REVIEW

RESPONDING TO PANDEMIC INFLUENZA IN CAMBODIA AND LAO PDR: CHALLENGES IN MOVING FROM STRATEGY TO OPERATION

Joia de Sa[1], Sandra Mounier-Jack[1], Chau Darapheak[2], Ly Khunbun Narann[3], Rattanaxay Phetsouvanh[4], Nyphonh Chanthakoummane[4], Sok Touch[3], Bounlay Phommasack[4] and Richard Coker[1]

[1]London School of Hygiene and Tropical Medicine, London, UK; [2]National Institute of Public Health, Phnom Penh, Cambodia; [3]Ministry of Health, Phnom Penh, Cambodia; [4]Ministry of Health, Vientaine, Lao PDR

Abstract. Low income countries in Southeast Asia are in a region at risk of emerging infectious diseases, notably SARS, H5N1 influenza and H1N1 influenza. Efforts have focused largely upon early outbreak response, though with the emergence of pandemic influenza, countries in the region are having to prepare to implement mitigation measures. We review the challenges for strategy and operation faced by two low income countries, Cambodia and Lao People's Democratic Republic (PDR), and highlight successes in planing and implementation to date as well as identifying needs and challenge that may hinder the future effectiveness of control measures.

Key words: avian influenza, challenges, strategy, operation, Cambodia, Lao PDR

INTRODUCTION

Concerns have been raised about the ability of low-income countries to cope with influenza pandemics (Oshitani *et al*, 2008; Fedson, 2009). Many low income countries are burdened by a weak public health infrastructure and competing public health priorities. They may find it a challenge to develop operational pandemic preparedness strategies that respond to international communicable disease control imperatives (such as International Health Regulations) and international policy recommendations, while responding effectively to domestic public health problems. The current H1N1 pandemic, as of 19 March 2010, has been documented in over 213 countries around the world and resulted in at least 16,813 deaths. The first cases in Southeast Asia occurred in late May 2009, among people who had recently travelled to affected areas. The experience of severe acute respiratory syndrome (SARS) and the current pandemic highlight the fact that national borders are often ineffective at preventing

Correspondence: Joia de Sa, Department of Global Health and Development Faculty of Public Health and Policy, London School of Hygiene and Tropical Medicine, 15-17 Tavislock Place, WC1H 9SH, UK.
Tel: +44 207 927 2431
E-mail: joia.desa@lshtm.ac.uk

the spread of communicable diseases (WHO, 2004; WHO WPRO, 2006).

Resulting from the SARS experience and the emergence of highly pathogenic H5N1 avian influenza in the region, low-income countries in Asia are finding themselves at the forefront of efforts to control emerging infectious diseases. The impact of a new pandemic among low-income countries is likely to be substantial (Murray *et al*, 2006). Though the World Health Organization has provided strong leadership in surveillance, the response to infectious disease outbreaks remains largely a national responsibility, bounded by concepts of national sovereignty (Fidler, 2008).

We review two low-income countries in Southeast Asia to explore how pandemic preparedness strategies were developed and how they are being implemented. We highlight strengths, weaknesses, and ongoing needs in operationalizing their national strategic plans. We explore how low income countries might best plan and implement their responses to pandemic influenza and, more broadly, to emerging infectious diseases of public health significance.

MATERIALS AND METHODS

This study relies on both a documentary review and the use of the Systemic Rapid Assessment Toolkit (SYSRA) which is a systematic approach for gathering information about structures and modes of operation from complex health systems (Mounier-Jack, 2008; Hanvoravongchai *et al*, 2010). The Toolkit was developed from the WHO's Rapid Assessment and Response approach (WHO, 2002) and the conceptual framework on health systems and communicable disease control that was initially developed for assessment of TB and HIV/AIDS prevention and control programs by Atun *et al* (2004).

