Perspective

Pandemic influenza preparedness in the WHO South-East Asia Region: a model for planning regional preparedness for other priority high-threat pathogens

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Abstract
Pandemic influenza preparedness has contributed significantly to building, strengthening and maintaining countries' core capacities to prepare for health emergencies. The Pandemic influenza preparedness framework for the sharing of influenza viruses and access to vaccines and other benefits (the PIP framework) was adopted by the World Health Assembly in 2011. The experiences and lessons learnt from the implementation of the PIP framework have provided insights that can be used to strengthen preparedness for epidemics of other priority high-threat pathogens in the World Health Organization (WHO) South-East Asia Region in line with obligations under the International Health Regulations, 2005 (IHR). Implementation has established policies, strategies, action plans, strengthened systems and operational readiness to promptly diagnose influenza virus strains with pandemic potential and ensure timely event notifications and management in compliance with the IHR. WHO collaborating centres and the annual bi-regional meeting of national influenza centres and influenza surveillance have strengthened the influenza laboratory diagnostic knowledge network in the region. After action reviews following influenza outbreaks have documented best practices, strengths, constraints and areas for improvement in pandemic preparedness. The pandemic in 2009 and recent seasonal influenza outbreaks have offered real-life scenarios for testing national pandemic influenza preparedness plans and deploying vaccines. The successful implementation of the PIP framework, along with strengthening of health systems and operational procedures and continued technical collaboration with global centres of excellence, should be tapped into to strengthen preparedness to respond to epidemics of other high-threat pathogens based on the influenza model. The political commitment reflected in the Delhi Declaration on Emergency Preparedness, signed by all ministers of health in September 2019 and supported by the Five-year regional strategic plan to strengthen public health preparedness and response – 2019-2023, should be a catalyst for guidance and support in developing a broad, long-term strategic plan for preparedness and response to high-threat pathogens in the region.

Keywords: high-threat pathogens, International Health Regulations (2005), pandemic influenza, preparedness, WHO South-East Asia Region

Background
One quarter of the world’s population resides in the World Health Organization (WHO) South-East Asia Region, with all its diversity and not only increasing risk of outbreaks of common diseases but also a high degree of vulnerability to emerging and re-emerging diseases with epidemic and pandemic potential, such as seasonal influenza, Zika virus disease, Nipah virus disease, Crimean Congo haemorrhagic fever and other priority high-threat pathogens.1 Furthermore, the frequent seasonal exposure of people to flash floods, land-slides and adverse consequences of climate change in the form of extreme weather conditions, and the limited capacity of systems to respond to outbreaks of high-threat novel pathogens of unknown aetiology or deliberate biological events, make it imperative that the region evaluate, re-strategize, plan and strengthen its emergency preparedness to ensure timely and effective responses to these biological threats.2

Both the International Health Regulations, 2005 (IHR),3 and the Asia Pacific strategy for emerging diseases and public health emergencies (APSED III)4 provide the impetus to address threats shared by Member States of the WHO
South-East Asia and Western Pacific regions. Other key global guidance tools for Member States in relation to preparedness for and response to priority high-threat pathogens include the Global influenza strategy 2019–2030, the Pandemic influenza preparedness framework for the sharing of influenza viruses and access to vaccines and other benefits (the PIP framework), the draft research and development roadmap for Nipah virus infections and Ending cholera: a global roadmap to 2030.

In view of the need for close alignment between IHR compliance and pandemic planning, this perspective paper provides insights into the essential elements of pandemic influenza preparedness in the context of strengthening IHR core capacities. We explore how lessons learnt and best practices developed during the implementation of the PIP framework can be translated into regional preparedness to respond to other high-threat pathogens and incorporated by Member States into their national action plans for health security (NAPHSs).

