts and increasing fragility. More and more countries are having to work against a backdrop of conflicts, displacements, disease outbreaks and natural disasters. More than half the countries in the Region are experiencing ongoing conflict, with 10 countries classified as fragile states by the World Bank. The Region is the source of two thirds of the world's refugees; and is home to more than half (53%) of world's population in need of humanitarian assistance. Today, there are 16 active emergencies ongoing in the Region. Complex contexts like these challenge the logistics of an influenza programme.

Tackling influenza in complex emergencies: Lessons from the field

Countries facing complex emergencies tend to have fragile health systems, displaced populations, limited health workforce, security concerns and limited or no laboratory networks. Business as usual will not work for influenza programmes in these situations. But progress can still be made; experience from the field suggests that the key lies in staying flexible and building on existing assets.

EMARIS participants shared practical advice for operating within complex emergencies:

- **Surveillance**. Start with ILI surveillance using whatever systems exist, such as the early warning, alert and response networks. Choose one sentinel site for SARI if the situation allows, using value judgements to choose the right site. Use data from neighbouring countries as proxies if needs be.
- **Laboratory capacity**. Integrate laboratory functions for influenza with other public health programmes, for example by drawing on ex-Global Fund projects. Maximise capacity-building opportunities for sample collection, shipment and laboratory testing through other programmes. Where available, use the polio network for sample shipment and transport.
- **Data analysis**. Build on existing infrastructure, including case-based measles surveillance, polio surveillance, and programmes for tuberculosis, malaria and HIV/AIDS. Make use of any data analysis systems that already exist for immunization, polio or other disease control programmes.
- **Response**. Tap into existing capacity for outbreak alert, detection and investigation, including field epidemiology training programmes and rapid response teams.
- **Preparedness**. Build influenza into the national action plan for health security (NAPHS) for implementing the International Health Regulations (2005); or into any other existing epidemic preparedness plans for infectious disease.

A dynamic virus with multiple hosts. Influenza can be found across a broad range of hosts from birds, bats and pigs to horses, tigers and seals. It constantly evolves and diversifies over time and space, and can jump across species anywhere, at any time. This limits our predictive power and is particularly challenging to vaccine composition, since recommendations have to be made in advance.

Variable host immunity. Immunity to influenza is known to vary significantly across individuals. In many cases, immunity is compromised by comorbidities and lack of vaccination. For example, recent data from Morocco, Oman, Tunis and Yemen show that SARI and deaths are more common among influenza patients with underlying chronic conditions, such as asthma, diabetes and heart disease. In other cases, variable immunity may be associated with waning immunity over time (of up to 7% per month) for some groups, the impact of repeat vaccination, or imprinting (where a person's first infection with influenza determines how they respond to influenza virus infection or vaccination for the rest of their life).

Patchy vaccine performance. Vaccine effectiveness varies from year to year. Since 2015, there has been a steady decrease in influenza vaccine effectiveness, largely driven by the decreasing effectiveness of the A(H3) vaccine. In part, this may be because the use of egg-based production introduces structural changes into the virus.

Slow manufacturing timelines. It takes around six months from the time vaccine recommendations are made by WHO to the time when vaccines are available for use. In the case of a pandemic, this is far too slow and means that vaccines can only be made available at late stages in the epidemiological curve. Manufacturing vaccines is a complex process, which needs to include a number of steps beyond producing the vaccine itself, such as packaging, potency testing, regulation and distribution.

Limited use and uptake of vaccines. This represents a gap in implementation: even in countries with vaccination policies, programmes are weak. The lack of vaccination programmes poses a double challenge to tackling influenza: it limits the use of vaccines for seasonal influenza; and evidence shows that it can also hold up access to a vaccine during a pandemic.

"Despite widespread policy recommendations on influenza vaccination, attaining high coverage rates remains a challenge in the Eastern Mediterranean Region."

Vaccine hesitancy. Listed by WHO as one of the top 10 threats to global health, vaccine hesitancy is a growing concern, and not only for influenza. The reasons why people do not choose to vaccinate are complex and vary significantly across different countries, contexts and communities. They are thought to include complacency, inconvenience in accessing vaccines, and lack of confidence.

Global barriers to sharing. Global treaties, trade sanctions and legal bindings can put up barriers to sharing data and viruses for influenza surveillance. For example, the recent trade sanctions against Islamic Republic of Iran have made preparing and shipping influenza specimens particularly difficult. In other countries, national influenza centres have had problems sharing influenza viruses because of conflicts with national legislation on access and benefit sharing arising from the recent implementation of the Nagoya Protocol that is part of the Convention on Biological Diversity.

Inconsistent and incomplete surveillance data. The timeliness, quality and representativeness of data shared with global and regional platforms varies from country to country. In many cases, data is reported too late to be included in the bi-weekly influenza updates issued by WHO.

"In competency building, we need both all-hazard capacities and hazard-specific capacities."

Lack of preparedness planning. Globally, more than half of the world (99 countries, including 14 in the Eastern Mediterranean Region) still have no publicly-available pandemic influenza preparedness plan. This represents a big gap in the fight against influenza; but is also an opportunity for introducing a multisectoral approach to planning that can simultaneously build IHR core capacities and address other hazards beyond influenza.

2. VIROLOGICAL SURVEILLANCE IN THE EASTERN MEDITERRANEAN REGION

2.1 Virological surveillance networks

Countries undertake virological surveillance for many reasons, including, for example, to:

- detect and characterize circulating influenza viruses;
- identify novel strains of influenza, including zoonotic ones with pandemic potential;
- contribute to global vaccine strain selection by isolating and sharing viruses;
- evaluate susceptibility of influenza viruses to antivirals;
- identify groups at high risk of severe disease to target education and prevention measures; and
- report data to ministries of health and WHO;

From physicians and national influenza centres (NICs) to WHO collaborating centres and regulatory laboratories, there are well-developed and developing global and regional networks of stakeholders involved in collecting and analysing data to support virological surveillance (see Fig. 5). The outputs of these networks feed into routine surveillance and virus characterization at country and global levels; and enable the development of country-specific risk assessments and recommendations for action. They also inform the biannual vaccine composition meeting convened by WHO.

The Eastern Mediterranean Region influenza laboratory network includes 17 NICs in 16 countries and a further four national influenza laboratories. The network forms the basis for regional preparedness; and it tests beyond influenza (including, for example, MERS-CoV, RSV and other high-threat pathogens).

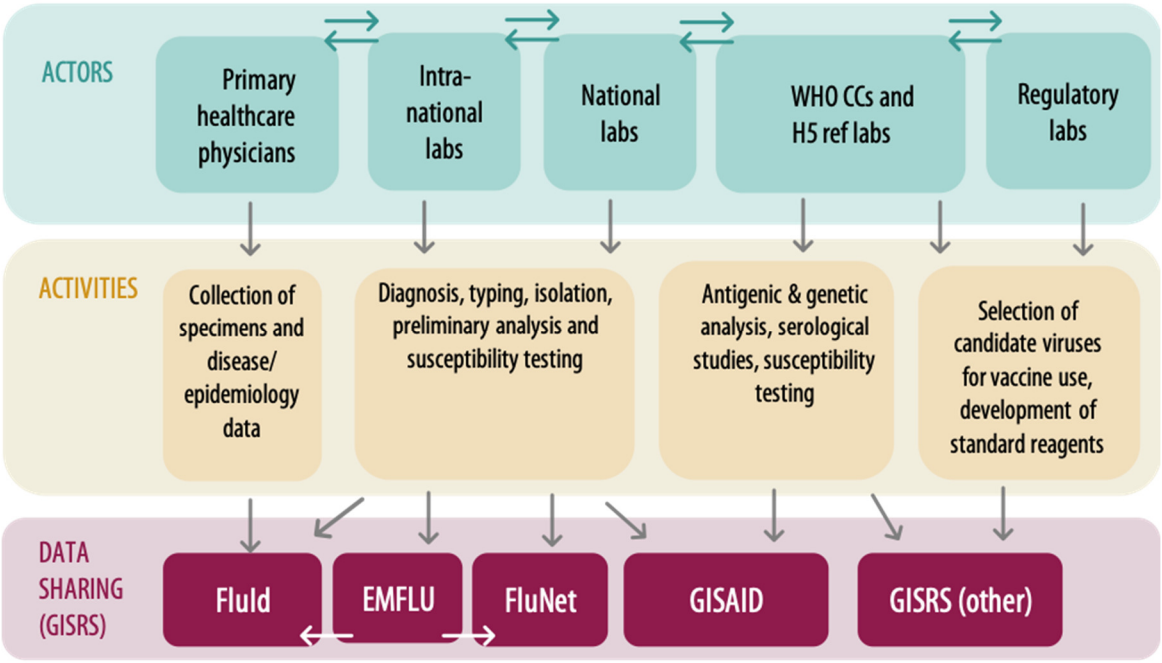

Fig. 5. Each link in the global and regional virological surveillance chain has a distinct role

To work effectively, virological surveillance relies on timely and consistent data sharing through GISRS. This, in turn, relies on rapid diagnosis and initial characterization (of both type and subtype) at NICs followed by timely reporting of data to FluNet and regular shipment of specimens to WHO collaborating centres and H5 reference laboratories. To support this, the WHO Shipping Fund project provides shipping services for all NICs and other influenza laboratories to cover the cost of sending samples to a WHO collaborating centre or H5 reference laboratory; and to provide logistical and technical support.

While most specimen collection is done within the public sector, private physicians supplement the public network in some countries, providing a huge asset to surveillance. In Morocco, for example, up to 24 long-term voluntary partners in the private sector collect samples and ship them (free of charge) to the NIC for testing. Experience suggests that good participatory involvement is critical to engaging the private sector in this way. Private volunteers in Morocco are given no rewards or incentives for contributing to influenza surveillance; but they are invited to all the relevant meetings, included in briefings and trainings, and regularly contacted through scientific organizations.

NICs are an important link in the surveillance chain, in the Eastern Mediterranean Region as elsewhere. In many countries, their role extends beyond diagnosis, typing, virus isolation and preliminary analysis or sequencing. For example, the NIC in Palestine has multiple other functions, including:

- providing epidemiological data to health directorates and government departments;
- providing physicians with equipment to collect, store and transport samples;
- detecting any significant shift in the virus type and informing national and global health officials; and
- providing technical help and training in the fields of sample collection, diagnosis, storage, transport, biosafety and biosecurity issues and good safe practices.

WHO collaborating centres and H5 reference laboratories are equally critical to the global surveillance network. In addition to providing detailed antigenic and genetic analysis, these laboratories support NICs by providing updated diagnostic reagents, reference viruses, ferret anti-sera and cell lines for isolation. They also provide technical support, training courses and learning exchanges; and develop updated protocols and sequences of primers for NICs to use.

CDC yearly laboratory work on influenza viruses

CDC's Influenza Division has served as a WHO collaborating centre since 1956 and is the world's largest reference centre for public health interventions to control and prevent pandemic and seasonal influenza. Every year, the centre:

- develops, manufactures and deploys diagnostic kits to support the testing of 100 000 specimens in 93 state and local public health laboratories;
- does full genetic sequencing on about 7000 influenza viruses;
- tests about 2000 influenza viruses for immune properties;
- prepares as many as 50 candidate viruses for use in vaccine production; and
- integrates all data from the same specimens to support vaccine virus selection.

2.2 Assessing and assuring laboratory quality

External quality assessment (EQA) is a system for objectively checking a laboratory's performance and is a critical aspect of laboratory quality management. Participating in an EQA programme gives laboratories objective evidence of their testing quality. It also delivers valuable data for comparing performance across sites, identifying systematic problems with kits or operations and highlighting training needs.

