



# Supporting national immunization technical advisory groups (NITAGs) in resource-constrained settings. New strategies and lessons learned from the Task Force for Global Health's Partnership for influenza vaccine introduction <sup>☆</sup>



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## ABSTRACT

National Immunization Technical Advisory Groups (NITAGs) are multidisciplinary national experts who provide independent, evidence-informed vaccine policy recommendations to national health authorities. An essential NITAG function is to ensure that these decisions are grounded in the best available evidence generated through a systematic, transparent process. However, in many low- and middle-income countries (LMICs), experience with this decision making method is limited. The Task Force for Global Health manages the Partnership for Influenza Vaccine Introduction (PIVI) program in collaboration with the Centers for Disease Control and Prevention, Ministries of Health, corporate partners and others. During 2017, PIVI worked with its country partners and the World Health Organization regional and local offices to assess NITAG strengthening needs and to provide technical assistance in 7 LMIC countries (Laos Peoples Democratic Republic, Mongolia, Vietnam, Armenia, Côte d'Ivoire; Moldova and the Republic of Georgia). Our workshops supported general NITAG capacity building and the evidence-based review process using vaccines of interest to the country. For NITAGs reviewing evidence on seasonal influenza, we developed an influenza resource package to support their review and provide country-relevant information in an easy to use format. Of the seven NITAGs trained, six have applied some of the concepts learnt: revision or development of formal transparent, systematic procedures for their operations; preparation of recommendations on seasonal influenza vaccination using quality-assessed data from systematic searches and local data; and have applied the principles learned for making other new vaccine recommendations. Our experience confirms that LMIC NITAGs are considerably under-resourced without adequate technical support or access to global peer-reviewed literature. Ongoing support from NITAG partners must be secured and creative approaches might be needed to help countries achieve the GVAP 2020 target and support development of sustainable vaccine policies and programs.

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## 1. Introduction

Public health interventions that prevent mortality and morbidity have greatly increased over the past decade. Immunization is

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the most cost-effective of these preventive interventions, with potential to bring broad economic benefits beyond health benefits [1,2]. Nevertheless, vaccination policy decisions are often challenging in the changing global immunization landscape (e.g., cost of new vaccines, perception of vaccination as a public good). Although new and underutilized vaccines targeting a variety of age groups beyond the traditional infant groups provide public health benefits to new populations, their introduction presents challenges in terms of cost and delivery.

Countries need the necessary evidence and clear processes to enable informed decision-making in order to introduce and sustain new vaccines in immunization schedules and to improve national immunization programs. Decisions should be unbiased, comprehensive, systematic and based on deliberate, rational, understandable and evidence-based criteria [3]. This process requires specialized skills and resources that need to be reinforced in many immunization programs in low- and middle-income countries (LMICs).

National Immunization Technical Advisory Groups (NITAGs) are multidisciplinary groups of experts responsible for providing independent, evidence-informed advice to national policy makers. High income countries have considerable experience with NITAGs issuing vaccine policy evidence-based recommendations [4–7]. Work to strengthen NITAGs in LMICs accelerated over the last decade following the 2012 endorsement of the Decade of Vaccines Global Vaccine Action Plan (GVAP) at the World Health Assembly, where all countries committed to have a functional NITAG by 2020 [8].

The main processes that NITAGs need to go through to make recommendations consist of (1) identifying topics and policy questions, (2) deciding on criteria for decision-making, (3) gathering evidence and assessing its quality, as necessary (global, regional, local), (4) synthesizing and deliberating on evidence and (5) formulating policy recommendations which are then transmitted to ministry of health. Technical and scientific support to NITAGs is provided by the Secretariat, which consists of one or more people from a technical agency appointed by the ministry of health, and requires substantial immunization related expertise and experience.

