

Developing a seasonal influenza vaccine recommendation in Kenya: Process and challenges faced by the National Immunization Technical Advisory Group (NITAG)

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ABSTRACT

Background: In 2014 the Kenya National Immunization Technical Advisory Group (KENITAG) was asked by the Ministry of Health to provide an evidence-based recommendation on whether the seasonal influenza vaccine should be introduced into the national immunization program (NIP).

Methods: We reviewed KENITAG manuals, reports and meeting minutes generated between June 2014 and June 2016 in order to describe the process KENITAG used in arriving at that recommendation and the challenges encountered.

Results: KENITAG developed a recommendation framework to identify critical, important and non-critical data elements that would guide deliberations on the subject. Literature searches were conducted in several databases and the quality of scientific articles obtained was assessed using the Critical Appraisal Skills Programme tool. There were significant gaps in knowledge on the national burden of influenza disease among key risk groups, i.e., pregnant women, individuals with co-morbidities, the elderly and health care workers. Insufficient funding and limited work force hindered KENITAG activities.

In 2016 KENITAG recommended introduction of the annual seasonal influenza vaccine among children 6 to 23 months of age. However, the recommendation was contingent on implementation of a pilot study to address gaps in local data on the socio-economic impact of influenza vaccination programs, strategies for vaccine delivery, and the impact of the vaccination program on the healthcare workforce and existing immunization program. KENITAG did not recommend the influenza vaccine for any other risk group due to lack of local burden of disease data.

Conclusion: Local data are a critical element in NITAG deliberations, however, where local data and in particular burden of disease data are lacking, there is need to adopt scientifically acceptable methods

Abbreviations: AMP, Agence de Médecine Préventive (Agency of Preventive Medicine); CDC, Centers for Disease Control and Prevention; HIC, High Income Countries; IVWG, Influenza Vaccine Working Group; NVIP, National Vaccines Immunization Program; KENITAG, Kenya National Immunization Technical Advisory Group; LMIC, Low and Middle Income Countries; MoH, Ministry of Health; NIP, National Immunization Program; NITAG, National Immunization Technical Advisory Group; SIVAC Initiative, Supporting Independent Immunization and Vaccine Advisory Committees Initiative; UNITAG, Uganda National Immunization Technical Advisory Group; WG, Working Group.

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of utilizing findings from other countries to inform local decisions in a manner that is valid and acceptable to decision makers.

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1. Introduction

Over the years, the range of vaccines available for human use has increased substantially. As a result, the need to establish National Immunization Technical Advisory Groups (NITAGs) that utilize evidence-based processes in choosing which vaccines to include into national immunization programs (NIPs) has gained greater importance [1]. Unfortunately, many countries, especially in the developing world, are yet to adopt clear guidelines for recommending new vaccines into national vaccination programs or revising the schedules of existing vaccines within vaccination programs [2]. And despite the fact that Africa bears the brunt of the world's vaccine-preventable diseases [3], African nations are least likely to have functional NITAGs in place that provide timely, locally relevant, evidence-based vaccine recommendations that influence national policy decisions [2].

The burden of influenza in the tropics has been documented in recent studies [4–9]. Paediatric respiratory hospitalizations associated with influenza are more than three times higher in low- and middle-income countries (LMICs) compared to high income countries (HICs) (150 vs 48 per 100,000 children annually) [4]. Moreover, deaths due to influenza infection are highest in sub Saharan Africa (2.8 – 16.5 per 100,000 individuals) when compared to other regions around the globe [10]. Yet for African nations tackling diseases such as HIV/AIDS, malaria, tuberculosis, and diarrheal illness, influenza is often perceived as a less important public health priority [11].

Based on evidence of significant burden of influenza disease globally, the availability of safe and effective influenza vaccine options and documented cost-effectiveness of vaccine programs from temperate countries, the World Health Organisation (WHO) recommended that all countries should offer annual influenza vaccination to those at risk of influenza related complications, including pregnant women, young children, the elderly, individuals with co-morbidities and health care workers [12]. These country level initiatives to prevent seasonal influenza would have the additional benefit of enhancing global preparedness to manage future pandemic strains of the virus [13].