The Eastern Mediterranean Region influenza laboratory network participates in several EQA programmes. Most recently, this has included:

- A CDC influenza molecular quality assessment. This started in April 2019 and is ongoing.
- An EQA of proficiency for isolation and identification of influenza viruses using three different cell culture techniques (CPE, HA assay and ID). Eight laboratories in the Region participated; only one got 100% correct results for all three techniques. Most participating laboratories could detect influenza virus growth and could identify virus amplified from samples. Some laboratories failed to isolate and identify viruses from samples with lower titres of virus, highlighting issues in the sensitivity of influenza virus isolation methods between laboratories.
- A second EQA for detecting MERS-CoV using molecular technologies, for which 17 out of 20 laboratories from the Region returned correct results. Follow up action includes onsite and subregional training, which will be conducted in 2020 in collaboration with CDC.
- The annual WHO EQA Project (EQAP) assessment for detecting influenza viruses by RT-PCR. Results from this show significant improvement over the past decade, with the proportion of correct results up from 50% in 2007 to 90% in 2019.

"The EQAP has allowed the Regional Office to identify the capacities and resources need by countries for sustainable improvement."

The results of annual assessments form the basis for the Regional Office to identify capacity and resource needs across the Region. And in all cases, EQAs in the Region are followed up by corrective actions, such as national or regional training. But capacity-building also happens across the laboratory network outside EQAs, for example through training in collaborating centres, regional exchange visits, technical missions and NIC assessments.

2.3 Challenges to virological surveillance

EMARIS participants raised several challenges to effective virological surveillance, as outlined below.

Limited animal surveillance. Animal surveillance is important for influenza, not least because of the pandemic potential that zoonotic strains can have. But systems for animal surveillance are weak in many countries; and the wide range of animal hosts (across wild and domestic populations) makes comprehensive animal surveillance very difficult in practice.

Barriers to EQAP. Several laboratories in the Eastern Mediterranean Region are excluded from participating in EQAP because they have no access to the resources required to meet stringent shipping requirements (for example, the use of dry ice). Other laboratories at a subnational level are excluded because the EQAP only targets national capacity; although this barrier can also be seen as an opportunity for reference laboratories to develop and run their own subnational assessments.

Other operational challenges. EMARIS participants from across the Region cited a range of operational challenges including the presence of complex emergencies as well as a lack of diagnostic and safety equipment, a lack of appropriate infrastructure (such as a biosafety level 3 laboratory), limited experience and training opportunities, a lack of funding and limited access to resources because of international sanctions.

2.4 Emerging technologies to watch out for

Active research and development throughout the global surveillance network drives continuous improvement. This includes the development of new techniques, methods and reagents, as well as innovations to resolve problems in specific tests or processes and analytical improvements to increase the potential use of data.

Asked to name the most exciting innovations on the horizon, speakers at EMARIS identified six emerging technologies that could make a big difference to influenza surveillance and understanding: next-generation sequencing (NGS), bioinformatics, increased computer power, MinION rapid sequencing, new vaccine technologies, and point of care diagnostics and molecular testing (see Fig. 6).

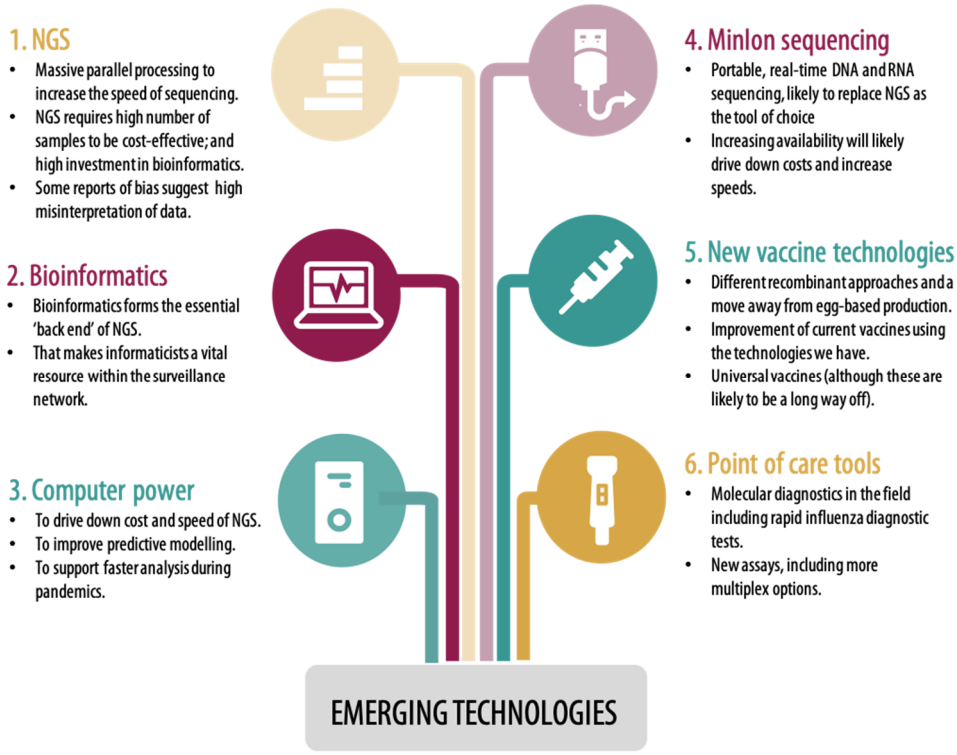

Fig. 6. Six areas of emerging technologies that could significantly improve influenza surveillance and understanding

3. ESTIMATING THE BURDEN OF INFLUENZA

3.1 Data reporting

Influenza surveillance data enable a range of activities, including monitoring disease, tracking viruses, establishing subtypes, identifying threats at the human–animal interface, informing decisions and guiding capacity-building. In all cases, surveillance data must be robust enough to be used with confidence. That means that data should be:

- of the best quality possible;
- up to date (with a historical record where possible);
- representative;
- easy to share;
- standardized; and
- interlinked.

WHO's Global Influenza Programme (GIP) collects multiple types of influenza surveillance data through global and regional platforms, including FluID, FluNET and EMFLU. To standardize these data and ensure they are easy to use, they are all combined into a single platform, FluMart. FluMart accepts data from multiple sources and in multiple formats; it can be managed and supported anywhere. Today, the platform includes data from 198 countries and 380 reporting sites.

FluMart data are used by GIP to develop outputs for different purposes and audiences, including:

- Outputs for countries, for example, severity thresholds and average curve applications.
- Outputs for modelling groups, including tailored data downloads.
- Outputs for influenza focal points, including charts on timeliness and consistency in reporting, analyses to support vaccine composition and virus selection, and pandemic preparedness indicators.

Every two weeks, the WHO uses FluMart data to publish a global influenza situation update.

3.2 Estimating burdens: tools and tactics

Reporting data is important to monitor disease and inform decisions on influenza prevention and control. EMARIS speakers described four further types of study that can be particularly useful in communicating the value of influenza policies and programmes.

Burden of disease studies

Burden of disease studies estimate the socioeconomic burden of influenza in terms of, for example, lives lost, impact on GDP, or cost-effectiveness of government action. They can be used to support policy development, communicate disease severity, strengthen surveillance and expand knowledge and understanding among other things. In particular, by estimating the national burden of influenza, countries can more effectively prioritize their resources, evaluate their influenza strategies, inform their treatment guidelines and support decisions about vaccination.

In the Eastern Mediterranean Region, work on estimating the burden of influenza has increased significantly over the past seven years. Since 2012, WHO has done four workshops on the subject in the Region and supported several countries to calculate their influenza burden. Today, five countries have published their results, with another seven countries almost ready to publish. All 12 studies have broadly followed the WHO protocol for estimating burden of disease, but with a flexible approach to allow for variable country contexts, since each country has its own way of thinking about influenza.

"WHO protocols are very good but they need to be modified to fit local contexts because each country is different."

Across the Region, work to estimate the burden of disease has already proved useful in securing investment in influenza prevention. This includes, for example, supporting decisions to implement vaccine policies and programmes, participate in the Partnership for Influenza Vaccine Introduction (PIVI), secure manufacturing capacity (even if only for a limited time), and ensure uptake among some target groups.

Impact modelling

Impact modelling estimates the value of a vaccination programme in terms of lives saved. It is done through a four-step process that begins with quantifying the number of observed influenza cases and estimating illness among the susceptible population before calculating the illness in a counterfactual population and finally working out the difference between the observed and estimated illnesses.

Impact modelling estimates can improve situational awareness about influenza activity and risk, especially among people targeted for vaccination. Experience from the United States,

where these estimates have been regularly calculated for nearly a decade, suggests that impact modelling can demonstrate huge benefits of vaccination to the economy. For example, the results of impact modelling during the 2017–2018 influenza season show that vaccination prevented seven million influenza illnesses and 8000 deaths.

Cost of illness estimates

"If you know the cost of illness, you can estimate the impact that flu vaccine would have."

Cost of illness studies estimate how much money is spent treating and diagnosing illness, and how much income is lost from patients or caregivers missing work. They also identify who pays for these costs. These estimates allow for an impact assessment of vaccination in terms of number of cases and total cost.

Studies on the societal costs of influenza in Mongolia and elsewhere suggest that:

- The direct cost of illness from seasonal influenza hits poorest households hardest; and is higher for influenza-positive patients.
- The costs of illness to government can be significant, amounting to 2–8% of national GDP.

Pandemic Influenza Severity Assessment (PISA) assessments

Developed by WHO in 2016, the PISA tool offers a standard, quantitative approach to defining whether an influenza outbreak is mild, moderate or severe. In PISA, severity is defined using three indicators that are based on surveillance data: transmissibility, seriousness of disease and impact. Data for each indicator are collected and used to establish thresholds for describing an influenza event as no, low, moderate, high or extraordinary severity.

Knowing the severity of an outbreak can help policy-makers decide what action to take. For example: at season onset, the government may remind people about vaccination; at low severity, the government confirms that beds are ready; at moderate severity the government starts using community messaging; at high severity the government considers more drastic measures such as closing schools and cancelling mass gatherings; and at extraordinary severity the government may call a meeting to decide whether or not to declare an emergency.

Today, 26 countries are using the PISA tool to set thresholds and report severity to WHO. Some countries have further linked thresholds to non-pharmaceutical interventions.

PISA in Morocco

Morocco started using the PISA tool in March 2019, with the triple aim of:

- describing the epidemiological situation and assessing the severity of an influenza outbreak;
- informing national and global risk assessments; and
- informing public health preparedness, response and recovery measures and resource allocation.

In the six months since the project started, the country has reached national consensus on the parameters to be used for each indicator; and, using a moving epidemic method, established thresholds for the transmissibility indicator. Next steps focus on achieving the same for the seriousness indicator.

3.3 Driving policy with data: Lessons learnt

Drawing on their experience in driving policy with data, EMARIS speakers and participants shared a number of the lessons learnt, both in the Eastern Mediterranean Region and beyond.

Timeliness of data sharing is critical.

In all cases, FluMart-derived products are only as good as the data available. This makes timely and consistent data sharing critical to these products' accuracy. Analysis of Eastern Mediterranean Region reporting in 2019 shows that 15 countries reported data to FluID and FluNet in 2019, but only two did so consistently and on time.

Estimating influenza burden requires a flexible approach.

Different countries have different data sources and different data requirements, so there is no one-size-fits-all protocol for estimating burden of disease. Each study must be carefully tailored to respond to country needs and priorities. In some cases, countries may need to devise an alternative method to estimate the burden on specific populations, such as refugees, who have no access to sentinel sites. To that end, the WHO Regional Office has developed a manual for estimating the burden of communicable disease in high-risk populations.

How data are communicated matters.

Communicating the value of influenza policies and programmes is important for all stakeholders, including leaders, government ministries, health care providers and the general public. Such communications should be user-friendly and tailored to meet the priorities and concerns of each audience. Preparing key messages and soundbites before the influenza season starts can help ensure that people talking to the media or others stay on-message. Media schools, where journalists are brought in for special influenza briefings, have been used successfully in the United States to ensure the media serves as an equal partner influenza control.