A major advantage of NITAGs is the rigor, transparency, and evidence-based processes for vaccine policy making, which in turn adds credibility to the national immunization program and to the government at large. According to guidance for establishing standard operating procedures, NITAGs are advised to establish working groups to systematically gather, analyze, interpret and prepare evidence on key elements to inform the development of recommendations on vaccine policy by the full NITAG [3]. The elements include disease burden, vaccine safety and efficacy/effectiveness, and ideally also include economic and programmatic implications, including vaccine acceptability [3]. NITAGs have access to some systematic evidence based reviews which may preclude the need to conduct their own reviews. However, they are usually interested in reviewing available local or regional data. For NITAGs in LMICs, conducting even limited literature reviews is resource-intensive and poses significant challenges for their members who may already be overcommitted and may not have adequate analytic and evidence-based decision-making skills, ready access to peer reviewed publications, nor an adequately staffed secretariat to support their reviews [9]. Since 2010, there has been considerable progress to establish NITAGs in countries [10]; by 2017, 134 (69%) countries (compared to 89 countries in 2010) reported having established a NITAG and the number of countries with NITAGs complying with the six WHO defined indicators of NITAG functionality reached 98 (51% of countries) [3,11]. However, it is recognized that these are process indicators and are not sufficient to reflect outputs or outcomes (i.e. performance with respect to characteristics of a high-functioning NITAG) including proper references to evidence, quality of work processes with use of a systematic approach leading to recommendations, and integration of the NITAG into the national health policy process. In an effort to better evaluate functionality of NITAGs, WHO collaborated with partners to develop a NITAG self-assessment tool that includes a proposed list of indicators including several that directly relate to performance of the data review process [12].

## 2. Initiatives for strengthening capacity for evidence-informed immunization decisions

In collaboration with WHO, several initiatives have provided technical assistance to build capacity and functionality of country NITAGs – The Supporting Independent Immunization and Vaccine Advisory Committees (SIVAC) and ProVac initiatives [13,14]. The SIVAC Initiative was established in 2008 and based in the *Agence de Médecine Préventive [AMP]*; the SIVAC project led to the creation of the Health Policy and Institutional Development Center, a WHO Collaborating Center for evidence-informed immunization decision-making. SIVAC was supported by the Bill and Melinda Gates Foundation (BMGF) and funding ended in June 2017. The Pan American Health Organization's ProVac initiative was launched in 2004 to provide technical cooperation for the promotion of evidence-based decision making prior the introduction of new vaccines, focusing on economic evaluation methodologies, tools and studies. Funding from BMGF for this initiative ended in 2015.

The Partnership for Influenza Vaccine Introduction (PIVI) is a public/private program of The Task Force for Global Health (TFGH) [15]. PIVI was launched in 2013, and is a partnership with the Centers for Disease Control and Prevention (CDC), Ministries of Health, corporate partners and others to support LMIC countries wishing to create sustainable, seasonal influenza vaccination programs. PIVI works with WHO to support countries' efforts to control and prevent seasonal influenza and to help countries prepare for pandemic influenza. This work also includes strengthening capacity for evidence-based vaccine policy review by NITAGs. In addition, through a separate but related program, CDC's Influenza Division provides direct technical and funding support to competitive grant recipients in LMICs to develop influenza vaccination policies and programs; NITAG capacity building is also a priority activity under this initiative. CDC's Global Immunization Division supports these and other NITAG strengthening initiatives. Support for NITAGs through these two programs (i.e., PIVI and Cooperative Agreement grants from CDC's Influenza Division) encompasses assessing NITAG level of functioning in partner countries, developing training materials and providing technical assistance to address gaps in general NITAG functions and also supporting evidence-based reviews of vaccines under consideration for introduction. In this paper, we describe a collaboration between the TFGH, CDC and WHO regional and local offices to support NITAGs in 2017 and highlight lessons learned to maximize the efforts of future work in this area, including the applicability of these efforts to recommendations relevant to influenza and other vaccines.

## 3. Collaboration to provide NITAG support in partner countries during 2017

### 3.1. Assessment of NITAG capacity

TFGH and CDC hosted an annual meeting for partner countries interested in developing influenza vaccine policy through PIVI and CDC policy cooperative agreement support; the 2017 meeting was held in Tbilisi, Republic of Georgia and 13 countries attended<sup>1</sup>. One objective of the meeting was to discuss evidence-based processes to provide recommendations for vaccine policy decision making in partner countries. Before the meeting, TFGH contracted with the SIVAC Initiative to survey partner countries to better understand the decision-making environment regarding immunization policies in their country and to enquire about the relationships between influenza vaccine activities conducted under Ministries of Health