In each of five health system modules (external context, governance and stewardship, financing, health care provision and information systems), data were collected based on a review of published data and interviews with key personnel in each country. The questions in the interviews explored past and current patterns of health program responses, primarily to H5N1 disease, changes in pandemic response and other historical information about outbreak management. The interviewed subjects were purposefully selected in each country based on their expertise regarding a broad range of health system and pandemic program components to provide in-depth information about these. They came from all administrative levels and from different institutions to provide a coherent view of the health system and pandemic management program. Information was triangulated to ensure content validity.

RESULTS

Cambodia is a country of approximately 14.3 million people bordering Thailand, Lao PDR and Vietnam. Recent political stability has allowed for a period of economic growth and improvements in human development indicators.

The first poultry outbreaks of H5N1 were reported in January 2004 and the first human case was detected (in Vietnam) in early 2006. Cambodia has had a total of 9 human cases, with 7 proving fatal (Buchy *et al*, 2007). As of December 2009, Cambodia had reported 472 cases of H1N1 influenza, with 5 deaths. Among the fatalities were a 51 year old woman with previous respiratory disease, a 25 year old pregnant woman and two 41 year olds.

Lao People's Democratic Republic

(Lao PDR) is a land-locked country of approximately 5.6 million people which borders China, Myanmar, Vietnam, Cambodia and Thailand. It is home to a large number of ethnic groups, most of whom live in rural locations.

Lao PDR has reported several poultry outbreaks of H5N1 and two human cases were reported in early 2007, both fatal (Puthavathana *et al*, 2009). There have been a total of 292 laboratory confirmed human cases of H1N1, as of the 7th January 2010 with 2 deaths. However individual cases are no longer being routinely tested.

Cambodia and Lao PDR are both classified as least developed countries by the United Nations (2009). They have a similar public health profile, with a high burden of infectious diseases. The majority of the population live in rural settings. Both countries have experienced both poultry and human cases of H5N1 avian influenza and H1N1. Both countries have conducted national level pandemic preparedness planning exercises.

The challenges facing health systems in low-income countries are multiple and varied. With the majority of the population rurally based, simply providing access to health care is difficult. Both Cambodia and Lao PDR are emerging from periods of instability and as such, have limited resources to invest in their health systems or to reform health care financing (HLSP, 2007; Thomé and Pholsena, 2008; WHO WPRO, 2008). Both rely on substantial donor support for health system strengthening and disease-specific programs, with subsequent challenges emerging around harmonization, integration and sustainability which are beginning to be addressed (the World Bank, 2008). Human health system resources are limited and unequally distributed, with rural areas least served. The communications capacity is weak, as are logistics regarding transport, storage and distribution of medical supplies, although these are now gradually being tackled.

The health system is structured similarly in both countries with a central governmental structure allocating responsibility to provinces (Lao PDR) and operational districts (Cambodia). Units of healthcare are hospitals at provincial and district levels, and health centers. Care is provided on a fee-basis, though the poor are notionally exempted. The private healthcare sector is growing, particularly in Cambodia. The countries spend very little on healthcare, with the majority coming from out-of-pocket payments and donor financing; government expenditure in 2006 reached USD6 per capita in Cambodia (with USD7 from donors and USD 15-25 from out-of-pocket payments) (WHO WPRO, 2008) and USD 5.5 in Lao PDR (1.1% of GDP) out of a total of USD 19.5 per capita health expenditure (Thomé and Pholsena, 2008).

From strategy to operation: management and co-ordination

In a low-income context, many disease programs compete for financial and human resources. Vertical programs often sit parallel to broader health system arrangements, particularly for HIV and TB, and reflect separate funding streams and donor influences(Oliveira-Cruz *et al*, 2004). Parallel programs, funded solely by donors, are likely to be unsustainable given the uncertainties in timing and public health impact of pandemic influenza and other emerging infectious diseases.

Both Cambodia and Lao PDR have benefited from, and are largely reliant on, financial contributions from the international community to boost influenza activities with no guarantee of financial

sustainability (UNSIC and the World Bank, 2008). In both countries, influenza response and preparedness programs have no direct or secure stream of domestic funding, and may have to compete with other disease programs in the future. The mobilization of financial resources during an outbreak and a subsequent pandemic remain challenges that need to be met (Chanthakoummane *et al*, 2009; Darapheak *et al*, 2009).