"The media can be a key ally in mobilizing communities to protect themselves."

Systems thinking could provide insights to behaviours.

While not yet widely used in this context, a systems approach could prove useful in understanding the drivers behind the behaviours of specific groups, such as health care workers who refuse to vaccinate. Similarly, mixed method approaches that combine quantitative data with qualitative approaches could also provide more explanatory information and enable a stronger understanding of the attitudes and perceptions behind certain behaviours.

Money is often the limiting factor in increasing investment in influenza.

Many countries—especially LMICs—have limited resources and many competing health priorities. In these countries, even with robust burden of disease data and compelling communications it can be difficult to secure a greater budget for influenza prevention and control. In all cases, it is the ministries of finance that hold the purse strings and they are a primary target for advocacy and communication.

4. LEVERAGING OUTBREAK STRUCTURES FOR INFLUENZA

4.1 Outbreak investigation and response networks

In considering how to leverage existing outbreak investigation and response structures for influenza, EMARIS speakers highlighted the potential contribution of three types of network: rapid response teams, field epidemiology training programmes and the Global Outbreak Alert and Response Network.

Rapid response teams

The overarching goal of rapid response teams is to swiftly detect and effectively respond to public health events. They fit into the response arm of the "prevent, detect, response" health security framework; and their value is emphasized in the IHR (2005). Rapid response teams have multiple roles; their presence enables countries to rapidly deploy people to the scene of an emerging outbreak, do timely field investigations and implement measures to control and contain the problem.

Having rapid response capacity has become a national priority across the Eastern Mediterranean Region and since 2015, WHO has supported countries throughout the Region to develop and strengthen their rapid response teams through targeted training. Tailored to fit each country's needs, this training emphasizes the development of a multidisciplinary team of people with complementary skills (see Fig. 7).

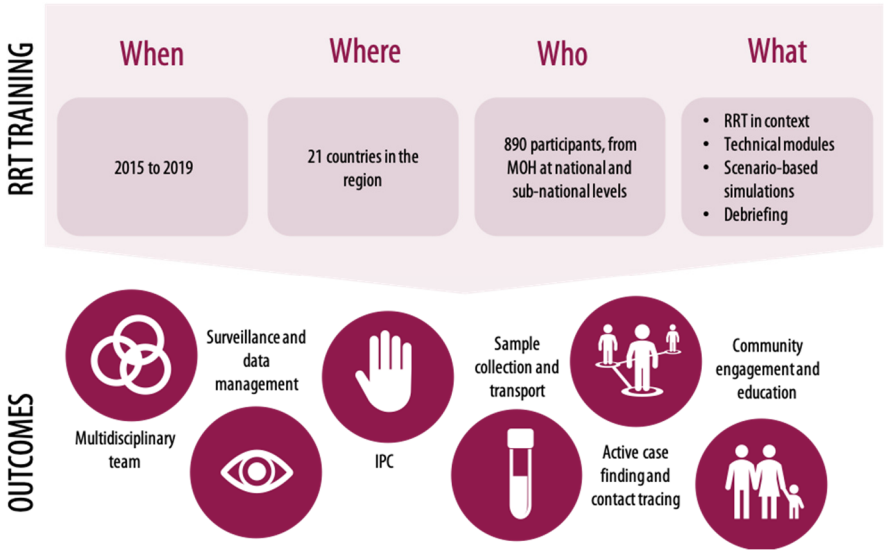

Fig 7. Rapid response team training in the Eastern Mediterranean Region

Field epidemiology training programmes (FETPs)

FETPs, which are typically two-year programmes, provide longer-term training opportunities for outbreak investigation and response. Rooted in practical education, these programmes focus on learning by doing, equipping residents with the skills they need through rotations in public health institutes or deployments to the field as first responders to outbreaks. Residents of FETPs also do research as part of their training, for example outbreak investigations or epidemiological studies.

"FETPs train 'disease detectives' that can detect and respond to outbreaks as and when they occur."

Harnessing FETPs for MERS-CoV in Saudi Arabia

In Saudi Arabia, MERS-CoV has provided a unique training opportunity for FETP residents. From 2014–2019, 38 residents of the national FETP investigated 13 outbreaks of MERS-CoV, spending more than 400 days in the field.

In supporting the country's MERS-CoV response, FETP residents have also conducted analyses of surveillance data and gained practical experience in the field. Through placements within the Ministry of Health, they have learned about communicating to the general public during outbreaks. And through scientific research and publication, they have also learned about communicating to the broader global community of experts.

In the Eastern Mediterranean Region, there are seven national FETPs, all linked through the Eastern Mediterranean Public Health Network. The presence of an FETP in a country is acknowledged as an important component of the IHR (2005) requirements for outbreak detection. But the benefits of an FETP extend much further than early detection. A strong FETP can deliver:

- better data, by contributing to surveillance;
- better policy, by providing guidelines and recommendations; and
- better action, by supporting the first response to an outbreak.

The Global Outbreak Alert and Response Network (GOARN)

GOARN is a global partnership for alert and response that is a network of technical partners coordinated by WHO. Established in 2000, the network has grown over two decades to include more than 250 partners around the world. GOARN pools human and technical resources for rapid identification, confirmation and response to outbreaks of international importance.

"GOARN wants to tap into networks like EMARIS to expand our collective ability to respond to global events."

Since 2016, GOARN's scope has expanded to include activities in risk assessment, rapid response capacity, outbreak response training, operational research and governance. And most recently, the network has been considering how it can provide more sustained support and contribute to pre-outbreak readiness efforts as well as post-outbreak follow-up activities. As GOARN continues to search for ways to increase its potential to respond to global events in the Eastern Mediterranean Region and beyond, there is a potential role for networks like EMARIS in contributing technical experience and expertise.

4.2 Lessons learnt from the Eastern Mediterranean Region experience

Reflecting on their experience in influenza outbreak investigation and response, speakers highlighted two key lessons learnt.

The media can both help or hinder influenza investigation and response.

In Morocco in 2019, the death of a pregnant woman with influenza A(H1N1) in Casablanca attracted enormous interest from the press and generated a lot of activity on social media. The media coverage caused panic among general public, increased pressure for data on influenza lethality and prompted a high demand for antiviral drugs. The crisis emphasized the power of the media in informing and influencing the public. It unveiled a clear need for more education and awareness on influenza among the media and the public and led the government to develop a social media plan and a sensitization strategy, which includes sharing information before the influenza season starts, adapting communications to local contexts and communicating quickly during any future event.

Community engagement and mobilization enables faster, more effective detection.

In Egypt, the Community Animal Health Outreach (CAHO) programme provides the foundation for detecting disease at village level. Through CAHO, veterinarians use participatory epidemiology tools and community outreach to engage households, avoiding stigma and ensuring cooperation in influenza surveillance. The programme has been so successful that it has even managed to detect diseases during the most disturbing situations when all other systems failed. While CAHO is primarily a veterinary-led programme, it has recently been expanded on a trial basis to include Ministry of Health and Population physicians.

5. MERS-COV AND OTHER EMERGING RESPIRATORY INFECTIONS

5.1 MERS-CoV

With the first human case reported in 2012, MERS-CoV is a relatively new disease. But it has already proved to be a deadly one, with a mortality rate of 34%. Over the past seven years, MERS-CoV in humans has been detected in 27 countries, mostly in the Middle East (85% of all cases reported have been in Saudi Arabia).

The disease has nonspecific symptoms that can range from no symptoms at all (in around a fifth of all cases) to severe pneumonia and death. Many patients present without any respiratory symptoms but with comorbidities, such as cardiac and renal disease; these are almost always the source of nosocomial transmission.

"Not all community-acquired cases of MERS-CoV have links to camels."

Outside health care settings, the source of human infection is dromedary camels, in which the virus is known to circulate widely, not only in Middle East but also across north, east and west Africa. This means that MERS-CoV infections are more likely to be present in areas where people are highly exposed to camels, for example in markets, farms, festivals, races, and abattoirs. Not all cases have links to camels though.

Despite being a recently emerging disease, there has been much progress in understanding MERS-CoV and in developing global tools to tackle it. There are good diagnostics available for humans and animals, including point of care testing solutions for camels. Therapeutics are advancing quickly, with most focus on monoclonal and polyclonal antibodies. And there are several human and camel vaccine candidates in development (camel vaccines are more promising at this stage, with two candidates already being evaluated in field trials).

WHO priorities for MERS-CoV

In the seven years since MERS-CoV emerged, efforts to strengthen surveillance, collaborate with animal and environmental sectors and implement new systems for treatment and response have had a direct impact on reducing human-to-human transmission and minimizing outbreaks in health care settings.

But there is much room for improvement. WHO identifies seven priorities for action in the global fight against MERS-CoV:

- significantly improving infection prevention and control measures;
- enhancing hospital readiness in affected and at-risk countries;
- building advanced laboratory capacity, including full genome sequencing in affected regions;
- improving cross-sectoral collaboration at regional and local levels;
- implementing clinical trials for MERS-CoV therapeutics and vaccines;
- progressing licensure of MERS-CoV camel vaccine candidates; and
- further implementing the public health research agenda.

5.1.1 MERS-CoV: Lessons learnt from country experience

At EMARIS 2019, presenters from Morocco, Oman, Qatar and Saudi Arabia shared their experience of investigating, detecting, preventing and controlling MERS-CoV. Some of their lessons learnt are summarized below.

Infection prevention and control (IPC) is the single most important area for improvement.

Experts broadly agree that failures in IPC have the potential to prompt superspreading outbreaks of MERS-CoV. This applies for humans and camels alike. A recent analysis of the drivers behind two hospital clusters of MERS-CoV infections in Oman during 2019 suggests that high traffic in affected wards, poor adherence to IPC measures and lack of terminal cleaning were all partially responsible. At the same time, camels living in crowded conditions where IPC is poor are also more likely to be MERS-positive compared with free range camels.

In many cases, the presence of MERS-CoV can serve as an opportunity for improving IPC. In Oman, for example, the 2019 outbreaks of nosocomial infection prompted the implementation of stricter IPC measures alongside an awareness and training programme for health care workers.

"We couldn't have done the competency-based IPC training without this [MERS-CoV] event."

Effective IPC measures for controlling and containing MERS-CoV in health care settings are thought to include: strict isolation and monitoring of IPC practices; enhanced triage; restrictions on visitors and attendants; contact screening; and environment decontamination.

Early detection is key, which requires quick and accurate case identification and good reporting.

Early diagnosis is complicated by the large number of asymptomatic cases which makes developing an effective case definition tricky. Yet clearly defined criteria for testing are important as outbreaks are known to prompt panic and a tendency to over-test. In Saudi Arabia, the case definition for MERS-CoV was revised in 2018 based on learning since 2012 and is more robust as a result. It is sensitive enough to detect most cases.

Timely and consistent reporting is also important to detect new outbreaks early. Experience in Saudi Arabia suggests that linking the provision of testing services to the status of reporting can improve compliance in reporting. Indeed, this was cited as one of the seven best practices used in the country to effectively tackle MERS-CoV (see Fig. 8).

Efforts should build on existing systems wherever possible.

When it comes to tackling MERS-CoV, there is no one-size-fits-all approach. Countries should look for solutions that require minimal adaptation and extra costs. Existing systems and structures should be adjusted to account for differences in risk (for example, by tweaking transportation systems to be more responsive, targeting risk communications at high-risk groups such as camel herders and owners, or expanding the laboratory network for testing to camel-dense areas).

An integrated approach is a more effective approach.

As with any zoonotic disease, a One Health approach that integrates activities across human health, animal health and the environment is essential. This is not always easy, especially as there remains some denial of camels being carriers for MERS-CoV. Countries that have successfully implemented an integrated approach cite joint ownership with clear roles and responsibilities as the basis for success.