<sup>1</sup> Albania, Armenia, China, Cote d'Ivoire, Georgia, Kenya, Lao DPR, Moldova, Morocco, Mongolia, Uganda, Vietnam and Sri Lanka.

and NITAGs. The survey, which was completed by Ministry of Health officials in consultation with NITAG members in their countries, gathered detailed information about country NITAG operations, including perceived needs for technical assistance and training workshops. All countries responded that the immunization decision-making process includes seeking advice from their NITAG and 7 of the 10 countries that responded to the question reported that their NITAG has a good or high level of integration with the national decision-making process. Among the challenges faced by NITAGs, uncertain or insufficient funding for NITAG operations including meeting logistics, and limited access to external technical resources and to scientific evidence, were cited most frequently. Only 2 of the 13 country NITAGs attending the meeting used standardized methods for quality assessment of scientific evidence. Six countries indicated that their NITAGs would benefit from capacity building support, especially in evidence gathering and assessment. Following the Tbilisi meeting, the TFGH sought input from NITAG focal points at WHO regional offices on the functional level of country NITAGs and on country requests for technical assistance, reviewing NITAG evaluation reports, if available. The comprehensive needs assessments resulted in plans to conduct NITAG capacity building workshops in 5 partner countries during 2017.

### 3.2. NITAG support

#### 3.2.1. General capacity building

The general NITAG support started during the Tbilisi meeting where a half-day session included a review of NITAG core functions and review of the methodology for issuing evidence-based recommendations. In particular, participants from the 13 attending countries were introduced to the first step for developing evidence-based recommendations; they reviewed a generic recommendation framework for influenza vaccine decision-making. Considering the question “should seasonal influenza vaccine be introduced in the national immunization program?”, meeting participants agreed on which elements of the framework were considered critical, important or not critical for decision-making related to as well as the likely data sources (i.e., from global-, regional- or local- level) that would be used to gather the evidence. The resulting NITAG influenza recommendation framework was used to conduct the literature search and was adapted to countries context during the individual workshops.

From June to October 2017, we conducted workshops in 5 partner countries (Box 1). Participants from 7 countries attended the workshops; 2 focused on general NITAG capacity building and 3 were designed primarily for NITAGs that were ready to conduct an influenza evidence-based review but also addressed gaps in general NITAG functions. The workshops were evaluated and reports were shared with collaborators and partners including WHO [15].

We revised training materials using existing SIVAC Initiative materials (translating some into Russian) and developed new materials as needed, in English and French. We prepared programs for the workshops in consultation with the country NITAG chair and the WHO local office. For general NITAG capacity-building workshops, the program addressed gaps identified through review of country specific NITAG materials and evaluations (e.g., gaps in internal procedures manual, process for issuing recommendations, conflict of interest statements and role of the secretariat). We selected vaccines to use as examples in practical sessions after review of Expanded Programme on Immunization (EPI) multiyear plans, reviews and applications to the Vaccine Alliance (Gavi), for new vaccine introduction and EPI strengthening. For example, in Laos PDR, we used rotavirus vaccine as the example for evidence search and review since the country was actively engaged in preparing a Gavi application for rotavirus vaccine introduction.

#### Box 1.

##### NITAG capacity building workshops.

##### General NITAG workshops.

Content: basic NITAG functions and activities, and principles of conducting an evidence based review (EBR).

- Vientiane, Laos PDR, June 26–30, 2017. The workshop used rotavirus as the example for the EBR.
- Ulaanbaatar, Mongolia, October 2–6, 2017. The workshop used influenza as the example for the EBR.

##### NITAG Influenza working group workshops.

Content: conducting EBR for seasonal influenza including how to search peer review literature on key elements, quality assessment of literature, writing the technical dossier for the full NITAG to review and discuss.

- Da Nang, Vietnam, August 29–31, 2017.
- Arzakan, Armenia, September 25–29, 2017, 2 staff each (NITAG and/or influenza) from Moldova and Republic of Georgia also attended.
- Grand- Bassam, Côte d'Ivoire, October 30 –November 3, 2017.