Governance arrangements are key to emergency response (SARS Expert Committee, 2003; The National Advisory Committee on SARS and Public Health, 2003). The Communicable Diseases Control Department of the Ministry of Health of Cambodia is currently taking the lead in human health activities, predominantly those strengthening surveillance and response capabilities. This lead is retained (in the national plan) in later stages of a pandemic (WHO phases 5-6). Although other ministries and technical agencies are involved in multi-sectoral preparedness coordination, the full responsibility for coordinating the non-health sector response lies with the National Committee for Disaster Management (NCDM), although this has been criticised for its weak infrastructure and limited clout (Darapheak *et al*, 2009).

In Lao PDR, the National Avian Human Influenza Co-ordinating Office (NAHICO), which has now changed its name to National Emerging Infectious Disease Co-ordinating Office (NEIDCO), was established in 2006 by Prime Ministerial decree. A separate decree also formalized its authority. Working groups have been set up to steer the five strategic elements of the national plan (Fig 2) working with international partners. This more "vertical" approach provided NEIDCO with greater autonomy and established a clear governance system for avian and human pandemic influenza preparedness and control, although its capacity remains limited. There is also a separate disaster management committee in Lao PDR, but the roles, responsibilities and linkages with NEIDCO remain operationally uncertain (Chanthakoummane *et al*, 2009).

The lack of institutional authority and financial capacity of the disaster response bodies reflects, to a large extent, the fact disaster management of public health crises is a relatively unfamiliar concept in some low-income countries. With the challenges of developing an effective health system (along with public policy needs beyond the health sector), the institutionalization of separate disaster management offices remains challenging and operational capacity is very limited. Significant challenges also result from a lack of preparedness at the regional level hindered further by limitations in communication capacity. Lao PDR and Cambodia have piloted innovative approaches to ensure an effective multi-sector response at the provincial level (UNSIC and the World Bank, 2008) (Fig 1).

Implementation and operation

Given the many challenges facing low-income countries, we have chosen to focus our analysis on the strengthening of surveillance and response systems because this is the main focus of both national plans.

Surveillance

The International Health Regulations (2005) endorsed by all WHO member countries have mandated strengthening surveillance in all countries to be able to detect public health threats of international concern (WHO, 2005). Cambodia and Lao

In Cambodia, a sub-national pandemic simulation exercise was held in Siem Reap in December 2008. This emphasised that although the plan was generally well understood, there was a lack of co-ordination between different sectors and a need for more operational preparedness. Command and control arrangements lacked clarity, resulting in further co-ordination difficulties (Government of Cambodia, 2008).

In an effort to address some of these challenges, WHO Cambodia has been supporting and testing strategic and operational planning in Siem Reap Province. Eight government sectors as well as civil society and private enterprises were involved. A major part of the planning focused on disaster management and phase 6 activities. The outcome of these meetings will be disseminated to other regions including a model provincial operational plan with standard operating procedures and lessons learned from the process (UNSIC and the World Bank, 2008).

In Lao PDR, similar conclusions were drawn from a national simulation exercise *PanStop II* held in December 2007 (UNSIC, 2008). WHO Lao country office has been supporting the country to develop operational plans at province level – the first was completed in Vientiane Province linking strategic aims to activities with designated responsibilities. It is planned to extend this to other provinces later this year.

Fig 1–Operationalizing pandemic preparedness.

PDR both employ a similar approach to surveillance: routine surveillance and event-based surveillance. Routine surveillance consists of weekly reports sent in from provinces and operational districts on a number of diseases including any clusters of cases. The timeliness of the system is challenged by a lack of information technology, though recent developments in Cambodia have included an SMS gateway for information to be sent directly to the system. In Lao PDR, there is new WHO-created software allowing electronic case and death data to be sent from province to national level, currently running to some extent in all provinces. An informal reporting system through the training of village health volunteers also exists in both countries and encourages reporting through a dedicated telephone "hotline" The success of this approach in highlighting outbreaks of infectious diseases in animals (WHO WPRO, 2006; UNSIC and the World Bank, 2008) has been noted but continues to be challenged by a lack of communications infrastructure. In a similar approach to other Asian countries, the integration of animal and human health surveillance has been emphasised in national planning, though in practice, this remains informal.