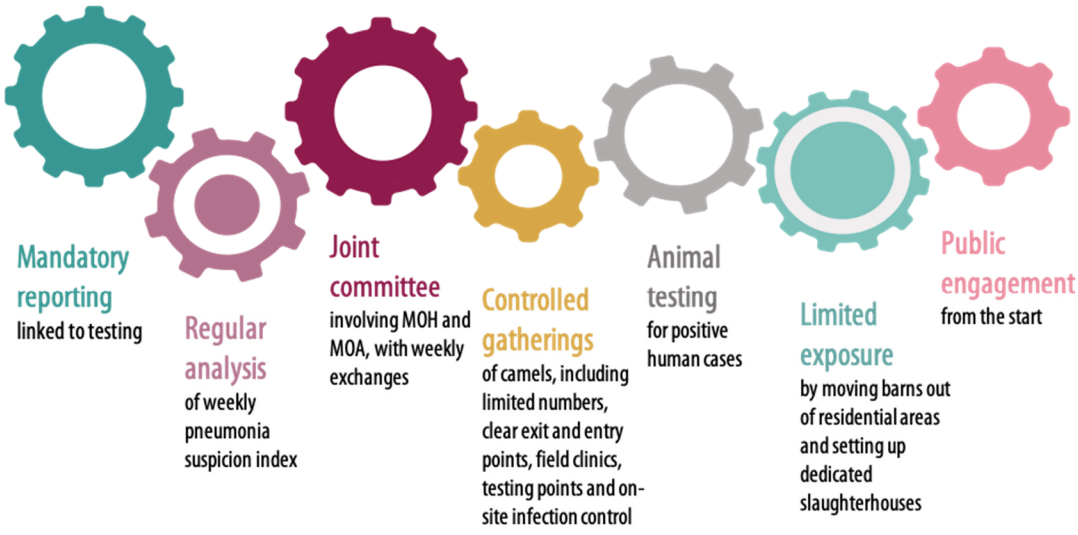

Fig. 8. Best practices for tackling MERS-CoV, tried and tested in Saudi Arabia

Efforts must include clear communications and strong community engagement.

Regular, transparent communications and community engagement are key to building awareness and trust, avoiding panic and over- or under-testing, and overcoming problems associated with stigma and denial. They can also help ensure that interventions such as contact tracing work in practice; and they can be instrumental in reducing risky behaviours. In Qatar, community service teams are regularly mobilized to help in education, risk communication, investigation, home quarantine and referral of suspected cases. Media awareness sessions and strategic use of social media have been proven to be effective in keeping the community updated before, during and after an outbreak. In all cases, communications and engagement must cover all relevant stakeholders, including individual camel owners, camel industry representatives, veterinarians, health care professionals and social workers.

5.1.2 MERS-CoV: Knowledge gaps

The WHO's roadmap for MERS-CoV identifies five areas of research that are needed to prevent human infection and reduce severe illness and death:

- Virus origin, characteristics and research in animals.
- Epidemiology and transmission.
- Clinical management and infection prevention and control.
- Product development and implementation of diagnostics, therapies and vaccines.
- Impact of interventions and operational research.

Within this framework, speakers at EMARIS 2019 highlighted the second of these areas (epidemiology and transmission) as a priority in the Eastern Mediterranean Region, pointing to four key "unknowns" (see Fig. 9).

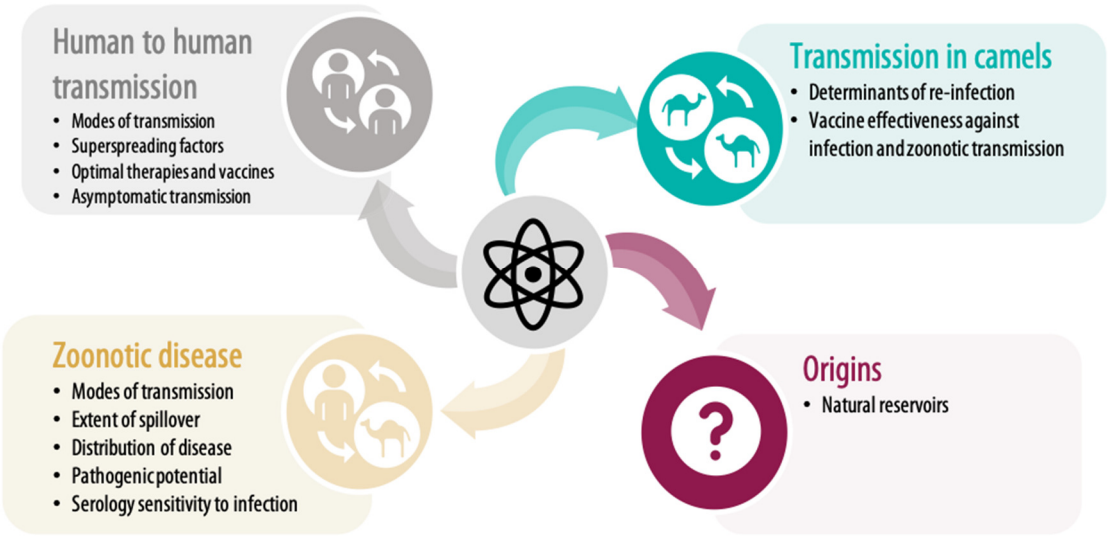

Fig. 9. Key knowledge gaps in our understanding of MERS-CoV

Our limited knowledge about zoonotic disease from MERS-CoV is particularly worrying, not least because while MERS-CoV is known to be widely circulating in north, east and west Africa, there have been no reports of disease in these areas. This may be because of behavioural differences in these regions; or it may be because the virus itself is different here. Or it may simply be that disease is there but is not being picked up because of a lack of awareness and testing.

"Why has no zoonotic disease been reported in Africa when 70% of the world's MERS-CoV infected camels are found there?"

Solving the African conundrum requires introducing and scaling up activities to collect and analyse epidemiological and virological data from areas in Africa where camel densities are high. This includes doing more testing of SARI surveillance samples in camel-herding areas (which may require the introduction of new sentinel sites), and the use of tests with a different index of infection (because not all patients with MERS-CoV have antibody responses, which makes serology tests unreliable).

5.2 Other emerging respiratory viruses

5.2.1 Respiratory syncytial virus (RSV)

RSV has long been recognized as the leading cause of illness and death from acute lower respiratory infections in young children and the elderly. Every year, there are 33 million cases of RSV in children under five, and around 60 000 RSV-related deaths.

RSV has many symptoms but importantly, fever may be absent; this makes case definition difficult. There are lots of products in development to treat and prevent RSV, with a vaccine nearly ready. But surveillance of the disease remains patchy, varying from country to country. Successfully deploying a vaccine once it is available requires a better understanding of seasonality, risk factors and burden of disease.

Harnessing GISRS for RSV surveillance

Amid concerns about the world's capacity to monitor RSV and target vaccines effectively, WHO launched a project in 2016 to test whether the influenza surveillance platform, GISRS, could be adapted to the task. The project, which was funded by the Bill & Melinda Gates Foundation, aimed to test the feasibility of using GISRS for RSV surveillance; and to establish standards and mechanisms for doing so in a cost-effective way that does not negatively impact influenza surveillance.

The first phase of the project (2016–2019) was about developing a strategy and piloting it. That included developing a case definition, establishing a new algorithm for transporting and testing, producing reagents, carrying out training, and trialing the system in sentinel sites and laboratories. Results from this phase show that the RSV case definition works well and that using the GISRS network for surveillance can be done with incremental costs to, and minimal impact on, influenza surveillance.

Phase 2 of the project (2019–2021) focuses on scaling up the number of countries involved, refining the target group (to concentrate on young inpatients) and expanding the scope (to include typing, gene sequencing and seasonality assessments).

5.2.2 Respiratory human adenovirus (HAdV)

HAdV is a DNA virus that is very diverse, covering seven species and more than 90 genotypes. It is a hardy virus that circulates all year round and can persist in the environment for a long time.

"Respiratory adenoviruses may be an overlooked cause of severe respiratory illness."

HAdV causes lots of different syndromes and has multiple manifestations depending on type; many cause ARIs. The epidemiology and severity of HAdV tends to vary by type and can be different in immunocompromised populations.

Recent studies suggest that several emerging and re-emerging HAdV types may be associated with outbreaks of ARIs, including severe respiratory illnesses in the United States and severe pneumonia in Asia.

5.2.3 Enterovirus D68 (EV-D68)

EV-D68 is one of more than 100 non-polio enteroviruses. An unpredictable virus, EV-D68 can cause mild to severe respiratory illness, or no symptoms at all. Until 2014, EV-D68 was poorly resourced: it was not a notifiable disease, there were no diagnostics for it and epidemiologic and clinical knowledge about it was limited. Then there was a major outbreak in the United States, during which there were more than 1100 confirmed cases, some of which were associated with acute flaccid myelitis. Since then, EV-D68 has received more attention, although it remains under-resourced. Recent studies suggest that the virus may have a role in severe respiratory infections among children with asthma.

6. VACCINATING HIGH-RISK GROUPS

6.1 Use of influenza vaccines in the Eastern Mediterranean Region

Expanding seasonal influenza vaccination programmes is an important objective of WHO and other global, regional and (increasingly) national stakeholders. This is because such programmes are increasingly recognized to serve as:

- A tool for reducing disease burden. Vaccination reduces hospitalizations and deaths, leads to fewer clinic visits, and minimizes the financial and societal costs of missed workdays.
- A mechanism for strengthening health systems. Influenza vaccination programmes build systems, capacities and infrastructure that can be equally used for other diseases, for example cold chain storage, health care worker skills and programme integration.
- A way of improving pandemic preparedness. Influenza vaccination programmes can serve as systems for timely delivery of vaccines during pandemics. Moreover, evidence from previous pandemics suggests that countries lacking seasonal vaccination infrastructure are less likely to receive pandemic vaccines first.

"Donors of vaccines may favour countries with proven records of strong vaccine programmes."

Across the world, the number of countries with influenza vaccine policies in place has steadily grown over the past decade, from 74 countries in 2006 to 115 countries in 2016. Yet, even in countries where policies exist, influenza vaccination programmes remain weak. Overall, vaccines remain significantly underused, especially in LMICs, where 47% of the world's population receive just 4% of the world's influenza vaccines.

In several regions, vaccine coverage is even low among high-risk groups such as health care workers. For example, a review of recent publications from the Eastern Mediterranean Region shows that coverage rates for seasonal influenza vaccination in health care workers is less than 30% across the Region as a whole, with large variability from country to country (ranging from 8.8% in Pakistan to 87% in Saudi Arabia).

6.2 Barriers to influenza vaccines in the Eastern Mediterranean Region

There are many reasons why countries may find it difficult to introduce or maintain a vaccination programme. Barriers tend to fall into four categories:

Political barriers include perceptions of affordability and relative value as well as lack of national policies, operational plans and regulatory experience and expertise. A lack of availability and the limited number of approved products can also dissuade policy-makers from embarking on a vaccination programme for seasonal influenza.

Industry constraints include the uncertainty of future markets, the low profit margins and high competition as well as the high costs of approval in many countries.

Technical challenges include difficulties in calculating the influenza burden and matching supply with demand, the increasing variety in products available and the fact that many target groups are not infants, which makes it hard to integrate influenza vaccines into existing routine immunization programmes. Measuring the impact of vaccination is also both complex and expensive.

Public hesitancy is driven by many complex factors that include doubts about efficacy, concerns about adverse effects, lack of understanding about influenza and the risks it poses, and limited availability of vaccines (or lack of awareness of availability).

6.3 Increasing vaccination coverage: Lessons from the Eastern Mediterranean Region

Establishing a sustainable seasonal influenza vaccination programme does not happen overnight. CDC identifies five critical steps in developing a national programme (see Fig. 10); and the agency works with various countries in the Eastern Mediterranean Region and beyond to support each of them.