Pandemic influenza preparedness framework and the IHR
Influenza pandemics are unpredictable but recurring events that can have severe health and non-health consequences worldwide. Despite this uncertainty, most, if not all, countries are ill prepared to face a pandemic. The PIP framework adopted at the 64th World Health Assembly in May 2011 became a landmark in country preparedness for pandemic response. The framework was designed to strengthen global pandemic influenza surveillance and response through private sector industry contributions, benefiting low- and middle-income countries by increasing access to technologies and strengthening countries’ capacities for pandemic response. A high-level implementation plan was developed to provide guidance on use of PIP framework partnership contributions, in part to achieve six outcomes: (i) detection, monitoring and sharing of influenza viruses with pandemic potential, (ii) timely influenza situational analysis, including risk assessment, (iii) estimating influenza disease burden for evidence-based policies, (iv) facilitating rapid approval and deployment of pandemic influenza products, (v) communicating risks during influenza pandemics and (vi) developing, testing and updating national influenza pandemic preparedness plans (NIPPPs).

In the past, planning for pandemic influenza has focused on activities to prepare for, respond to and recover from a pandemic. The 2017 guideline Pandemic influenza risk management applies the principles of an all-hazards emergency risk management for health (ERMH) approach to pandemic planning. The objectives of ERMH are to (i) strengthen capacities to manage health risks posed by all hazards, (ii) embed comprehensive emergency risk management in the health sector and (iii) enable and promote multisectoral linkage and integration across the whole of government and the whole of society. The guideline therefore aligns more closely with the disaster risk management structures already in place in many countries and underscores the need for appropriate and timely risk assessment for evidence-based decision-making at national, subnational and local levels.

Pandemic influenza risk management also defined pandemic emergency response phases in terms of disease risk and preparedness, response and recovery (see Fig. 1), and WHO will refer to these phases when communicating the global situation. The global phases – interpandemic, alert, pandemic and transition – describe the spread of the new influenza subtype around the world. As pandemic viruses emerge, countries and regions face different risks at different times. For that reason, the guidance emphasizes that countries need to develop their own national risk assessments based on local circumstances, taking into consideration the information provided by the global assessments produced by WHO. Countries’ risk management decisions should be informed by global risk assessments but based on local risk assessments. This approach provides countries with the opportunity to revisit national plans in different phases of a pandemic and modify them depending on lessons learnt in each phase.

In 2018, WHO produced A checklist for pandemic influenza risk and impact management. This publication updates...
strengthening the IHR core capacities, with a view to translating State parties in the region is described below in the context of various elements of pandemic influenza preparedness by Member States of the WHO South-East Asia Region. The adoption of essential preparedness and response. The adoption of essential capacities needed to manage pandemic influenza with the core capacities required to manage broader health security threats. Second, risk and severity assessments have been added to the document, to emphasize the importance of performing these assessments at national level. Aligned with Pandemic influenza risk management, this approach means that countries can determine national pandemic response actions in the context of their own experience, resources and vulnerabilities, rather than being directed by global risk assessments and pandemic phases, as was the case previously. Third, the 2018 checklist integrates the principles of ERMH into pandemic preparedness planning through an emphasis on multisectoral and multidisciplinary approaches. It includes activities to help planners integrate ethical considerations into pandemic planning and to ensure risk communication and engagement with affected communities and the general public.

Guided by the PIP framework and States Parties’ obligation under the IHR to notify all cases of human influenza of a new subtype and all cases of an influenza virus with pandemic potential, Member States of the WHO South-East Asia Region have long been involved in building capacities for pandemic preparedness and response. The adoption of essential elements of pandemic influenza preparedness by Member States in the region is described below in the context of strengthening IHR core capacities, with a view to translating them into preparedness to respond to other high-threat pathogens.

### Strengthening IHR core capacities

#### Legislation, policies and plans

The initial NIPPPs in the region focused primarily on avian influenza. However, since the influenza pandemic in 2009, the region has been focusing on systematic pandemic planning. Global drivers such as the PIP framework,6 the Global Health Security Agenda,15 financial and technical support from the United States of America Centers for Disease Control and Prevention and other initiatives have accelerated and strengthened the planning process.

Member States standardized their NIPPPs using the technical guidance offered by the WHO Global Influenza Programme, first through the WHO checklist for influenza pandemic preparedness planning (2005)19 and later through Pandemic influenza risk management (2017).20 All countries of the region have NIPPPs, although they are at different stages of maturity. However, conducting regular testing of NIPPPs and frequently updating them with links to the test results is essential and challenging.