#### 3.2.2. Capacity building for evidence-based review using influenza as an example

For workshops dedicated to NITAGs considering the introduction of seasonal influenza vaccine, we addressed identified gaps in general NITAG functions as described above and focused on the methods and tools for developing evidence-based recommendations. For teaching evidence-based review for influenza, we referred participants to the generic recommendation framework for seasonal influenza vaccine that had been reviewed at the Tbilisi meeting (Table 1). The key elements of the framework covered four major topics: disease including burden of disease and clinical characteristics; vaccine and immunization characteristics including cost, safety and efficacy/effectiveness; economic and operational considerations including cost effectiveness; and health policy and programmatic issues including vaccine acceptability. Judgement of the evidence on all these elements is central to considering the potential benefits and harms from using a vaccine.

#### 3.2.3. Development and use of a resource package of reference materials

The survey results from partner countries highlighted lack of access to scientific evidence as a critical challenge for NITAGs, and highlighted evidence gathering and quality appraisal as the key area for capacity building. Therefore, to further assist countries in reviewing evidence on the critical and important elements of the framework (as defined by consensus of the countries), PIVI provided additional resources, consisting of an “influenza resource package” (Box 2), which was comprised of literature reviews with systematic and documented search strategies and quality reviews using the Critical Appraisal Skills Program (CASP) tool [3]. The content encompassed key elements of the influenza recommendation framework including disease burden, influenza vaccine safety and efficacy/effectiveness, cost effectiveness and influenza vaccine acceptability. This package covered the 2012–2017 time-period

**Box 2.**

**INFLUENZA RESOURCE PACKAGE.**

The Influenza Resource Package is a summary of scientific evidence on essential issues to consider in issuing a policy recommendation on seasonal influenza vaccination. The evidence presented in this package comes from quality-assessed published articles, vaccine textbooks and other advisory group reviews (the WHO Strategic Advisory Groups of Experts-SAGE, the US Advisory Committee on Immunization Practice- ACIP).

**How was the Resource package developed?**

The resource package was developed using the recommended NITAG methodology process as guided by WHO principles i.e.

1. Listing all the data needed to support the recommendation (recommendation framework) and indicating the source of the data (global, regional or local levels).
2. Defining a search strategy for data requiring a systematic literature search, for all the key elements in the recommendation framework considered critical and important.
3. Screening of search results i.e., titles and abstracts, against a defined inclusion-exclusion criteria to retrieve relevant articles.
4. Assessing the quality of the evidence presented in the selected articles, using Critical Appraisal Skills Programme’s (CASP) checklists.
5. Summarizing the selected articles according to the research questions stated in the recommendation framework.
6. The results obtained at each step above were recorded in separate word documents to allow for transparency and reproducibility by NITAG working groups.

**How can the NITAG use the Resource package?**

Individual country NITAGs decide which elements are critical/important to include in their seasonal influenza vaccine technical report and based on this they then select from the resource package the relevant articles and summaries to include in their report. However, the NITAG working group is still required to obtain and fill in the relevant local data in order to complete their technical report. In addition, as the process of development of the resource package for seasonal influenza has been fully documented, the NITAG can also refer to it to prepare similar background documents for other vaccines or vaccination strategies.

**Does the resource package include a final recommendation?**

As the name suggests, the resource package is purely a resource material for NITAGs and does not provide a recommendation on seasonal influenza vaccination. Although its purpose is to assist NITAG members to understand key issues on seasonal influenza safety and effectiveness, it is left to the NITAG to interpret the evidence and decide on the vaccine policy recommendations based on the overall body of information collected including local data.