There are also several programmes across the Region that offer models for successful implementation. Speakers from Egypt, Morocco, Oman, Pakistan and Saudi Arabia shared tools and tactics for increasing vaccination coverage based on their experience. The key enablers that they cited are listed below, although they all agreed that there is no single action that will enable a sudden surge in vaccine uptake. Rather, it is a mix of interventions that is required to succeed.

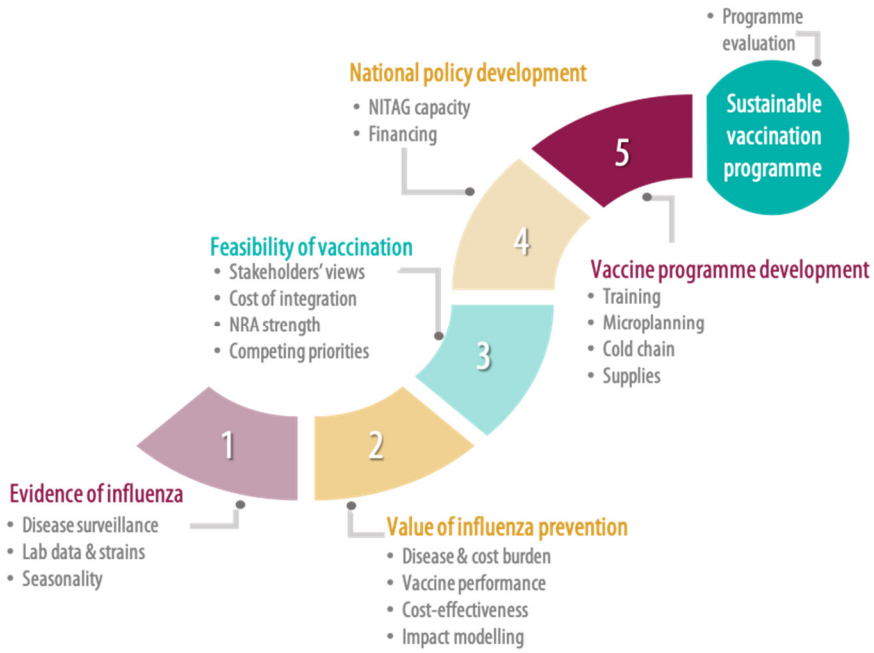

Fig. 10. Five key steps to establishing a national influenza vaccination programme

Strong leadership and oversight.

At the highest level, this includes political will, understanding and endorsement. A strong recommendation from the national immunization technical advisory group (NITAG) is often critical to gaining the political backing for an influenza vaccination programme. Visible participation of country leaders, business leaders and other key influencers in the programme can help secure public buy-in. For some target groups, including health care workers, mandated vaccines in the workplace have been proven to be effective in improving vaccine uptake.

"Ensuring that the NITAG has the right, evidence-based, information to make a decision can make a huge difference in driving policy."

Robust planning and evaluation.

Both before and after a new vaccination programme is established, a range of activities are needed to plan for and later evaluate success (see Table 2).

Strategic targeting of high-risk groups.

WHO recommends starting with a single target group when establishing an influenza vaccination programme for the first time. Several EMARIS speakers echoed this advice, suggesting the need to plan vaccination programmes according to the target groups selected. For example, in Saudi Arabia, Hajj pilgrims have been a target group for influenza vaccination since 2016. Freely available at fixed health centres across the country, the vaccine is linked to the Hajj permit application process as a way of improving vaccine uptake. The approach seems to be working: uptake among local pilgrims has increased from 29% in 2016 to 50% in 2019, including 90% among health care workers.

Table 2. Activities to support planning and evaluation of a new seasonal influenza vaccination programme

Activity	Why it's important
PLANNING	
Understanding acceptability and communication needs of target groups	• To forecast uptake and demand • To decide in which group to launch a programme • To design effective communication campaigns
Developing the local and regional evidence base	• To understand the out-of-pocket costs to patients • To calculate the cost to government • To assess the indirect, societal costs
Strengthening NITAGs	• To improve technical expertise • To secure a recommendation
EVALUATION	
Monitoring, evaluation and follow-up	• To monitor safety • To develop key messages • To ensure growth
Economic evaluations, effectiveness evaluations and impact modelling	• To build the evidence base on value for money • To convince policy-makers to invest

Health care workers are often among the first groups targeted for vaccination, not least because vaccination among this group is known to reduce health care-associated infections and save treatment costs. Health care workers are also known to be key influencers in securing public uptake. For example, a study to assess the acceptability of influenza vaccines in Morocco among pregnant women found that a recommendation by a health care worker was among the top three factors that would persuade pregnant women to get the vaccine.

Communications rooted in behaviour change theory.

While communications are important to increase awareness and understanding of influenza, experience suggests that they rarely work on their own but require other interventions to be implemented at the same time (for example, the introduction of mobile vaccination clinics to increase availability).

"Vaccine hesitancy is complex, context-specific and varies across time and place."

The drivers of vaccine hesitancy are diverse and complex and in many cases changing current practices will require communication approaches and tools that are grounded in behaviour change theory. This includes, for example, the use of COM-based strategies that assume vaccine behaviour is influenced by capability, opportunity and motivation (COM) and that identify and target deficits in these areas to increase vaccine uptake.

Increased access and availability.

Regardless of which group may be targeted for influenza vaccination, experience suggests that making vaccines free and easy to access (both in space and time) is a basic step to securing uptake.

Increasing vaccine coverage in Oman: Best practices

In 2005 Oman introduced seasonal influenza vaccines for health care workers, Hajj pilgrims and immunocompromised patients. Since then the programme has expanded to include pregnant women and the elderly. All vaccines are provided free of charge through fixed immunization centres throughout the country.

The programme achieves extremely high coverage rates (80–100%) in most of the target groups, with the exception of older patients (65%) and those with underlying conditions (45%). The country's success is down to a combination of approaches including:

- A strong surveillance system that provides real-time digital information on severity of disease, risk categories, morbidity and mortality.
- Robust estimates of disease burden calculated through a WHO-modified method to assess hospitalization and mortality data and regularly analysed to better understand risk groups.
- Tailored vaccination strategies for different target groups (for example, vaccinating health care workers in health facilities, pregnant women in fixed clinics as part of their prenatal care and immunocompromised patients at disease-specific clinics).
- Increased vaccine stocks and improved deployment to ensure sufficient and efficient supply for the target populations.
- Effective communication for acceptance in health facilities and in communities, for example through workshops, awareness-raising campaigns, educational materials and the use of peer vaccinators and mobile teams.
- Public–private partnerships to share guidelines and ensure vaccines are available for all target groups in the private sector.
- Ongoing evaluations for continuous improvement.

7. BIOSAFETY AND BIOSECURITY

7.1 Biosafety and biosecurity in the Eastern Mediterranean Region

Interest in biosafety and biosecurity in the Eastern Mediterranean Region has grown steadily over the past decade as recognition grows that working with dangerous pathogens and chemicals in laboratories involves a lot of risk to workers, the public and the environment at large. The importance of biosafety and biosecurity has been further underscored by the global health security agenda, where it is listed as one of the requirements for core competency in laboratory systems under the IHR (2005).

In the Eastern Mediterranean Region, as elsewhere, access to biosafety laboratories varies from country to country. The infrastructure available for implementing biosafety and biosecurity is diverse and so too are the legal frameworks in place. Most countries have access to a Biosafety Level 2 laboratory. There is one Biosafety Level 3 laboratory in the Region, in the United Arab Emirates.

7.2 Global guidance and standards

7.2.1 WHO Laboratory Biosafety Manual

The *WHO laboratory biosafety manual* was first published in 1983, as a means to provide the global community with practical guidance on how to implement biosafety in laboratories. The manual has evolved over time, establishing four levels of biosafety that define proper laboratory techniques, safety equipment and design, depending on the types of biological agents or toxins being studied.

The latest revision remains in progress, with an expected publication date of 2020. The new manual will differ from previous editions in several ways. In particular, it will move away from making a direct relationship between risk group of pathogen and biosafety level (BSL) of laboratory. Instead, the new manual will support a more practical risk-based approach where control measures increase with increased risk. Under this new method, each laboratory will evaluate the pathogens and procedures it deals with and assess the risks these pose in terms of likelihood of exposure and severity of harm. The risk will never be zero; and depending on the results, the laboratory will then adopt appropriate control measures.

"You can't ever completely eliminate the risk unless you don't do the work."

The new manual describes what risk assessment is, how it should be performed and what control measures should be in place depending on the results, including:

- Core requirements: these set out the minimum requirements for safe working practices at any facility. They include good microbiological practices and procedures, competent and appropriately trained staff, availability of laboratory and personal protective equipment (PPE), and effective decontamination and waste management.
- Heightened control measures: these can be anything from extra PPE, a segregated workspace, limited staff entry during processing, a biological safety cabinet, an anteroom, or a combination of these.
- Maximum containment measures: these are the highest type of control measures available and will only be required in a small number of cases.

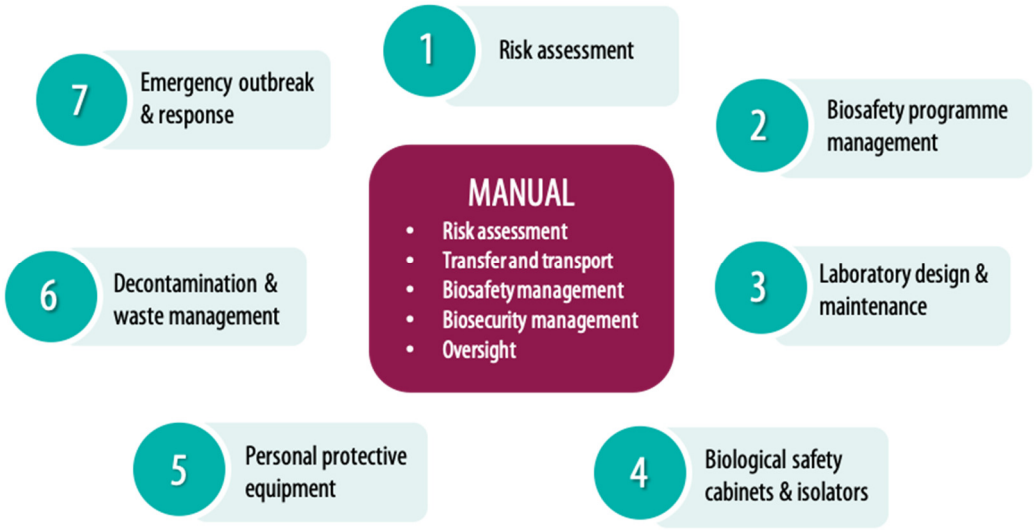

Fig. 11. Topics covered by the new WHO biosafety manual and accompanying monographs

Beyond risk assessment, the new manual covers various other elements of biosafety and biosecurity, including transfer and transport, programme management and national oversight. It will be accompanied by seven monographs that provide more detail on related topics such as laboratory design and maintenance, PPE and emergency response (see Fig. 11).

7.2.2 CWA 15793 Standard

The CWA 15793 is a voluntary laboratory biorisk management standard that can be adopted by any facility handling biological agents or toxins. Developed by a global group of biosafety and biosecurity experts in 2008, the standard is based on a management system approach and articulates expectations for all aspects of the system including: policy, planning, implementation and operation, checking and corrective action, and review.

While CWA 15793 takes a risk-based approach, it does not use any type of risk classification for pathogens; nor does it use laboratory safety levels. The standard is fully compatible with related standards developed by the International Organization for Standardization and the Occupational Health and Safety Assessment Series, as well as WHO guidance on biosafety and biosecurity.

7.3 Implementing biosafety and biosecurity: Lessons learnt

The IHR (2005) can open the door to better biosafety and biosecurity.

