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Short communication

Progress toward sustainable influenza vaccination in the Lao Peoples' Democratic Republic, 2012–2018

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ABSTRACT

Despite global recommendations for influenza vaccination of high-risk, target populations, few low and middle-income countries have national influenza vaccination programs. Between 2012 and 2017, Lao PDR planned and conducted a series of activities to develop its national influenza vaccine program as a part of its overall national immunization program. In this paper, we review the underlying strategic planning for this process, and outline the sequence of activities, research studies, partnerships, and policy decisions that were required to build Laos' influenza vaccine program. The successful development and sustainability of the program in Laos offers lessons for other low and middle-income countries interested in initiating or expanding influenza immunization.

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Influenza vaccination remains underused in low and middle-income countries. While the number of countries with national vaccine policies has increased in recent years, in 2014 only 59% of countries had policies for use of influenza vaccine. Among those with policies only 18% were among low and low-middle income countries [1]. Lao Peoples' Democratic Republic (Laos) initiated a national influenza vaccination program in 2012. Although Laos is now a lower-middle income country, at that time it was the first low-income country to do so. Laos first used influenza vaccine during the 2009–10 influenza A(H1N1)pdm09 pandemic, during which one million doses of the monovalent influenza A(H1N1)pdm09 vaccine donated from the World Health Organization (WHO) were used to vaccinate pregnant women, health care workers, people living with chronic medical conditions, and persons aged 65 and older [2]. The pandemic experience generated interest among government officials for further strengthening influenza monitoring and pandemic preparedness systems [3], and provided the impetus to initiate a seasonal vaccination program in the country. Programmatic lessons from the 2009 vaccine delivery experience were reviewed, and provided the foundation for initiation of the seasonal vaccination program in 2012. Working with the U.S. Centers for Disease Control and Prevention (CDC) and WHO, the Government of Laos (GOL) undertook research and surveillance activities to create the evidence base for vaccination, and engaged in an innovative partnership to support the development of a seasonal vaccination program in the country. We review the key steps in the emergence of a sustainable influenza vaccination program in Laos, and discuss challenges that have been, or will need to be, addressed for longer-term sustainability.

An essential component of the work has been an ongoing effort to create the evidence for a national decision to introduce influenza vaccination. Since 2007, Laos has had a robust influenza surveillance system that has contributed substantially to global influenza vaccine strain selection. During this time period Laos has tested over 22,000 sentinel specimens, with 96 shipments of specimens to the WHO Global Influenza Surveillance and Response System [4,5]. Laos has also published data on circulating viruses and seasonality to support decision-making about the timing of vaccine delivery, and to define priority vaccine target groups for vaccine delivery. These data demonstrated year-round influenza circulation with primary peaks in the rainy season from July to December,

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and secondary peaks during the cold season of February to April [6]. Data from this system were made available weekly as reports to government and international stakeholders, increasing awareness of influenza among key stakeholders in the country. As a result of these data, the Laos National Immunization Program (NIP) made the decision to use southern hemisphere formulations of vaccine in annual campaigns during April - June.

At the request of national policy makers, these surveillance data were augmented by studies that have been (and are being) designed to provide local data to further support influenza vaccine prioritization, procurement, and uptake. During the initial year of vaccination, the prevalence of adverse events following vaccination were studied to ensure that local vaccine safety data were available for review by policy makers [7]. Next, because pregnant women were an early target of the vaccination program [8], data on birth outcomes in the country, including birth weights and the frequency of low birth weight and preterm labor, were collected from 2004 to 2013 [9]. These data were a foundation for a 2013–14 study evaluating the effects of maternal influenza vaccination for these outcomes [10]; and were the first findings of an association between maternal vaccination and birth outcomes in a national vaccine program. In addition to evaluating vaccine performance, work to understand the disease and economic burden of influenza have been conducted, or are underway. Using the WHO manual for estimating disease burden associated with seasonal influenza as a guide, data from the national sentinel surveillance system, coupled with health care admission surveys, have been used to estimate the rates and burden of influenza hospitalizations, by age group. Studies are ongoing to estimate the direct and indirect economic costs of influenza hospitalizations from the family and governmental perspectives, and to conduct cost-effectiveness modeling of vaccine use for recommended priority groups. Other practically relevant work is focusing on understanding the knowledge, attitudes, and practices of vaccine target groups to improve seasonal influenza vaccine uptake. Finally, plans for 2020 include undertaking a post-implementation evaluation with the World Health Organization to generate data to further optimize vaccine delivery.