**Table 1**  
Generic Recommendation Framework For Seasonal Influenza Vaccine<sup>a</sup>.

Issue	Element	Specific data	Specific queries	Source of data and comments
1. Disease	1.1 Burden of disease	Incidence of morbidity & mortality  Implications on health care use	Incidence (as lab confirmed influenza cases, severe disease outcomes (SARI <sup>††</sup> ) and Influenza-associated ICU admissions) in the target population. Impact on health facility attendance and hospitalisations, workload for health care workers	1. <b>Global data</b> – WHO, CDC <sup>††</sup> , ECDC <sup>††</sup> sites 2. <b>Systematic literature search</b> – AFR-West <sup>††</sup> , EUR-NIS <sup>††</sup> & WPR-Asia <sup>††</sup> regional data 3. <b>Local data</b> from country reports <b>Global data</b> CDC, ECDC or WHO sites
	1.2 Clinical characteristics of the disease	Signs and symptoms of disease, severe forms, long term complications	Symptoms, severity, complications in risk groups and in co-morbidities	
	1.3 Regional and international considerations	Existence of regional and global recommendations	Policy in place in the region	
2. Vaccine and immunization characteristics	2.1 Vaccine characteristics	Vaccine presentation, formulation, dosage and route of administration Administration schedule and possibility of co-administration with other vaccines and drugs Cold chain and logistic requirements	Presentation, formulation, route of administration and dosage for WHO prequalified vaccines Recommended schedule for available vaccines; possibility of co-administration with existing infant and adult vaccines Additional cold chain and logistic requirements for available vaccines, type of vaccine to be stored, single or multi-dose vials	<b>Global data</b> – information regarding influenza vaccines from WHO website <b>Global data</b> – information from WHO website  <b>Local data</b> – National Immunization Program – Supply Chain and Logistics Systems <b>1. General data</b> – for healthy adults, pregnant women, children, elderly, chronic illness patients and HCWs <sup>†</sup> <b>2. Systematic literature search</b> – for healthy adults, pregnant women, children, elderly, chronic illness patients and HCWs <sup>†</sup> <b>Global data</b> WHO, manufacturer inserts
	2.2 Safety	Type, consequences and frequency of short and long-term adverse events following vaccination; risk groups or risk factors for adverse events	Severe Adverse Events & AEFIs in target population Adverse events in pregnant women i.e. severe adverse events, AEFIs <sup>†</sup> , maternal morbidity and mortality & foetal outcomes Serious adverse events when co-administered with other vaccines in the target populations	
		Contraindications	Contraindications for use of influenza vaccines	

(continued on next page)

Table 1 (continued)

Issue	Element	Specific data	Specific queries	Source of data and comments
	<b>2.3 Efficacy and effectiveness</b>	Efficacy against strains circulating in the country  Duration of protection and waning of immunity in general and risk groups	Efficacy i.e., lab-confirmed influenza and severe outcomes e.g. SARI, hospitalization and death in the target population (excluding the general population)  Duration of protection of available vaccines for recommended schedules	<b>1. General data</b> – for healthy adults, pregnant women, children, elderly, chronic illness patients and HCWs <b>2. Systematic literature search</b> – for healthy adults, pregnant women, children, elderly, chronic illness patients and HCWs <b>Global data</b> – WHO Position paper
Issue	Element	Specific data	Specific queries	Source of data and comments
<b>3. Economic and operational considerations</b>	<b>3.1 Vaccine related costs and resource use</b>	Direct and indirect costs	Cost to administer the vaccine as they compare to those of other existing vaccines or other prevention or control measures; cost using different strategies	<b>Systematic literature search</b> – AFR-West, EUR-NIS & WPR-Asia regional data
	<b>3.2 Vaccine availability</b>	Sources of funding Availability	Sustainability of government funding; reliability of partners support	<b>Local data</b>
	<b>3.3 Vaccine affordability</b>	Availability of fiscal space to effectively implement and sustain the recommendation in the programme	Reliable supply chain for the vaccines to the country Annual fiscal implications to the government	<b>Local data</b>
	<b>3.4 Socio economic and social impact of the disease</b>	School and work absenteeism; indirect cost to patients and families, productivity losses	Productivity losses to patients and families	<b>1. Local data</b> - national reports <b>2. Systematic literature search</b> – AFR-West, EUR-NIS & WPR-Asia regional data
	<b>3.5 Economic impact of intervention on immunization program as well as health sector</b>	Health Gain Reduction in healthcare costs	Cost benefit, cost effectiveness, DALY <sup>#</sup> , QALY <sup>#</sup> Potential in health care costs if the vaccine is introduced in the programme	<b>1. Local data</b> - national reports <b>2. Systematic Literature search</b> – AFR-West, EUR-NIS & WPR-Asia regional data
Issue	Element	Specific data	Specific queries	Source of data and comments
<b>4. Health policy and programmatic issues</b>	<b>4.1 Feasibility</b>	Accessibility of target population (health system organization), number of individuals in target pop Impact on resources	Feasibility of possible delivery strategies to reach target population; coverage of interventions currently provided to the target population Human, technical and financial requirements i.e. cold chain, supply chain requirements	<b>Local Data</b> – EPI <sup>‡</sup> reports  <b>Local data</b> – Immunization Program – Supply Chain and Logistics
	<b>4.2 Ability to evaluate</b>	Vaccine registration and regulations Surveillance system for disease AEFI monitoring	NRA <sup>‡</sup> requirements to register available vaccines for use in target population Reliability and sustainability of surveillance system for flu disease AEFI definition Program capacity to carry out AEFI monitoring of vaccines given at the proposed schedule	<b>Local data</b> from National regulatory bodies <b>Local Data</b> – in-country situation <b>1. Global data</b> – WHO, CDC, ECDC <b>2. Local data</b> – National Immunization Program and Surveillance Systems
	<b>4.3 Acceptability</b>	Availability of information systems to measure coverage & vaccine utilization Perception of the public and medical community about disease and vaccine	Quality of data collected for coverage of other vaccines given in the immunization programme Perception about flu and vaccination in target population Influenza care seeking behaviour in the community	<b>Local data</b> – National Immunization Program and Surveillance Systems <b>1. Local data</b> <b>2. Systematic literature search</b> – AFR-West, EUR-NIS & WPR-Asia regional data
	<b>4.4 Pandemic preparedness</b>	Country capacity for pandemic preparedness	Existence of pandemic influenza plan with prioritized risk groups; capacity building needed	<b>1. Global data</b> - WHO, CDC <b>2. Local data</b> – pandemic plan and identified risk groups for vaccination