Experience from several countries shows that a joint external evaluation (JEE) under the IHR (2005) framework can prompt action to strengthen biosafety and biosecurity. For example, in Pakistan, a national laboratory working group was established to guide policy development and planning to strengthen the country's laboratory sector after a JEE in 2016 emphasized the need for stronger biosafety and biosecurity systems. The development of a national action plan for health security (NAPHS) can also be used as an opportunity for better biosafety and biosecurity by endorsing their importance, establishing a national focal point and including objectives to develop a national biorisk management system.

Establishing a biorisk management system requires a flexible approach.

A flexible approach includes action to:

- Decouple risk group from biosafety level. This will avoid the desire for unnecessarily complex and unsustainably expensive facilities that are often underused. Experience in working with the Ebola virus proves that although the virus is often categorized as risk group 4, not all procedures for handling it require a BSL-4 environment.
- Prioritize improvement plans according to need. Where resources are limited, biorisk management should be based on the specific biosafety needs of individual laboratories. Having a dedicated department for biorisk management can help in this regard; in Sudan such a department uses gap analyses to identify needs, develops action plans based on results and implements them gradually.

"The department reviews the effectiveness of action plans and modifies the system accordingly to improve biosafety and biosecurity."

- Adapt systems to local contexts. For example, in Abu Dhabi, where the United Arab Emirates built a BSL-3 laboratory, temperatures can rise to 50°C, with 85% humidity. To ensure proper air conditioning in this kind of environment the laboratory was equipped with a double back-up air conditioning system. It was also given extra filters to account for sand in the air, which is not a usual concern.

Much can be achieved with low-cost changes.

Biorisk management plans may include several types of activity. But they can be implemented incrementally; and many activities can be done with little to no budget. Morocco's NIC, the Institut Naitonal d'Hygiène, has been improving biorisk management consistently for a decade and a 2019 audit shows 80% compliance against the CWA 15793 across 16 areas of biosafety and biosecurity. Talking about their experience in improving biosafety, speakers from the institute stressed the importance of starting with low-cost, easy-to-implement activities. This includes, for example, defining roles and responsibilities, establishing housekeeping rules, delineating technical areas, carrying out inventories of biological agents and toxins, disposing of obsolete chemicals, and establishing a washing system for laboratory coats, among other things.

"Our first activities focused on things that didn't require budget."

8. THE HUMAN–ANIMAL INTERFACE

8.1 Regional tools and tactics for implementing One Health

Zoonotic diseases and emerging pathogens pose a significant threat to public health: at least 75% of emerging infectious diseases, including influenza, have an animal origin. The Eastern Mediterranean Region is home to endemic and emerging zoonoses and lies at the epicentre of many zoonotic disease outbreaks.

In past two decades, emerging zoonotic diseases were reported in 18 out of 22 countries in the Region. Across the Region, the prevalence of zoonotic disease and the emphasis placed on cross-sectoral collaboration by international frameworks such as the Pandemic Influenza Preparedness Framework and the IHR (2005) are fuelling interest in, and action towards, a One Health approach to tackling ARIs. There are several global tools available to support countries in their efforts; EMARIS speakers highlighted two in particular.

8.1.1 WHO's regional One Health framework

WHO's One Health operational framework for action for the Eastern Mediterranean Region was developed to help countries integrate human, animal and environmental systems for a joint approach. It is designed to allow for incremental implementation and covers nine potential areas for integration:

- Governance and management: mechanisms to ensure a system for joint leadership and decision-making, including managing, coordinating and overseeing all joint activities.
- Networks and partnerships: collaborations between governments, partners and stakeholders to implement joint activities at all levels, from local communities to global forums.
- Capacity assessment: activities to identify capacity needs for joint working.
- Capacity-building: collaborative training and infrastructure strengthening to develop multidisciplinary capacity for tackling infectious diseases at the human–animal interface.
- Links to other plans: integration of joint activities and systems into national plans, including NAPHS, pandemic influenza preparedness plans, and sectoral plans for animal health, public health and the environment.
- Coordinated surveillance: mechanisms to support coordinated surveillance, including integrated databases for reporting, data sharing across animal and human health laboratories and joint community outreach.
- Preparedness and response: mechanisms for joint planning (for example, integrated strategies and action plans) and response (for example, joint investigation teams).
- Applied research: joint research agendas and activities to generate evidence for addressing priority disease impacts.
- Risk communications: activities to align key messages and disseminate them to all stakeholders.

The framework includes other tools that have been developed to support specific components of integration. This includes, for example, a framework for translating research into policy that supports One Health integration across the four steps of putting research into use (see Fig. 12).

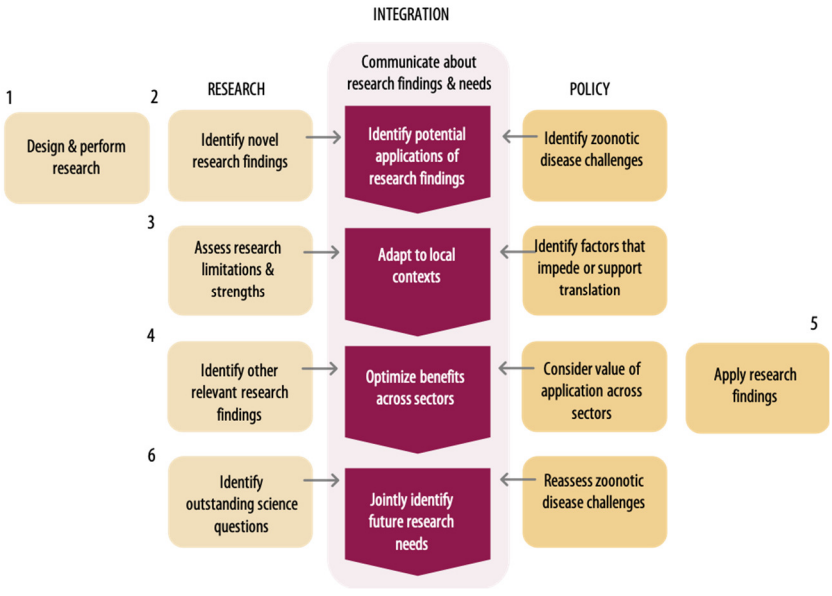

Fig. 12. An integrated approach to translating research into policy

8.1.2 One Health Zoonotic Disease Prioritization Tool (OHZDP)

In the face of finite funding, little cross-sectoral collaboration and limited equipment, many countries cannot afford to tackle all zoonotic disease threats at once. In these cases, developing a thoughtful list of priority disease threats can help countries allocate their limited resources to maximum effect. It can also help donors and partners direct their efforts to match country-specific needs.

To that end, the OHZDP enables countries to use a multisectoral approach in identifying their most urgent zoonotic disease threats and planning how to address them. Developed by CDC, the tool is both flexible and scalable so that it can be easily adapted to suit many different country contexts. It emphasizes transparency, soliciting equal input from human, animal and environmental health sectors as a way of building mutual trust and cooperation.

"The process of collaborative prioritization builds the foundations for mutual trust and joint action."

Through the OHZDP, countries can develop a list of priority disease threats that are accepted by all One Health sectors, which makes subsequent action planning and strategy implementation more likely to succeed. The tool is also proven to help establish communication channels, clarify roles and responsibilities and strengthen coordination mechanisms across One Health sectors.

8.2 One Health in practice: Examples from the field

Efforts to implement One Health come in all shapes and sizes. Some countries are investigating different risk factors for influenza at the human–animal interface. This includes studies to track and characterize circulating strains of H9N2 viruses in the Region, as well as studies to identify risky practices and inappropriate behaviours.

Some countries are implementing One Health on a broader scale as a means to tackle disease. For example, in Egypt, the government is integrating action across human and animal health to try and understand what is happening at the human–animal interface and address the threat of avian influenza there. Its approach integrates activities in six areas: laboratory systems, surveillance, data sharing, risk assessment, investigation and response.

In Qatar, the government is using a One Health approach to tackle MERS-CoV, implementing a range of activities to turn integration from theory into practice (see Fig. 13). Here, it is not only government stakeholders from animal health, human health and environment sectors that are involved. Industry and community participation in both planning and implementing activities have been instrumental in enabling success.

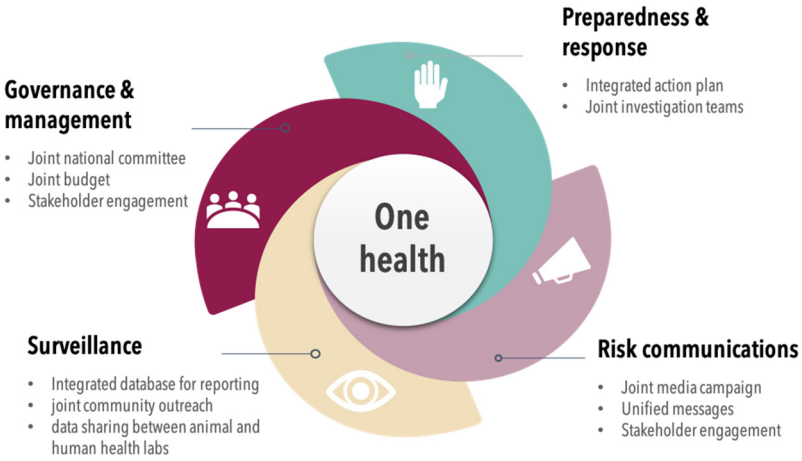

Fig. 13. Mechanisms that enable a One Health approach to tackling MERS-CoV in Qatar

8.3 Challenges for one health

EMARIS speakers and discussants highlighted three key challenges in adopting a One Health approach to tackling influenza.

Surveillance in animals.

Assessing risk of zoonotic disease and developing control strategies is impossible without effective surveillance in animal populations. Such surveillance is important not only because it poses a public health threat, but also because of the threat it poses to animal health, agricultural productivity, food security and livelihoods. And yet influenza surveillance in animals remains patchy across the Eastern Mediterranean Region (and beyond), dependent on multiple factors ranging from the capacity of veterinary services and whether the disease is notifiable or not, to local geographies and the availability of control strategies.

Carrying out influenza surveillance in animals is particularly difficult because of:

"The wild reservoir is as relevant as domestic animals."

- the diversity of viruses involved and their continued evolution both genetically and antigenically;
- the wide range of hosts and huge reservoir of potential viruses, including in wild animals;
- the complexity in host population contexts, which depends on the local behaviours of farmers, market workers and traders, as well as local trade networks; and
- the limited veterinary services capacity in some countries.

It may be unfeasible to achieve fully comprehensive influenza surveillance across all potential animal hosts, but surveillance can still be fit for purpose if it is well-structured to address key populations and if it includes stakeholders beyond public health and animal health. Compensation policies are known to support surveillance by improving self-reporting of sick animals, although these are not always practical or affordable.

Limited political leadership and commitment.

Across the Eastern Mediterranean Region, there is plenty of informal collaboration across human and animal health that happens through individual networks and interests. But few

countries have formal mechanisms, or dedicated resources, for conducting or coordinating One Health activities. The ad-hoc nature of collaboration means that it is often under-resourced and unsustainable because it relies on personal relationships rather than established channels.

Limited cross-sectoral involvement.

Many One Health initiatives tend to focus on linking human and animal health. Involvement of environment stakeholders is often minimal, and other stakeholders are very rarely involved. And yet an effective response to influenza requires the active participation of many different stakeholders, from government ministries and departments (for example, the ministries of finance, trade and education) to industry representatives (industry associations) and communities (influencers, leaders and opinion makers).

9. PANDEMIC INFLUENZA PREPAREDNESS

9.1 Pandemic threat

Influenza pandemics carry the threat of enormous impact, both for health and society as a whole. The cost of a major outbreak far outweighs the price of preparedness. A severe pandemic could result in millions of deaths globally, and cost as much as US$ 570 billion. By comparison, the cost of pandemic preparedness has been estimated at less than US$ 1 per person per year.