Regional experience demonstrates that limited resources make it difficult to develop multiple contingency plans for priority risks. A practical solution is to link NIPPPs to NAPHSs using the IHR platform. This approach was tested in Timor-Leste, where the exercise proved that making this link is feasible and efficient. The NIPPP within the NAPHS in Timor-Leste serves as a blueprint for responding to, or an adoptable framework for contingency planning for, other high-threat pathogens.16

### Coordination, communication and advocacy

As part of the pandemic planning process, with the aim of strengthening in-country coordination and communication capacities, multisectoral coordination and communication mechanisms have been established between various government ministries, competent authorities, nongovernmental organizations and non-state actors in the countries of the WHO South-East Asia Region. The 2009 pandemic and subsequent seasonal influenza outbreaks in some countries (the Democratic People’s Republic of Korea, India, Maldives, Myanmar, Sri Lanka) have provided opportunities to operationalize these mechanisms, with strong links to national emergency management structures through public health emergency operations centres. The 2009 pandemic also provided a real-life scenario in which to apply incident management systems across all sectors of pandemic response to coordinate functions including management, planning, operations, logistics, finance and administration. However, active, operational links between different ministries within countries and establishing mechanisms linking neighbouring countries for cross-border activities remain areas for further strengthening in the region.

### Surveillance systems

As part of pandemic influenza preparedness, countries of the region have established, improved and used influenza surveillance systems for early warning and alert, detection, timely reporting, risk assessment and response decision-making during interpandemic and pandemic phases. These include indicator-based and event-based surveillance systems. Notwithstanding the successes achieved, constant efforts are needed to ensure the sustainability of these surveillance systems, the generalizability of their findings to the all-countries context and their further improvement, including with regard to the quality of the data generated and data sharing for regional and global risk assessments and response decision-making.

In parallel with the global initiative on Pandemic Influenza Severity Assessment (PISA),17 countries of the region are assessing the feasibility of using their surveillance systems for PISA. This exercise has been a learning experience, involving identifying gaps and areas for improvements in surveillance systems to ensure that adequate high-quality data can be collected to conduct PISA in the countries. There is also a need for a focus on strong event-based surveillance systems in all Member States and on using surveillance systems for influenza burden estimation studies for evidence-based policy development, as has been done in Bhutan and Thailand.

### Zoonotic events and the human–animal interface

The detection of human cases of avian influenza in the region in Bangladesh, Indonesia, Nepal, Myanmar and Thailand has underscored the importance of effective and functional non-seasonal (novel) influenza surveillance systems and of further strengthening them as a pandemic early warning system to detect these new viruses as they enter human populations.19,20 However, regional experience indicates that this is an area...
for further strengthening through collaboration, cooperation, coordination and timely sharing of information between sectors to generate information that supports joint risk assessments for informed decision-making. In this regard, as well as in relation to using the human–animal interface for early detection and response to other zoonotic diseases, activities such as leveraging the tripartite collaboration in the Asia-Pacific region will be critical. With a coordination group in Bangkok, the tripartite comprises the WHO Regional Offices for South-East Asia and the Western Pacific in collaboration with the Food and Agriculture Organization of the United Nations (FAO) and the Pacific and World Organisation for Animal Health (OIE). Key activities of the tripartite will be scaling up the One Health approach, sharing good practices and lessons learnt, operationalizing the One Health mechanism through, for example, joint capacity-building and deployment of multidisciplinary outbreak investigation teams.

National laboratory systems
Concerted efforts on the part of Member States, WHO and partners have resulted in significant improvements in influenza virus diagnostic capacity in the region. Some of the success stories resulting from investments in pandemic influenza preparedness are (i) the establishment of national laboratory systems that are essential for the identification of circulating seasonal influenza virus strains and their subtypes, and (ii) improved access of countries to specialized laboratories with the diagnostic capacity required to quickly confirm suspected human cases of a new influenza strain. As a result, ten national influenza laboratories have been recognized as national influenza centres within the Global Influenza Surveillance and Response System (GISRS) in eight countries. Continuous efforts and investments have improved diagnostic capacities in national influenza laboratories in the other three countries (Bhutan, Maldives and Timor-Leste); these laboratories are seeking to achieve recognition as national influenza centres.