In this report, we describe the Kenyan experience in formulating a national seasonal influenza vaccine recommendation. The findings are relevant to governments and funders who would wish to understand the factors that influence the success of NITAGs in LMICs when introducing new vaccines into NIPs.

2. Materials and methods

We retrospectively reviewed data from the Kenya NITAG (KENITAG) internal procedures manual, minutes of KENITAG and influenza vaccine working group (IVWG) meetings, and reports generated from June 2014 through June 2016. We used the data to describe the establishment of KENITAG, the decision making process, and outputs of KENITAG deliberations in regards to the seasonal influenza vaccine recommendation. The content of data collected was informed by Duclos' (2010) publication on the key elements to consider during the establishment and operationalization of NITAGs. Duclos' publication is endorsed by WHO as a reference document for NITAGs [14]. We then selected the most

important challenges in the KENITAG process and discussed the circumstances that could have contributed to them.

3. Results

3.1. Establishment and organisation of KENITAG

KENITAG was established in June 2014, in accordance with the Kenya National Health Sector Strategic and Investment Plan, July 2013 to June 2017, and the National Policy Guidelines for Immunization, 2013. KENITAG was established to provide recommendations on national vaccine policy to the Ministry of Health (MoH). KENITAG is composed of 12 core members, non-core members and a technical secretariat hosted by the National Vaccine and Immunization Program (NVIP) and Disease Surveillance and Response Unit (DSRU) of the MoH (Fig. 1).

Core members are local experts from a range of professions (immunology, adult medicine, paediatrics, epidemiology, microbiology, public health, pathology and law) who serve in their individual capacity. Core members do not receive salaries for their participation in KENITAG, but do receive *per diem* payments which are daily monetary allowances to cater for travel and incidental expenses during meetings. Core members serve three year renewable terms, for a maximum of two terms. Non-core members either represent government agencies (*ex-officio* members), or non-government organisations (liaison members). Non-core members provide technical expertise, share their institutions' points of view with KENITAG, propose agenda items on behalf of their institutions, and report KENITAG decisions back to their institutions.

Members of the secretariat are drawn from NVIP and DSRU. The secretariat is tasked with ensuring that the functions of KENITAG are adequately coordinated, in addition to facilitating working group activities by preparing background documents and technical reports.

The advisory group is required to meet at least four times a year, the schedule for which is determined in the annual work plan. KENITAG meetings are not open to the public.

3.2. KENITAG procedures related to issuing an evidence-based vaccine recommendation

The vaccine questions considered by KENITAG in its annual work plan are either posed by the Ministry of Health or by KENITAG members in response to public health problems identified in the country or vaccine developments that are likely to be considered by the government in the foreseeable future.

KENITAG has an internal procedures manual to guide its operations that is adapted from a Supporting Independent Immunization and Vaccine Advisory Committees (SIVAC) Initiative manual [15]. The internal procedures manual provides a detailed description of the process of issuing a vaccine recommendation.

In order to issue a vaccine recommendation, the chair of KENITAG tasks one or two working groups to compile available evidence on the disease and vaccine, and prepare a report that will form the basis on which KENITAG decisions are made. Working groups are led by a KENITAG core member and may include external experts. Membership in a working group is voluntary.