Many of these studies have been conducted following donation of influenza vaccines in the country rather than before, and indeed, were made possible by the implementation of seasonal influenza vaccination among the Lao target groups. Seasonal influenza vaccine donation was initiated in Laos in 2012, with collaboration from the US CDC and the Partnership for Influenza Vaccine Introduction (PIVI) [11]. PIVI is a public–private partnership between Ministries of Health, corporate partners, and technical agencies to create sustainable, routine, influenza vaccination programs in middle-income countries; and to build the immunization infrastructure, capacity, and vaccine delivery systems required for future influenza pandemics and other infectious disease epidemics. In 2012, the NIP received 375,000 influenza vaccine doses through a pre-PIVI collaboration between the CDC, the WHO Country Office in Laos, UPS, and Walgreens as a pilot donation program. Based on this experience, PIVI was formed and has worked with Laos and CDC from 2013 to 2018 to grow and evaluate the national vaccination program. PIVI has supported the vaccine programs through a donation, but the Government of Laos has incrementally taken over vaccine purchase (Fig. 1).

During this time the annual number of influenza vaccines wasted has also been relatively low (Table 1) due in part to high demand among target groups and microplans for vaccine distribution that have been informed by local hospitals, clinics and EPI program managers. With the microplans, vaccination teams had an accurate understanding of target group numbers by village during vaccine campaigns. The cold chain also remained intact, and single-dose pre-filled syringes further reduced wastage.

While PIVI and CDC supported some of the costs for program delivery in 2012 and 2013, NIP has assumed all program costs, other than vaccine purchase, since 2014. By 2019, Laos plans to purchase the majority of its vaccine (150,000 doses purchased