For quick confirmation of novel influenza strains that require timely notification to WHO under the IHR for appropriate action to be taken, the ten national influenza centres and national laboratories in the other three countries of the region collaborate and share specimens/genetic data with three WHO collaborating centres.

As part of sustainable influenza-specific laboratory capacity development, national influenza centres and laboratories have undergone improvements in molecular testing capacity, laboratory biosafety and biosecurity, safe transport of biological substances in accordance with the International Air Transport Association regulations, etc. These laboratories participate in the annual global external quality assurance programme for reverse transcriptase polymerase chain reaction tests, and their overall performance has been very strong. In addition, they share laboratory data for global and regional policy-making, while 10 of the countries share influenza virus strains or genetic data with the GISRS.

Health service provision
Lessons learnt from communicable disease outbreaks in the region have highlighted overwhelmed health facilities leading to a lack of access to appropriate care for patients. For many countries of the region, establishing functional triage systems to identify patients at risk of severe disease and complications, and systems for community management of less severe cases, is challenging. The chronic shortage of medicines and a lack of stockpiles could also confound health service provision in a pandemic.

In this context, health services planning is essential for managing patients in overwhelmed health facilities during seasonal influenza outbreaks and for managing human cases of zoonotic influenza in interpandemic periods. In addition, specific plans for providing health services during a pandemic should be set out in NIPPPs, with supplementary business continuity plans to ensure that the health sector can continue services. Risk analysis indicates a need for additional planning for care for vulnerable groups such as children, pregnant women, the elderly and people with chronic conditions.

Although the influenza pandemic in 2009 was caused by a less virulent strain, the vulnerability of health facilities to an increased load of patients was evident. In spite of WHO's technical support in the form of treatment guidance, training on intensive care and training on managing patients with severe acute respiratory infections at peripheral-level hospitals, there remain critical gaps in planning for health service provision during seasonal influenza outbreaks, care for patients with non-seasonal influenza and uninterrupted provision during a pandemic (including through business continuity plans for the health sector). These areas require further attention from national health authorities in terms of both planning and "real-life scenario" operations. Given the experience of Indonesia in managing zoonotic influenza cases, Thailand having the first WHO-verified emergency medical team in the region, and Sri Lanka's experience in hospital-based management of severe dengue cases during outbreaks, Member States need to take advantage of collaboration opportunities to learn from each other's experiences to further strengthen health service delivery during pandemics.

Medical countermeasures, critical for pandemic response, have been identified as priority technical areas in eight joint external evaluations conducted in the WHO South-East Asia Region. With experience in conducting large-scale immunization campaigns, lessons learnt from pandemic vaccine deployment in 2009 and outbreak response immunization against influenza in recent years, countries are well placed to deploy pandemic vaccines in the region. With regard to local influenza vaccine manufacturing, India, Indonesia and Thailand have increased their capacities, having been beneficiaries of WHO's initiative to increase vaccine production capacity under the Global Action Plan for Influenza Vaccines during 2006–2016.

As part of pandemic preparedness and response, the WHO Regional Office for South-East Asia has considered possibilities for regional production of oseltamivir to increase the likelihood of its availability by fostering and strengthening public–private partnerships. The fact that Indian companies are involved in production of oseltamivir to ensure its availability for stockpiling in low- and middle-income countries is a step towards better regional preparedness. WHO has been involved in regional stockpiling of oseltamivir, while the countries of the region stockpile it as a part of their pandemic influenza preparedness planning.

Risk communication and community engagement
Lessons learnt from the 2009 influenza pandemic called for a proper understanding of risk perception, the development of
targeted messages based on risk perception, the identification of key people for risk communication in the community, good planning, efforts to ensure the availability of resources, and a coordinated, systematic approach to risk communication. These lessons learnt and countries’ experiences of risk communication activities carried out during the pandemic were important in guiding the development of the Risk communication strategy for public health emergencies in the WHO South-East Asia Region: 2019–2023. While the regional risk communication strategy is being rolled out, funds available through PIP partnership contributions and United States Centers for Disease Control and Prevention cooperative agreements could be leveraged to plan and pilot influenza-specific risk communication plans through exercises and during outbreaks in the interpandemic period.