Influenza pandemics always come as a surprise; yet the threat of one is ever-present and another influenza pandemic is inevitable. It could emerge anywhere in the world. That is why all countries and all health systems must be prepared. Countries suffering from active conflict or protracted emergencies both natural and man-made—including many of those in the Eastern Mediterranean Region—face additional constraints to pandemic influenza preparedness, including limited access to affected populations, insecurity, high operational costs and staff shortages.

In the Eastern Mediterranean Region, five countries (23%) have updated their pandemic influenza preparedness plans since WHO released its new guidance on pandemic preparedness in 2013; two have made their plans publicly available online. All countries in the Region have, however, committed to develop or update their plans, using a multisectoral approach, as a matter of priority.

9.2 Global tools for preparedness

9.2.1 The Pandemic Influenza Preparedness (PIP) Framework

The PIP Framework was established in 2011 to improve global pandemic influenza preparedness and response. Adopted by all WHO Member States, the Framework works as a policy and finance enabler by balancing virus sharing by countries with benefit sharing by companies. The benefit sharing raises US$ 28 million each year in preparedness funds, which are used to strengthen capacities at global, regional and country levels.

The PIP Framework's capacity-building work covers six areas of activity:

- Laboratory and surveillance strengthening, including establishing new NICs, increasing the number of countries contributing to GISRS by sharing data and viruses, and supporting the shipment of specimens to WHO Collaborating Centres through WHO's Shipping Fund Project.
- Burden of disease estimates, including global estimates for respiratory deaths as well as country estimates of burden of disease.
- Regulatory capacity-building activities, such as self-benchmarking, training and accelerated approval pathways to ensure rapid access to products during emergencies.
- Risk communications and community engagement, including the development of a global online learning resource, OpenWHO, as well as guidance materials, advocacy events and technical support to integrate risk communications and community engagement into national preparedness plans.
- Planning for deployment activities, such as gaming exercises, sustainability assessments, the development of global guidance and technical support to establish a national deployment and vaccination plan for pandemic influenza.
- Influenza pandemic preparedness planning, with a focus on supporting countries to develop, test and update their pandemic influenza preparedness plan.

9.2.2 Pandemic influenza vaccine production

In the event of an influenza pandemic, vaccine production would essentially follow the same process that is currently used for seasonal vaccine production. This includes several steps that begins with surveillance and strain selection and continues with reassortant and reagent preparation and production, and then, finally, formulation, filling and distribution.

"There is no single fix to improving the timeliness of current systems; it needs lots of smaller improvements."

The biggest concern in pandemic influenza vaccine production remains the timeline involved: it takes a minimum of five or six months to make a pandemic vaccine available using current platforms. This is too late to help most people hit by a pandemic.

But speeding up the process is not easy. This is because the production process is very complex, involving many different entities, activities and actions. Two elements in particular are very challenging:

- Candidate vaccine virus (CVV) development, which follows the typical GISRS vaccine composition meeting process for seasonal influenza and which is constrained by the limited global capacity for CVV production.
- The "switch", that is, the point at which manufacturers switch from producing seasonal vaccine to producing pandemic vaccine. Production facilities cannot be used for both, but defining the switch date is complicated by several factors, including downtime requirements, uncertainties about decision-making authority and the need to balance risks.

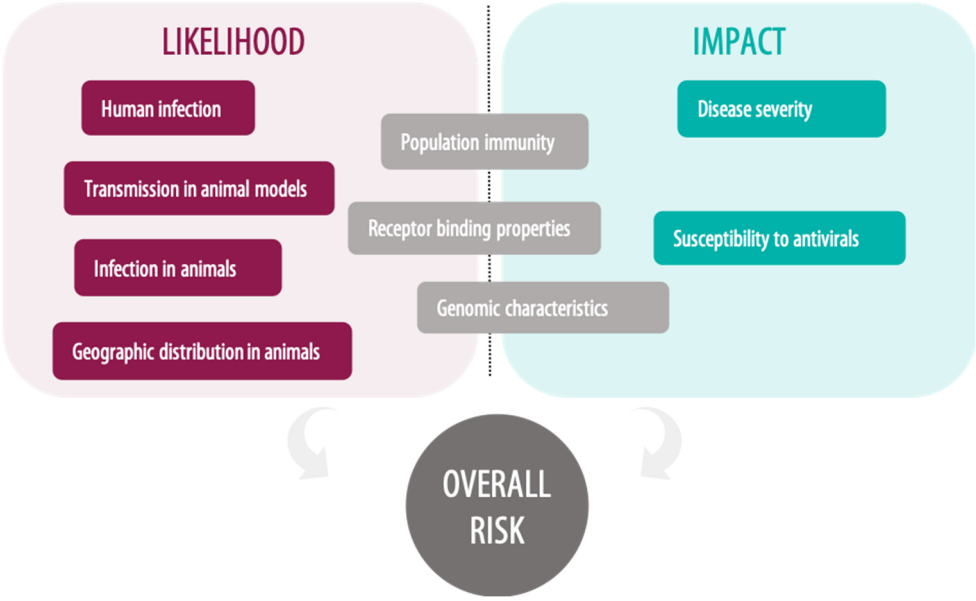

Fig. 14. Nine risk elements used to assess the overall risk of an influenza virus with pandemic potential

9.2.3 Tool for Influenza Pandemic Risk Assessment (TIPRA)

TIPRA is a global tool that is used to assess the pandemic risk of influenza viruses with pandemic potential. Launched in 2016, the tool is based on nine risk elements that together assess the likelihood and impact of an influenza virus leading to a pandemic (see Fig. 14).

TIPRA provides a qualitative assessment that can be used to compare viruses. It has been used regularly by WHO since 2016 to assess known and emerging viruses, including H5N6, H1N1, H7N9, H9N2 and H5N1. It is designed to consider the general extent to which a specific virus will cause a pandemic and as such does not take national contexts or capacities into account.

9.3 Essential readiness activities

In considering whether the world is ready to face another influenza pandemic, experts at EMARIS 2019 agreed that despite much progress over the past decade, many gaps in preparedness remain. Speakers pointed to seven types of readiness activity that countries should focus on.

Surveillance

Surveillance is one of the cornerstones of preparedness. It can be indicator-based or event-based and can be collected from formal and informal sources, both within and beyond the health system.

Vaccination

Having a seasonal vaccination programme in place is known to facilitate the acquisition and deployment of pandemic vaccines. An effective programme requires robust systems and processes for keeping vaccine records, managing the supply chain, monitoring population health, addressing coverage gaps and reaching target groups.

Risk communications

Effective risk communications during a pandemic encourage individuals and communities to make decisions and engage in practices that minimize the spread of disease. This type of communications is not simply about disseminating information to the public about health risks and events. Rather, it is about two-way and multi-directional communications and engagement with affected communities using appropriate and trusted channels.

Managing surveillance and vaccinations: best practices from Qatar

The Surveillance and Vaccinations Electronic System (SAVES) is an electronic platform for managing surveillance and vaccinations information in Qatar. It is an integral part of Qatar's e-health system and is used for real-time community surveillance. Linked to laboratories and registries across the country, SAVES supports complex data sharing and provides seamless integration at national level.

The framework has been customised to meet Qatar's needs and is designed to allow users to:

- Detect outbreaks and monitor trends.
- Provide policy-makers with situational awareness updates.
- Investigate incidents and implement control measures.
- Trace contacts and track disease transmission.
- Manage treatment and administer vaccines.
- Share data across public and private sectors.
- Meet reporting standards on timeliness and completeness
- Assess performance and plan for improvement.

Community engagement

During a pandemic, community engagement at all levels is required to help detect, prevent and treat outbreaks. Experience with outbreaks of other infectious diseases suggests community engagement is also essential to building trust and public confidence.

Non-pharmaceutical interventions (NPIs)

In the early stages of an influenza pandemic, NPIs may be the only set of countermeasures available to countries. Such measures, which include social distancing, staying at home when sick and hand and respiratory hygiene, will not stop a pandemic, but their use could slow its spread and potentially give more time for the development and deployment of a vaccine.

Research

Research to support pandemic preparedness includes studies to better understand the determinants of pandemics. It also includes studies on the effectiveness of different interventions, which can serve as evidence to support government action.

"As we learn more, we can do more."

Planning

A national pandemic influenza preparedness plan serves as a country's guiding document for planning, prioritizing and implementing strategies for preparedness and response. Such plans are only effective if they are routinely tested through tabletop exercises and drills and kept up to date. They may include plans within the plan, including, for example, deployment plans to make sure that vaccines reach those who need them, plans for mass gatherings and plans for vulnerable and high-risk groups, such as health care workers and migrants.

Integrating migrants into influenza plans

Across the world, 250 million people are migrants whose social vulnerabilities can heighten the risk of illness, disease spread and death. It is important to include migrants in all influenza plans and programmes. It is not always easy to do but has been achieved in several cases, using tools such as mobility mapping. Mobility mapping identifies the profiles of travellers and finds out where they gather and interact to assess where transmission can happen and project the potential risk of health threats such as influenza.

Such information can be used to deliver more targeted and evidence-informed public health measures at critical locations. For example, by prioritizing locations for capacity-building, infrastructure improvement and stockpiling, as well as identifying key sites for enhanced surveillance and additional control measures such as health screening or IPC.

PART 3. CONCLUSION

1. RECOMMENDATIONS FOR ACTION

Across the four days of EMARIS 2019, much of the discussion focused on exploring options for practical action to strengthen influenza detection, prevention and control. Participants considered what could be done—by Member States, WHO and partners—to improve efforts to tackle influenza in the Eastern Mediterranean Region. A broad range of recommendations emerged from their deliberations. These are listed below, grouped by broad category but presented in no particular order.

To Member States

1. Support early detection by strengthening human and animal epidemiological and virological surveillance, filling related knowledge gaps strategically, and building laboratory capacity to support the Global Influenza Surveillance and Response System (GISRS).

2. Enhance and expand influenza prevention by improving seasonal vaccination programmes and investing in non-pharmaceutical preventive measures.

3. Prepare for pandemic influenza through updating and testing national preparedness plans, including the development of national pandemic vaccine deployment plans.

4. Strengthen the national evidence base to improve understanding of influenza seasonality, estimate burden of influenza in more countries, scale up severity assessments and, ultimately, translate research outcomes into policy.

5. Search for synergies across diseases by using the influenza infrastructure to strengthen other respiratory disease surveillance capacities and integrating influenza into national disease surveillance systems.

6. Work together to align efforts by building partnerships in research and practice, fostering regional collaboration, aligning plans with global strategies and promoting greater data sharing.

7. Promote the One Health approach through building political will for animal health, prioritizing zoonotic disease threats collaboratively and developing mechanisms for integration.

8. Boost awareness and influenza seasonal vaccine uptake by tailoring and targeting messages to key groups, engaging new partners in communication and harnessing behaviour change theory.

9. Engage and mobilize communities by involving them in prevention, detection and control of influenza as equal partners, and engage marginalized groups and political leaders.

10. Be flexible and pragmatic by adapting systems to evolving situations and tailoring solutions to local contexts.

To WHO

11. Continue to support countries in building capacities to strengthen influenza systems and structures for influenza prevention, detection and control.

12. Facilitate research for policy by promoting and supporting national influenza burden estimations and other studies to build the relevant national evidence base for meaningful policies.

13. Incorporate country priorities into regional and global guidance and strategies.

14. Facilitate knowledge exchange and collaboration through forums and opportunities for exchanging experience and expertise across the Region, including for other respiratory diseases beyond influenza.

15. Continue to promote the One Health approach through capacity-building and the development of standard operating procedures and other guidance documents.

2. CLOSING SESSION

Three researchers received special awards for their exceptional contribution to EMARIS 2019:

- Hind Bouguerra from Tunisia, for the best oral presentation.
- Fatimah Alghawi from Saudi Arabia, for the best poster.
- Farag Elmoubasher from Qatar, for the most innovative abstract.