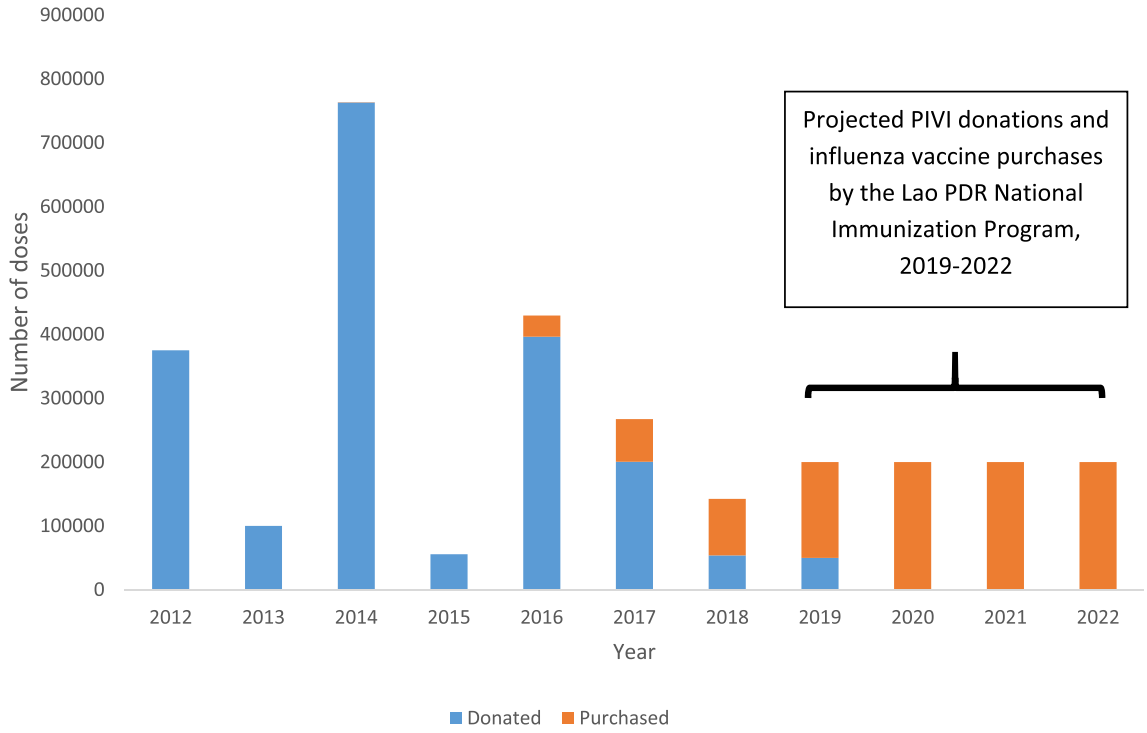

Fig. 1. Donated and Purchased Influenza Vaccines, Lao PDR, 2012–2018, with projections from 2019 to 2022*. * Donated vaccines have come from Walgreen's (2012), CSL Australia (2013, 2014), Green Cross and Hualan (2015) and Seqirus (2016–2018). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 1
Donated, purchased, and wasted influenza vaccine, Lao PDR, 2012–2022.

									Estimated procurements and donations		
Year	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Donated vaccine	375,000	100,000	763,000	55,760	396,309	200,333	50,000	50,000	0	0	0
Purchased vaccine	0	0	0	0	33,333	67,000	150,000	200,000	200,000	200,000	200,000
Wasted vaccine	45,444	3474	20,113	6781	6129	–	–	–	–	–	–

and 50,000 doses donated), using its evidence to inform efficient vaccine delivery to priority target groups.

Variability in vaccine doses used in the program during the 2012–2015 was due to unpredictable donations of vaccines. In 2015, a multi-year sustainability plan was developed by Laos and PIVI which explicitly stated program goals in terms of target groups and coverage goals from 2016 to 2022. In this plan target vaccine coverage of key populations with the currently available 200,000 doses includes 50% coverage of pregnant women and health care workers, and 15% coverage of persons aged >= 60 years. Laos plans to purchase all 200,000 doses necessary to achieve these goals during the years of 2020–2022. The more predictable demand for vaccine for the Lao program enabled PIVI to work with manufacturers to provide a more stable vaccine supply based on the sustainability plan. PIVI now works with all countries to create such plans at the beginning of the collaboration.