**Points of entry**

Strengthening and maintaining capacities to prevent, prepare for and respond to public health risks at designated key points of entry (PoEs) under the IHR is an area that needs solid support in the region. As countries of the region are now in the process of either developing their NAPHSs or updating their NIPPPs, an intense focus is needed on measures to prevent, detect and control transmission of high-threat pathogens, including pandemic influenza, at PoEs. Influenza-related activities designed for PoEs need to be linked to national health authorities and need to include regular testing and exercises with a view to continually improving contingency plans for pandemic influenza at PoEs, standard operating procedures, human resources and infrastructure.

**Human resources**

Human resources are required to implement, manage and coordinate pandemic influenza response activities. To fulfil this need, in addition to general capacity-building activities in relation to health emergency preparedness and response, a variety of influenza-specific training activities (including on highly specialized areas such as laboratory diagnosis) have been facilitated in the region. However, high staff turnover, the need for regular training on rapid response to seasonal influenza outbreaks and pandemics, a lack of adequate specialized personnel (in field epidemiology, virology, clinical management and behavioural science) and the difficulty of ensuring surge capacity for deployment for rapid response in a pandemic/epidemic are issues to be addressed.

**IHR notifications and event management**

WHO has been working closely with national influenza programmes in the region on their pandemic influenza preparedness planning, facilitating links with the IHR national focal points to ensure timely and accurate notifications of all human infections caused by a new influenza subtype required to be reported under the IHR. WHO, together with WHO collaborating centres and partners, supports countries to diagnose these strains in a timely manner and notify events in compliance with the IHR.

In addition, the annual bi-regional meeting of national influenza centres and influenza surveillance acts as a bi-regional knowledge network on seasonal and non-seasonal influenza with pandemic potential. The forum, in addition to discussing issues, challenges and solutions in relation to prevention, detection, early warning and alert, preparedness, response and recovery with regard to influenza outbreaks/pandemics, facilitates effective mechanisms for linking up influenza programme managers and IHR national focal points for timely event notifications to prevent the international spread of influenza viruses.

The recently established regional laboratory network on influenza and other high-threat pathogens and the South-East Asia Regional Knowledge Network of International Health Regulations National Focal Points also contribute to strengthening detection and notification of non-seasonal influenza viruses and other priority high-threat pathogens.

**Strategizing for other priority high-threat pathogens**

The global experience of Ebola, Middle East respiratory syndrome and severe acute respiratory syndrome and the regional experience of Crimean Congo haemorrhagic fever and Nipah virus disease emphasize the need for regional preparedness to respond to high-threat pathogens. The opportunities created by increased preparedness for pandemic influenza through strengthening plans, health systems and operational capacities for prevention, detection, early warning and alert, preparedness, response and recovery could form the basis for increasing regional preparedness to respond to other high-threat pathogens.

After action reviews conducted following (i) the influenza pandemic in countries of the WHO South-East Asia Region (2009), (ii) seasonal influenza outbreaks in Myanmar (2017), Maldives (2017), Sri Lanka (2018) and the Democratic People’s Republic of Korea (2018); and (iii) human cases of zoonotic influenza in Indonesia and Nepal (2019) have created opportunities to document best practices, strengths, weaknesses and challenges in response, resulting in recommendations for specific, actionable improvements to NIPPPs. These findings can be used to improve preparedness for other high-threat pathogens in the region through countries’ NAPHSs.

The considerable progress made by the Member States on IHR core capacities, the openness in implementing the IHR monitoring and evaluation framework in the region and the availability of the Five-year regional strategic plan for strengthening public health preparedness and response – 2019–2023 are enabling factors for the successful implementation of such an initiative. The required leadership is provided by the Regional Director’s strategic vision, in which the four strategic imperatives – (i) addressing persisting and emerging epidemiological and demographic challenges, (ii) promoting universal health coverage and building robust health systems, (iii) strengthening emergency risk management for sustainable development and (iv) articulating a strong regional voice in the global health agenda – are strongly linked to and facilitate combating high-threat pathogens in the region.