NIC awards went to:

- NIC Oman: for sharing viruses consistently in 2018–2019 and achieving annual targets.
- NIC Saudi Arabia: for reporting data regularly and in a timely manner for all weeks.
- NIC Islamic Republic of Iran: for maintaining functions despite very challenging circumstances.

Other recognitions for contributions made were given to the Centers for Disease Control and Prevention (US), Francis Crick Insitute (UK), Moroccan Ministry of Health, Professor Malik Peiris (University of Hong Kong), US Influenza Division for Prevention and Control, influenza team at WHO headquarters and WHO Morocco country office.

Dr Abdinasir Abubakar, Acting Programme Area Manager for Infectious Hazard Preparedness at the WHO Regional Office, congratulated the winners and thanked the planning committee, judges and Regional Office team for their hard work in making EMARIS 2019 happen.

Dr Mohamed Youbi from the Moroccan Ministry of Health congratulated all EMARIS participants and organizers for a successful meeting and wished them safe travel home.

Next steps

Before the close of the meeting, WHO articulated its next steps, which included:

- producing a meeting report and sharing it with all participants;
- meeting with colleagues and partners to review and prioritize suggestions for action; and
- convening a planning committee for EMARIS 2021 and starting the planning process.

ANNEX 1

PROGRAMME

12 November	Session	Facilitators/Presenters
8.00–8.30	Registration	
8.30–9.30	Message from WHO Regional Director	*Ahmed Al-Mandhari Richard Brennan, Daniel Jernigan, Maryam Bigdeli, Ehsan Mostafavi, Abdinasir Abubakar*
Session 1. Global influenza strategy		
9.30–9.45	The Global Influenza Strategy	*Ann Moen*
9.45–10.00	Challenges in influenza prevention and control	*Daniel Jernigan*
10.00–10.15	Influenza in the Eastern Mediterranean Region	*Abdinasir Abubakar*
10.45–11.00	Current and regional status of influenza subtypes	*Rodney Daniels*
11.00–11.15	GISRS	*Wenqing Zhang*
11.15–11.30	Tackling influenza in emergencies	*Sk Md Mamunur Malik*
11.30–11.45	CDC's International Influenza Program	*Kinda Zureick*
11.45–12.15	Panel discussion: Reducing the threat of seasonal influenza: where do we stand in the Eastern Mediterranean Region?	*Moderator: Richard Brennan Ann Moen, Daniel Jernigan, Wenqing Zhang, Sk Md Mamunur Malik, Abdinasir Abubakar*
13:15–14:15	Oral abstract presentations	*Moderator: Muhammad Safdar*
	• Factors associated with LRTI, Pakistan, 2018–2019	*Asim Minallah*
	• Influenza morbidity & mortality, Tunisia, 2017–2018	*Hind Bouguerra*
	• Influenza epidemic, Yemen, 2018–2019	*Mohamed Al Amad*
	• SARI database, Lebanon, 2018	*Nada Ghosn*
	• ILI and SARI, Pakistan, 2008–2017	*Nadia Nisar*
Session 2. influenza dynamics and characteristics in the Eastern Mediterranean Region		
14.30–14.45	Virological surveillance networks	*John McCauley*
14.45–15.00	Detection and characterization of zoonotic influenza	*David Wentworth*
15.00–15.15	EQAP for influenza	*Amal Barakat*
15.15–15.30	Improving surveillance: NIC in Palestine	*Ibrahim Salem*
15.30–15.45	Detecting influenza in NIC Oman	*Amina Al Jardani*
15.45–16.15	Panel discussion: How can emerging technologies enhance surveillance and understanding?	*Moderator: Wenqing Zhang David Wentworth, John McCauley, Rodney Daniels, Amal Barakat, Amina Al Jardani*

13 November	Session	Facilitators/Presenters
9.00–10.00	Oral abstract presentations	*Moderator: Omar Elahmer*
	• Genetic characterization of influenza, Oman, 2018–2019	*Samira Al Mahrouqi*
	• Detecting non-influenza in Hajj pilgrims, Islamic Republic of Iran, 2017	*Kaveh Sadeghi*
	• Non-influenza respiratory viruses, Pakistan	*Hamza Mirza*
	• ILI in public and private sectors, Morocco, 2016–2019	*Hicham Oumzil*
	• EV-D68 and rhinovirus C, Islamic Republic of Iran	*Farhad Rezaei*
Session 3. Estimating influenza burden		
10.30–10.45	Reporting platforms	*Maja Lievre*
10.45–11.00	Estimating national influenza burden in the Eastern Mediterranean Region	*Amgad Elkholy*
11.00–11.15	Impact modelling	*Eduardo Azziz-Baumgartner*
11.15–11.30	PISA threshold setting	*Katelijn Vandemael*
11.30–11.45	Measuring the cost of seasonal influenza	*Bill Davis*
11.45–12.30	Oral abstract presentations	*Moderator: Leila Bouabid*
	• SARI cases, Jordan, 2015	*Nasha'at Ta'anni*
	• SARI cases, Morocco, 2014–2019	*Hind Ezzine*
	• Influenza in Hajj pilgrims, Saudi Arabia, 2019	*Ahmad Alowfi*
12.20–13.00	Panel discussion: How can burden data be used to advocate for better public health policies?	*Moderator: Mahmood Nabavi Eduardo Azziz-Baumgartner, Katelijn Vandemael, Bill Davis*
Session 4. Leveraging outbreak investigation and response structures		
14.00–14.15	Rapid response teams in the Eastern Mediterranean Region	*Evans Buliva*
14.15–14.30	Saudi FETP experience investigating MERS	*Sami Almudarra*
14.30–14.45	Influenza upsurge, Morocco, 2018–2019	*Mohamed Youbi*
14.45–15.00	Human-animal surveillance in Egypt	*Amira Abdelnabi*
15.00–15.15	Oral abstract presentations	*Moderator: Abdulkader Afrah*
	• MERS-CoV outbreak, Saudi Arabia, 2017	*Nada Saeed AlGhawi*
15.15–15.45	Panel discussion: Can the Eastern Mediterranean Region investigate and respond to potential novel flu outbreaks?	*Moderator: Abdulkader Afrah Evans Buliva, Sami Almudarra, Mohamed Youbi, Amira Abdelnabi, Rana Asghar*
16.15–18.15	Skill-building workshops	
	• Pandemic preparedness in fragile contexts	
	• Data quality and epidemiologic analysis	
	• Increasing vaccine coverage	
	• Outbreak investigation and response	

14 November	Session	Facilitators/Presenters
Session 5. MERS-CoV and other emerging respiratory infections		
9.00–9.15	Response to MERS in Saudi Arabia	*Abdullah Assiri*
9.15–9.30	MERS-CoV: global perspective	*Maria Van Kerkhove*
9.30–9.45	Fulfilling knowledge gaps on MERS	*Malik Peiris*
9.45–10.00	WHO global RSV surveillance	*Wenqing Zhang*
10.00–10.15	Beyond influenza: RSV, HaDV, EV-D68	*Holly Biggs*
10.30–11.20	Oral abstract presentations	*Moderator: Badar Al-Rawahi*
	• MERS-CoV surveillance, Saudi Arabia, 2016–2019	*Abdullah Al Zahrani*
	• Zoonotic MERS-CoV, Morocco	*Anass Abbad*
	• MERS-CoV outbreak, Oman	*Amal Al-Maani*
	• One Health for MERS, Qatar, 2012–2017	*Elmoubasher Farag*
11.20–11.50	Panel discussion: How do we leverage influenza surveillance infrastructure for other diseases?	*Moderator: Ann Moen Abdulla Assiri, Maria Van Kerkhove, Malik Peiris, Holly Biggs, Wenqing Zhang*
11.50-12.50	Poster presentations	
Session 6. Vaccination of high-risk groups		
13.30–13.45	Expanding vaccination in the Eastern Mediterranean Region	*Joseph Bressee*
13.45–14.00	Improving uptake for Hajj and Umra visitors	*Abdullah Assiri*
14.00–14.15	CDC's support for influenza vaccination	*Margaret McCarron*
14.30–14.45	Successful vaccination among health care workers	*Hassan Zaraket*
14.45–15.00	Increasing vaccine uptake and use in Oman	*Fatma Al-Yaqoubi*
15.00–15.50	Oral abstract presentations	*Moderator: Amjad Mohamed*
	• Vaccination among health care workers in the Eastern Mediterranean Region	*Mohamed Farouk Allam*
	• Vaccination in health care workers, Egypt, 2018	*Shereen Elghazaly*
	• KAP in pregnant women, Morocco, 2018	*Loubna Alj*
	• Influenza B lineages, Pakistan, 2011–2019	*Nazish Badar*
15.50–16.15	Panel discussion: How to improve vaccine introduction and uptake in the Eastern Mediterranean Region?	*Moderator: Hadeel Al Sayeh Joseph Bressee, Hassan Zaraket, Fatma Al-Yaqoubi, Abdulla Assiri, Sonja Olsen*
Session 7. Biosafety and biosecurity		
16.30–16.45	The revised WHO laboratory biosafety manual	*Uzma Bashir*
16.45–17.00	Biosafety and biosecurity system in Pakistan	*Aamer Ikram*
17.00–17.15	Biosafety and biosecurity in Morocco	*Rhizlane Selka*
17.15–17.45	Oral abstract presentations	*Moderator: Ghada Flaieh*
	• Compliance with CWA 15793, Morocco	*Hassan Ihazmade*
	• The role of biorisk departments, Sudan	*Siza Obied Mukhtar*
	• Establishing a BSL-3 laboratory, United Arab Emirates	*Stefan Weber*

15 November	Session	Facilitators/Presenters
Session 8. The human-animal interface		
9.00–9.15	One Health Framework in the Eastern Mediterranean Region	*Ghazi Kayali*
9.15–9.30	Animal surveillance: implications for human health	*Nicola Lewis*
9.30–9.45	Prioritizing zoonotic diseases to One Health	*Salah AlAwaidy*
9.45–10.25	Oral abstract presentations	*Moderator: Nada Ghosn*
	• Risky practices for avian influenza, Egypt, 2014–2017	*Hend Elsheikh*
	• Evolution of LPAI H9N2 in north Africa	*Mariette Ducatez*
	• H9N2 infection in poultry, Lebanon, 2017	*Rebecca Badra*
10.40–11.00	Panel discussion: How can we help improve and integrate human and animal surveillance systems?	*Moderator: Manal Morcos* *Ghazi Kayali, Nicola Lewis, Salah AlAwaidy, Amira Abdelnabi*
Session 9. Pandemic influenza preparedness		
11.00–11.15	Progress in PIP Framework implementation	*Gina Samaan*
11.15–11.30	Pandemic influenza threat among refugees	*Alice Wimmer*
11.30–11.45	Can we get pandemic preparedness right?	*Stephen Morse*
11.45–12.00	Influenza readiness for World Cup 2022, Qatar	*Hamad Al Romaihi*
12.00–12.15	Pandemic influenza vaccine development	*Richard Webby*
12.15–12.30	Pandemic preparedness from regulatory perspective	*Houda Langer*
12.30–12.45	Using TIPRA to assess the potential for pandemic	*Magdi Samaan*
12.45–13.00	GOARN	*Patrick Drury*
13.00–13.30	Oral abstract presentations	*Moderator: Eyad Muhanna*
	• Defining influenza thresholds, Afghanistan, 2018–2019	*Mohammad Nadir Sahak*
	• Using PISA in Morocco, 2018–2019	*Soumia Triki*
13.30–14.00	Panel discussion: Are we ready for the next pandemic?	*Moderator: Said Saddat* *Hamad Al Romaihi, Stephen Morse, Gina Samaan, Richard Webby, Alice Wimmer*
14.00–14.30	Closing session	*Moderator: Ibrahim El-Kerdany* *Rana Hajjeh, Abdinasir Abubakar, Mohamed Youbi*

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