A review of H5N1 human case histories (Nora, 2007; WHO, 2007; Ear, 2009) reveals profound problems inherent in the system. All human cases but one were diagnosed at a very late stage of the disease and the first cases in each country were actually diagnosed in bordering middle-income countries (Vietnam and Thailand) where patients had gone to seek treatment. This raises several issues: first, that communication for surveillance between countries is currently based on (good) informal relationships and though facilitated by relationships formed through regional networks, such as Mekong Basin Disease Sur-

Fig 2–Information campaign, Cambodia (Source : Author).

veillance Project (MBDS), is not formalized; second, the surveillance systems are working, but slowly (it will be interesting to see how investment in information technology impacts the timeliness and breadth of surveillance); third, the majority of cases tend to seek health care late and predominantly in the private sector first [H5N1 cases in Cambodia averaged 2.5 private health care visits before diagnosis (Government of Cambodia, 2007)], highlighting an urgent need to incorporate the private sector into surveillance (and improve clinical awareness and knowledge).

With the emergence of H1N1 influenza, both Cambodia and Lao PDR have instituted border screening. H1N1 cases have continued to be reported through the systems described above. However, the relatively mild nature of the disease and the non-specific nature of the signs and symptoms (fever, cough, sore throat and runny nose) mean the disease is likely to be substantially under-reported. WHO guidance has now advised against laboratory testing of individual cases unless they have severe disease, have high risk conditions or live in a province without a confirmed cases (WHO Lao PDR, 2010).

Outbreak investigation and health care system response

The response to avian influenza in Cambodia and Lao PDR has been coordinated by rapid response teams. These teams are operational at province and district levels and are trained in fieldwork and outbreak investigation. Suspected cases are sent to the nearest designated hospital for appropriate medical care and treatment (including antiviral drugs) and epidemiological investigations are conducted in the areas, often in conjunction with animal health representatives and with technical support from central government and UN agencies. Rural communities have been educated by outreach campaigns,

such as SuperMoarn and Super Gai (Super Chicken – Fig 2) and compliance with outbreak investigations and subsequent measures, such as culling of infected poultry, remains high (Ear, 2009).

The public health infrastructure of Cambodia and, particularly of Lao PDR is weak. There is currently no formal training program in epidemiology in Lao PDR, although the WHO is supporting field epidemiology training, which was launched in 2009, with the first trainees helping in outbreak response. There are several provincial rapid response teams; the National Center for Laboratory and Epidemiology houses the national rapid response team. It also contains the national reference laboratory, responsible for bacteriology, virology and serology. There are plans to upgrade the laboratory with support from the Pasteur Institute of Paris, the US CDC and the WHO. The new Pasteur Institute is scheduled to open soon in formal affiliation with the Ministry of Health. Currently H5N1 specimens can be confirmed in country and are sent to Japan for further analysis.

Cambodia is in a more fortunate position having a functional Pasteur Institute National Influenza Center and has recently upgraded the National Laboratory of Public Health with the support of the US CDC in the capital Phnom Penh. Rapid response teams are operational in all provinces.

The mainstay of case management for both H1N1 and H5N1 is medication with antiviral drugs and the use of protective personal equipment (PPE) by healthcare and Rapid Response Team staff for suspected cases of severe disease. Both countries have central stockpiles of a few thousand doses of the antiviral drug oseltamivir, recently boosted by distribution from the regional ASEAN stockpile and donations; some stock has been distributed down to province and district level. However, it is unclear what the location and quantity of this stock is. Field visits showed the PPE and antiviral drugs had expired and staff were unsure about how to get further supplies (Darapheak *et al*, 2009).