\* Framework was developed at the Task Force for Global Health's Partnership for Influenza Vaccine Introduction (PIVI) partner meeting, Tbilisi 2017.

\*\* SARI = severe acute respiratory infection; ICU = intensive care unit; WHO = World Health Organization; CDC = Centers for Disease Control and Prevention; AFR West = African western sub-region, EUR- NIS = European region- Newly Independent States; WPR-Asia = Western Pacific region-Asia; ECDC = European Centre for Disease Prevention and Control.

† AEFI = Adverse event following immunization; HCW = Healthcare workers.

# DALY = Disability-adjusted life year, QALY = Quality adjusted life year.

‡ EPI = Expanded Program on Immunization; NRA = National Regulatory Agency.

and thus updated the literature since publication of the Strategic Advisory Group of Experts (SAGE) on Immunization influenza recommendations and accompanying background document and GRADE (Grading of Recommendations, Assessment, Development and Evaluation) tables [16,17]. Due to the large volume of literature on seasonal influenza and vaccines, reviews on influenza vaccine efficacy/effectiveness and safety were global in scope and were limited to systematic reviews and meta-analyses. Vaccine effectiveness outcomes were limited to those with laboratory-confirmed influenza, while non-specific outcomes such as influenza-like illness and hospital admissions were not included. Safety outcomes focused on serious adverse events and for pregnant women, fetal outcomes were also included. For disease burden and other elements, the reviews focused on regional or sub-regional data relative to the countries where the workshops were conducted. For Vietnam, the review focused on countries in the Western Pacific region that were PIVI or CDC influenza vaccine policy cooperative agreement partner countries. For Armenia, the sub-region was the newly independent states and for Côte d'Ivoire, it was West Africa. WHO European Region staff arranged translation into Russian of slides and other key materials used for the workshop in Armenia. The full process (search strategies, results and quality appraisal) was documented and made available to the participants during the workshops and for their planned influenza working group.

As part of building the NITAG's capacity, for the 3 countries (Vietnam, Côte d'Ivoire and Armenia) ready to conduct an evidence-based review of influenza disease and vaccine for consideration of a NITAG recommendation, during workshops, participants were taken through the entire process used to develop the resource package including developing search terms, saving and screening of search results and performing a quality assessment of relevant articles. Thereafter, participants were expected to begin the write-up of their respective sections of the influenza vaccine technical dossier using summaries of articles relevant to their specific recommendation. Our senior NITAG consultant provided follow up support, in person and remotely, to the influenza working-groups in Côte d'Ivoire and Armenia.