Concurrent with the creation of an evidence base and the delivery of vaccine, the NIP undertook a series of activities and actions to create the foundation for national support of the program. First, a policy about vaccine target groups was developed. Given some limitations in the availability local data, the 2012 WHO SAGE influenza vaccination recommendations were important to initial decision-making by the Lao PDR National Immunization Technical Advisory Group (NITAG) [8]. Healthcare workers were also considered particularly important given the ease with which they could be vaccinated, their importance during epidemics and pandemics, and the impact that their own attitudes and behaviors may have on the vaccine decision-making of their patients. Vaccine was prioritized for pregnant women, older adults with chronic conditions that put them at risk for severe influenza complications, and healthcare workers. Recognizing that national vaccine decision-making [12], especially the prioritization of limited influenza vaccine resources, requires careful consideration by an independent NITAG, CDC and WHO have supported increasing the capacity of the Lao NITAG to make evidence-based national vaccine (including influenza vaccine) recommendations. A knowledge exchange visit for the Lao NITAG to observe national vaccine-decision-making processes was organized for Canberra, Australia in February 2017. The Lao NITAG returned with an updated perspective on NITAG roles, and the Government of Laos recognized the need for the independence of NITAG members to avoid conflicts of interest. Laos then re-formed its NITAG in June 2017 with support from PIVI. Twenty-three new NITAG members were recruited and trained, representing a diverse knowledge base, and meeting international criteria for independence and expertise. Replacements for each specialty were also trained in case a primary member were not available at the time of a NITAG meeting. This reformed NITAG would be tasked with refining influenza and other vaccination policies, and to help prioritize vaccines to those most in need when there may not be sufficient amounts to reach all priority groups. Indeed, much of the current work on the burden of influenza, KAP studies, and the economic cost-effectiveness of the seasonal influenza vaccine is being undertaken to inform future NITAG recommendations and NIP influenza policy decisions about expansion of the national influenza vaccination program. Notably, the enthusiastic response during the pandemic vaccination in 2009 by the elderly provided Laos with an ability to reach this population not only with vaccines, but with other health and social interventions as well. In addition, the NITAG is charged with considering recommendations for influenza vaccination in the context of Laos' other vaccine introductions and the phased reduction of GAVI vaccine alliance support.

An influenza vaccine policy recommended by the NITAG must exist in a legal framework that binds public and private health and non-health sectors to standard implementation of a vaccine program. A multi-sectoral team led by the NIP drafted a first National Immunization Law in 2015. This law included eight chapters and 87 articles covering all aspects of Lao vaccine program implementation including vaccine technologies allowed in Laos, responsibilities for vaccine program management and delivery, mandatory and optional vaccines including enforcement strategies, private sector responsibilities for vaccine delivery and quality control, vaccination schedules, required funding for vaccines, legal management of adverse events following immunization, and other issues. A series of regional consultative meetings for this law were held in 2017 and this was subsequently approved by the Minister of Justice and the Prime Minister's Office. In 2018, this law was presented to the parliamentary assembly for a final vote and approved. This made possible the subsequent development of a national influenza vaccine policy, as well as negotiations for appropriate pricing with pharmaceutical companies.

Despite the substantial progress, significant challenges remain. Currently only 35% of pregnant women, 12% of elderly with chronic conditions, and 90% of health care workers are vaccinated given available amounts of influenza vaccine. As a result, access to the limited doses delivered has been considerably higher in easier-to-reach urban populations, and lower in rural populations which have been impacted by severe seasonal epidemics. Stable funding for program growth is now aided by the recent approval of the National Immunization Law, which will allow for expanded vaccine delivery to include public sector hospitals, after-hours clinics, and private pharmacies. This should make vaccine more accessible to rural populations and priority groups. The NIP has also pioneered the integration of influenza vaccine delivery with Tetanus Toxoid (TT) vaccine to better access pregnant women visiting ante-natal care clinics. This move had contributed to an increased uptake in TT vaccinations in that population as well. Despite considerable variation in the amount of influenza vaccine available to Laos in the past, the sustainability plan created for influenza vaccine purchases through 2022 will facilitate a modest yet consistent supply of vaccine to allow appropriate planning for vaccine prioritization by the NITAG, and to engender trust among selected target groups that a consistent vaccine supply will be available. At first, this may require further scrutiny of the existing evidence base to focus limited vaccine supplies toward just those that will provide the greatest cost-benefit from targeted vaccination. Continued communication campaigns will also help to alleviate any misconceptions regarding influenza vaccines in high risk populations and health care providers.

An influenza vaccination program, or any other vaccine program, does not mature in just five years. Nevertheless, Laos has implemented a model of 1) working with partners to amass the

evidence for the program; 2) creating the government structures and funding for sustaining the program; and 3) working with PIVI to ensure early access to the vaccine. This model has successfully generated the local desire for influenza vaccination and be transferrable to other middle-income settings.

Declaration of interests

None of the authors have a conflict of interest to declare.

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