This reliance on antiviral drugs has been criticised, because it is unlikely low-income countries will have sufficient financial resources to stockpile enough antiviral drugs to meet their population's needs (many developed countries have stockpiled enough to meet treatment needs of at least 25% of their population); secondly, the logistics of effectively delivering antiviral drugs are extremely challenging (Ferguson *et al*, 2005); and finally, the emergence of resistance may limit the effectiveness of antivirals. Neither country anticipated accessing or stockpiling, pre-pandemic or pandemic vaccines. Countries rely on the WHO antiviral emergency stockpile, that has been recently partially distributed to countries in Southeast Asia, to mitigate the logistical hurdles and strengthen outbreak response. In recognition of the inter-connectedness of the region, particularly through transport networks, the Association of Southeast Asian Nations (ASEAN) has, at the time of writing, acknowledged that a regional strategy is necessary for obtaining sufficient pharmaceutical and vaccine doses (Treerutkuarkul and Charoenpo, 2009). The WHO has distributed 300,000 H1N1 vaccine doses to Cambodia and (donated) 600,000 H1N1 vaccine doses to Lao PDR with a planned distribution program to health-care providers and pregnant women.

In common with many other national plans in the region (Coker and Mounier-Jack, 2006), both countries' plans imply rapid containment is both feasible and

necessary. Rationing of scarce resources, or ensuing ethical considerations are not mentioned. It is assumed the international community will provide the necessary assistance. In terms of service provision, staff report anxiety over treating highly infectious cases and absenteeism is likely to be high. Infection control "has not received much attention"(Government of Cambodia, 2007); however, training sessions have been initiated, supported by national infection control committees, and basic medical supplies have been boosted.

In the current H1N1 pandemic, there has been promotion of non-pharmaceutical interventions, such as hand washing and not spitting in public. International NGOs have been working with the Ministry of Health to help educate and inform the population using campaigns, such as those seen in Fig 2.

Summary of operational capacity

Both Cambodia and Lao PDR have developed a response for avian influenza but only partly addressed the planning and operational needs for pandemic influenza. The current H1N1 pandemic continues to have a fairly low impact, with the majority of cases having mild illness. Surveillance and outbreak investigation capacity have been strengthened, but the health system capacity to respond with containment, and especially mitigation, remains profoundly limited. An illustration of this is the lack, in both countries, of surge capacity planning. With limited available resources and an existing high disease burden, health systems in both countries face competing priorities, and pandemic influenza preparedness has naturally been limited. There are benefits to strengthening outbreak response that go beyond pandemic preparedness, including the development of capacity amongst rapid response teams to respond to outbreaks of food poisoning, dengue fever and other infectious diseases (NCLE and WHO, 2008). The integration of surveillance and outbreak response in low-income countries within their wider health systems and the broadening of their functionality beyond single diseases will likely be key to developing capacity to respond to emerging infectious diseases.

DISCUSSION

The World Health Organization (WHO) has been energetic in its calls for global preparedness, and has recently updated its guidance on preparedness and response, specifically calling for pandemic preparedness to be integrated into disaster management and emphasising a "whole of society" approach (WHO, 2009). The WHO influenza pandemic preparedness checklist (WHO, 2005b), published in 2005, was intended to help facilitate national preparedness and was discussed at an informal consultation among countries with limited resources (WHO, 2004a), but no formal guidance for low resource countries has been published to specifically respond to these countries' needs.

Regionally, the Asia Pacific Strategy for Emerging Infectious Disease (APSED) (WHO SEARO, 2005) was launched following the ratification of the International Health Regulations (IHR) (2005) as a road map for Asian countries. It aims to ensure a coherent, minimum response to emerging infectious diseases in a region which is noted to be an area with emerging infectious diseases "hotspot"(Jones *et al*, 2008). Minimum capabilities have been set out for five areas of focus: surveillance and response, laboratory, infection control, zoonoses, and risk communication. Lao PDR was chosen from the Western Pacific

Regional WHO Office (WPRO) to be reviewed in terms of progress, having achieved significant results as measured by APSED benchmarks in a relatively short time.