#### 4. Lessons learned: Successes and challenges

NITAGs make an important contribution to sustainable national immunization programs [3,19]. During 2017, the TFGH, through their PIVI program, along with CDC and WHO, provided considerable capacity-building and support to NITAGs in LMICs that are considering introduction of seasonal influenza vaccine in their national immunization programs. From experiences providing this support, we learned three main lessons: (1) capacity building needs time and should be tailored to country specific needs and resources – many countries considering influenza vaccine introduction needed general NITAG support before they were ready to examine evidence related to any new vaccine, (2) key gaps in NITAG functioning include ability to gather scientific evidence and interpret it which is especially true for influenza given the complexity and volume of the evidence, and (3) commitment from Ministries of Health and collaboration with many partners is needed to build country NITAG capacity.

For all the workshops, including those for NITAGs ready to conduct an evidence-based review on influenza, we addressed identified gaps in general NITAG functions and we focused on country priorities. The impact of our general NITAG workshop in Laos PDR, where rotavirus vaccination had been used as the example to teach the evidence-based review process, was reflected when the NITAG applied the principles learned during this training to their preparation of a recommendation on human papillomavirus (HPV) vaccination. Building capacity for NITAG and secretariats

to conduct an influenza evidence-based review should also translate into a broader capacity to conduct evidence-based reviews on another disease and vaccine topic.

To be successful, capacity building is a process that needs adequate time, an approach tailored to specific needs, and adequate resources. Providing effective technical assistance develops capacity for NITAGs to understand the value of their committee because of the rigorous process through which they arrive at their recommendations without any external pressure. Recent reviews on progress towards the GVAP 2020 goal and on strengthening and sustaining NITAGs have noted that countries value the work of these committees in providing technical advice generated through a transparent and unbiased process that is more likely to result in nationally owned evidence-based decision-making [16,18–20]. However, challenges remain. A number of countries have yet to establish NITAGs and in many others, their NITAGs will continue to need technical support [18]. It is important to note that in relation to the GVAP goal for every country to have a NITAG, subsequent global dialogue has further refined this goal, noting that all countries should have access to a NITAG [21]. For example, some small countries may rely on a neighboring country NITAG (e.g. Lichtenstein's participation in the Swiss NITAG) or several countries may form a sub-regional NITAG (e.g. Caribbean Immunization Technical Advisory Group – CITAG).

Many countries rely on WHO's SAGE recommendations for specific vaccines such as seasonal influenza and the accompanying evidence-based review [22]. However, a critical NITAG need is having the capacity to interpret the data provided by SAGE and to select, assess and synthesize evidence tailored to the country situation. Each country needs to define the question for their country and the specific data needed to make an informed policy decision. Furthermore, having adequate evidence is not enough; expertise to interpret the evidence must be present [11] and the basic concepts of epidemiology, and disease and vaccine specific expertise are often in short supply in LMICs.

Influenza vaccination is a particularly complex topic on which to conduct an exhaustive literature review due to its unique challenges with annual vaccination requirements, changing influenza virus strains in circulation and, resources permitting, the need to monitor and evaluate vaccine effectiveness and safety annually. Considerable subject matter expertise is essential to selecting articles among the huge volume of publications and interpreting the complex literature. The expectation that every NITAG will conduct an evidence-based review of the literature from scratch seems unrealistic and inefficient. To provide a head start for countries, we used WHO recommended methodology [3] to develop an influenza resource package comprised of quality reviewed summaries of scientific evidence on essential topics to consider in issuing a policy recommendation on seasonal influenza vaccination. This concept has potential for use for other vaccines. Technical briefings for decision-makers on rotavirus and pneumococcal conjugate vaccines have been developed for national-level technical policy-making around the use of these two childhood vaccines, with a focus on low- and middle-income countries [23,24]. These briefings, although not carried out using systematic reviews and formal quality assessment, provide high-level summaries of evidence compiled by experienced subject matter experts which are presented in a format adapted to a NITAG-focused decision-making framework. The 3 NITAGs that received training on influenza evidence based review with the influenza resource package reported considerable benefit from the evidence summarized according to the framework and used it to develop their NITAG influenza dossier. With additional in person and remote technical support, each of the three countries made progress on their vaccination programs. Côte D'Ivoire developed national recommendations for use of influenza vaccine and began a phased introduction of vaccine among

health workers in 2019. Vietnam has developed a multi-year plan of introduction of vaccine among health workers and will begin vaccination in three provinces in 2019. Armenia has expanded its use of vaccine since the workshops, using the influenza resource document as a reference for its decisions to invest more resources in the vaccination program.