The systematic and ongoing support to countries of the region through GISRS, and a strong network of WHO collaborating centres and other centres of excellence, has contributed immensely to the success of pandemic influenza preparedness regionally. The region’s efforts to develop a comprehensive roadmap for combating Nipah virus infection, facilitated by the WHO South-East Asia Regional Office, need to learn from the systematic support for pandemic preparedness planning and allied platforms, such as GISRS and WHO collaborating...
centres. However, such efforts to address Nipah virus and other regionally important high-threat pathogens need the support of the three levels of WHO, centres of excellence, partners and donors to achieve success similar to that of pandemic influenza preparedness in the long run. While investments in robust and functional health systems are a prerequisite, as experiences of increasing pandemic influenza preparedness clearly demonstrate, funding, technical expertise, experts/ laboratory networks, and new diagnostics, therapeutics, vaccines and technologies are needed to improve surveillance methods, laboratory diagnosis capacities, epidemiological capacity for detection, early warning and alert systems, and overall capacity with regard to preparedness for and response to a broad set of high-threat pathogens.

Technology transfer and enhancing regional manufacturing capacity of influenza vaccines and oseltamivir have boosted regional response capacity enormously. This regional success in enhancing local manufacturing capacity was partly a result of investments in health security by Indonesia and Thailand and investments in the pharmaceutical industry in India.34 However, in relation to Nipah virus and other high-threat pathogens, the commercial potential that could drive significant private sector investments in key components of preparedness and response other than medical countermeasures is limited. Nonetheless, many governments, such as those of Germany, Japan, Norway and the United States of America, as well as private entities, for example the Bill and Melinda Gates Foundation and the Wellcome Trust, have been involved in some activities relating to high-threat pathogens relevant to the region, such as Nipah virus, from a global health security perspective.33 The WHO South-East Asia Region has the potential to tap into such resources if a comprehensive, long-term strategic framework and country action plans for preparedness and response to high-threat pathogens are in place.

However, as the lessons learnt during the development of pandemic influenza preparedness demonstrate, there are many challenges. Regular, consistent, ongoing, functional mechanisms for health sector and non-health sector coordination, addressing existing health system issues, establishing and sustaining functional networks of regional laboratories and reference laboratories, participation in verticalized global support systems such as GISRS for influenza and ongoing capacity development of the health workforce in relation to specific novel infections are key regional priorities. The challenges are consistent with the suboptimal IHR core capacities identified in joint external evaluations conducted in the region.

Conclusions

Lessons learnt from the implementation of the PIP framework could serve as a basis for introducing polices, strategies, national plans and systems to ensure operational readiness to combat high-threat pathogens. In terms of planning, as demonstrated by Timor-Leste, NAPHSs can be an overall framework for planning to prepare to respond to these high-threat pathogens, and an NIPPP can serve as a blueprint with the flexibility to be adapted to the specific risks posed by the high-threat pathogen of concern. Alternatively, countries could also consider several contingency plans for infectious hazards covering different methods of transmission of the disease; these plans could be quickly operationalized for response while overall health system capacity development and increased operational readiness for detection and response could happen in alignment with efforts to ensure pandemic influenza preparedness. National action plans aimed at strengthening the implementation of the IHR can facilitate reviewing and revising legislation and regulations to address high-threat pathogens. The current mechanisms of governance, management and coordination established for pandemic influenza preparedness could be extended and effectively integrated following a multisectoral approach, involving national disaster management stakeholders and One Health stakeholders (where relevant) in managing high-threat pathogens including pandemic influenza.

Member States, WHO and partners need meticulous thinking on utilizing the opportunities provided by the Five-year regional strategic plan to strengthen public health preparedness and response – 2019–202330 and the ministerial-level Delhi Declaration on Emergency Preparedness,34 which reflect the political commitment of the Member States of the region to developing a broad, long-term strategic plan for investments in building capacity for minimizing the danger and impact of high-threat pathogens not only in the WHO South-East Asia Region but also beyond.

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