While an initial review of pandemic influenza preparedness in the Asia-Pacific region showed neither Cambodia nor Lao PDR had a national plan available in 2006 (Coker and Mounier-Jack, 2006), both countries have since published national and provincial (in Lao) avian and human pandemic influenza plans (Government of Lao PDR, and UN, 2006; Government of Cambodia, 2007). Both plans have benefited from high-level government support and have been endorsed by their governments. Countries have received significant technical support from UN agencies in drafting their plans (Royal Government of Cambodia and UN Team Cambodia, 2005). With the H5N1 avian influenza virus being endemic in the region and the fact that both countries have limited financial and technical resources with which to respond, both countries' plans focus on early surveillance and detection of influenza and subsequently early response to outbreaks in humans. However, plans place limited emphasis on mitigation strategies to respond to pandemic influenza, an event that has overshadowed avian influenza outbreaks, and lack operational guidance to support a response to the pandemic arising from beyond their borders.

The frailty of mitigation planning is consistent with other evidence that indicates pandemic preparedness is correlated with a country's income level (Hanvoravongchai *et al*, 2010). For instance, a World Bank report showed that fewer than 40% of low income countries surveyed were planning to use a pharmaceutical response, while 95% of high income countries were planning to do so (UNSIC and the World Bank, 2008). For low income countries acquisition of pharmaceuticals may not be feasible, but even if purchased the logistical hurdle of delivering drugs effectively would likely be insurmountable, especially in remote rural regions (Coker and Mounier-Jack, 2006; Lee and Fidler, 2007; UNSIC and the World Bank, 2008).

Low-income countries, such as Cambodia and Lao PDR, are likely to find themselves substantially challenged by a highly pathogenic influenza pandemic. They have significant needs and are experiencing profound gaps in planning for a pandemic. However, relative to their income level, significant progress has been made toward preparation efforts (UNSIC and World Bank, 2008).

In a low-income context, pandemic preparedness is an additional burden to other health priorities and the country's development agenda. Given the current economic climate, domestic and donor funding is likely to be scarcer. In terms of response, access to pharmaceutical resources for a pandemic is mostly limited by domestic economic constraints, access to donor funds, sustainability of donor funds, or to a finite international stockpile of pharmaceuticals and vaccines. Therefore, there is an acute need for specific guidance regarding the allocation of scarce resources. To date there has been little guidance for low-income countries to draw upon in terms of practical implementation of control measures, both in containment and mitigation efforts.

The current H1N1 pandemic highlights the challenges associated with early containment. It might be argued that much of the modelling, upon which global policy is formulated, made unrealistic assumptions regarding surveillance systems and

the logistics of delivering care and halting spread in low-income countries. (Ferguson *et al*, 2005, 2006). There is now an even more urgent need to support not only surveillance and outbreak investigation but also operational response in low-income countries, such as Lao PDR and Cambodia. Beyond pandemic planning, low-income countries need investment in health system "fundamentals"(Kruk, 2008), not only for pandemic influenza, but as part of a broader effort to build capacity to respond to all public health threats.

The issue of which governance model is more suited to emergency response can only be approached in the context of country governance arrangements and should be cognisant of the wider socio-political and cultural context. The choice by both Cambodia and Lao PDR to rely on a specific agency to lead the response helps ensure clear lines of responsibility but means sustainability may potentially be compromised. The piloting of provincial multisectoral planning in both countries is encouraging and should be further assessed before being expanded.

The H1N1 pandemic originating in Mexico has shown, once again, that pathogens do not respect national boundaries. In a region with a high prevalence of emerging infectious diseases, low-income countries are particularly vulnerable. Pandemic preparedness efforts so far must be applauded but support is necessary from the international community to ensure effectiveness.

In the chain of global responses to a pandemic we are all, as a global community, potentially at the mercy of the weakest link. We suggest there needs to be a debate on how to allocate resources not only to contain an outbreak but to mitigate the consequences of a pandemic, a debate that is both domestic and global in nature. The global inequities of resource distribution, whilst they will likely impact most on the poorest of the poor, have their genesis in global governance arrangements for global public health threats.

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