Our experience confirms the well-described problem of NITAGs in LMICs being considerably under-resourced without adequate technical support and access to global peer review literature [10,16,25]. We support sharing of systematic evidence-based reviews across regions and globally; such collaboration can be facilitated by NITAG partners, through the NITAG resource center [26] now maintained at WHO, and by regional NITAG networks and the Global NITAG Network [16,19,25]. Our experience also highlighted lessons learned from other NITAG capacity-building initiatives and partners including that NITAG strengthening work is a partnership that involves close coordination with country NITAGs and key NITAG partners particularly WHO regional and local offices [13,16]. We used materials developed by the SIVAC initiative and found them to be invaluable and easy to modify to meet individual country needs [26]. Providing reliable technical assistance and for the needed duration is costly. More than two full-time equivalents (FTEs) were needed to provide the overall capacity building and technical assistance required during 2017, and this does not include considerable CDC technical support. Although about half this time was related to developing the influenza resource package, each workshop required preparation time, the use of two expert trainers and one to two facilitators, time for evaluation and report writing and when feasible, follow-up technical assistance. Therefore, identifying NITAG experts who can provide training and technical assistance, in coordination with WHO and other key partners, is essential. Such expertise needs to be donor-supported and is in short supply since the SIVAC initiative ended [19]. There are likely also to be efficiencies in providing technical expertise in a coordinated fashion by all partners. In addition, partners need to ensure that these efforts maintain focus on the main goal of providing this type of technical assistance to NITAGs, which is to support country decision-making, not make decisions for the country. Indeed, PIVI's mission is accomplished equally if countries decide to introduce or not introduce influenza vaccination programs, as long as the decisions are evidence-based. We were fortunate in acquiring the services of two former SIVAC contractors but without additional resources and continued work, their expertise may be lost to other fields. Workshops alone are not sufficient to build capacity. Ideally, these should be followed up with additional technical assistance as we did in Côte d'Ivoire to reinforce key principles and to assist with developing core NITAG documents as well as technical working-group dossiers. Since the conclusion of their workshop, the NITAG secretariats in both Armenia and Mongolia have also sent requests for technical assistance in the write-up of their influenza technical dossier, using the influenza resource package.

The SAGE 2017 Assessment Report of GVAP proposes that core aspects of a multidimensional framework for a sustainable immunization system includes NITAGs and evidence-informed technical advice, and suggests including this aspect in evaluations of national immunization programs. However, there remains a need to ensure that NITAGs function effectively [18]. The report also states that in order to perform their roles as independent advisory bodies, NITAGs need to maintain high levels of transparency and of disclosure and management of relevant interests. Reviews of NITAG functioning have stressed that external support will be needed over the next decade to continue NITAG capacity building [16,19]. While good progress has been made in the number of countries meeting the six process indicators as defined by WHO for NITAG functionality, it is unlikely that the 2020 global goal of

all countries having or having access to a functional NITAG will be met without considerable investment in ensuring NITAGs have the required skills and support to respond to the expectations of national authorities. Experience in building NITAG capacity for LMICs has demonstrated the needs for long term investments and technical assistance as demonstrated in Côte d'Ivoire and countries in Latin America [27,28]. Ongoing donor support needs to be secured and creative approaches may need to be taken by multiple NITAG partners including WHO, CDC, Gavi, Bill and Melinda Gates Foundation, the Global NITAG Network and TFGH. We're optimistic that the work that TFGH supports in strengthening evidence-based recommendations in resource-constrained settings will be an important step towards countries achieving the GVAP goal of a functional NITAG but even more importantly, in supporting sustainable immunization policies and programs.

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## Declaration of Competing Interest

None of the authors have conflicts of interest to declare.

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