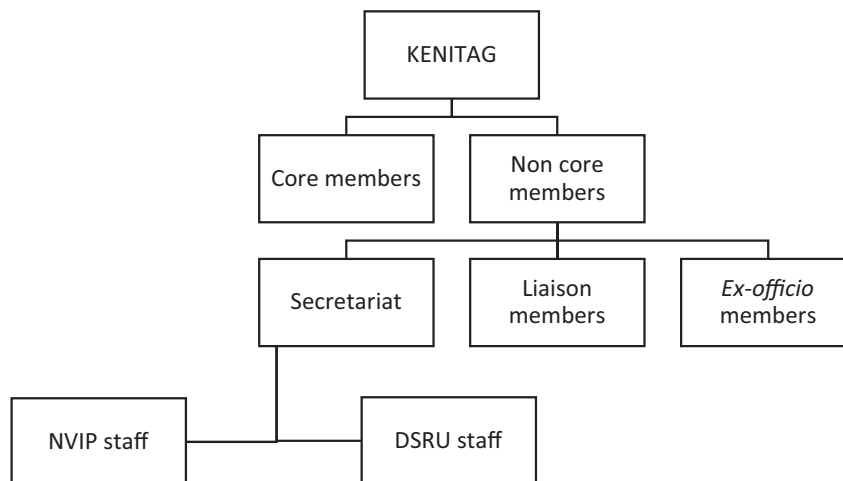


Fig. 1. Structure of Kenya National Immunization Technical Advisory Group. DSRU - Disease Surveillance Response Unit; KENITAG - Kenya National Immunization Technical Advisory Group; NVIP - National Vaccines Immunization Program.

The report developed by the working group is guided by the KENITAG recommendation framework that encompasses the following broad topics: (i) the disease (which includes the morbidity and mortality associated with the disease, its socio-economic impact, as well as available alternative control measures), (ii) vaccine and immunization characteristics, (iii) economic and operational considerations of the proposed vaccination program and, (iv) health policy and programmatic issues (such as the feasibility of an immunization programme, the ability to evaluate the programme, acceptability and equity). Each of the specific data elements within these 4 broad topics is ranked as either critical, important or non-critical. Critical data elements are essential for any recommendation to be made, while important data elements would be beneficial to the process of making the recommendation but not to the same degree as critical data elements. Information on non-critical data elements is not mandatory for the recommendation.

Once the working group report is presented to KENITAG, the decision on whether to introduce a vaccine into the NIP or modify the schedule of a vaccine within the NIP is made through a process of voting by core members. To ensure that the recommendations made by KENITAG are independent and transparent, members are required to declare any conflicts of interest at the start of each

meeting and only core members vote on the final decision. To ensure the results of the technical report are reproducible, the methods used to compile the data are documented in detail at each step. The MoH is not bound to the recommendations made by KENITAG. A summary of the characteristics of KENITAG is provided in [Table 1](#).

3.3. Establishment of the influenza vaccine working group

In September 2014, three months after KENITAG's establishment, the MoH through the NVIP requested KENITAG to provide a recommendation as to whether the seasonal influenza vaccine should be introduced into the NIP. This was the first assignment given to KENITAG on the introduction of a new vaccine into the NIP.

An influenza vaccine working group (IVWG) was formed in September 2014 to compile the available evidence and develop a report. This report would then inform KENITAG deliberations on the seasonal influenza vaccine. One core member of KENITAG, a subject matter expert in the field of paediatrics and respiratory disease, was appointed to chair the working group by the KENITAG chair. Later, an additional KENITAG core member was added to the working group to ensure that at least one core KENITAG member was available to attend each of the working group meetings. The chair of the working group in collaboration with the KENITAG secretariat, nominated external members of the following expertise to the working group: paediatrics, infectious diseases, social sciences, virology, and health economics. Liaison members were drawn from the SIVAC Initiative, of the Agency for Preventive Medicine (AMP). The KENITAG secretariat was appointed to provide secretariat services to the IVWG. The IVWG structure is illustrated in [Fig. 2](#).

The working group was provided with clear terms of reference which stated that the IVWG would need to:

- i. develop a work plan within 14 days of their formation with a deadline of submitting their report to KENITAG by November 2015.
- ii. develop a recommendation framework for formulation of the technical report that would be presented to KENITAG core members for approval before proceeding with the literature review.

Table 1
Characteristics of KENITAG over the period June 2014 to June 2016.

Item	Response
Year NITAG established	2014
NITAG established through an administrative process	Yes
Clear terms of reference provided to NITAG	Yes
Number of core members	12
Duration of term for core members (years)	3
Permissible to renew terms of core members	Yes
Presence of permanent non-core members without voting rights	Yes
External experts temporarily invited for specific topics	Yes
Pharmaceutical industry invited as occasional experts	No
Declaration of conflict of interest practiced	Yes
Framework in place for systematic development of vaccination recommendation	Yes
Number of meetings per year	1 to 4
Meetings open to public	No
Minutes published online	No
Government funding available	No

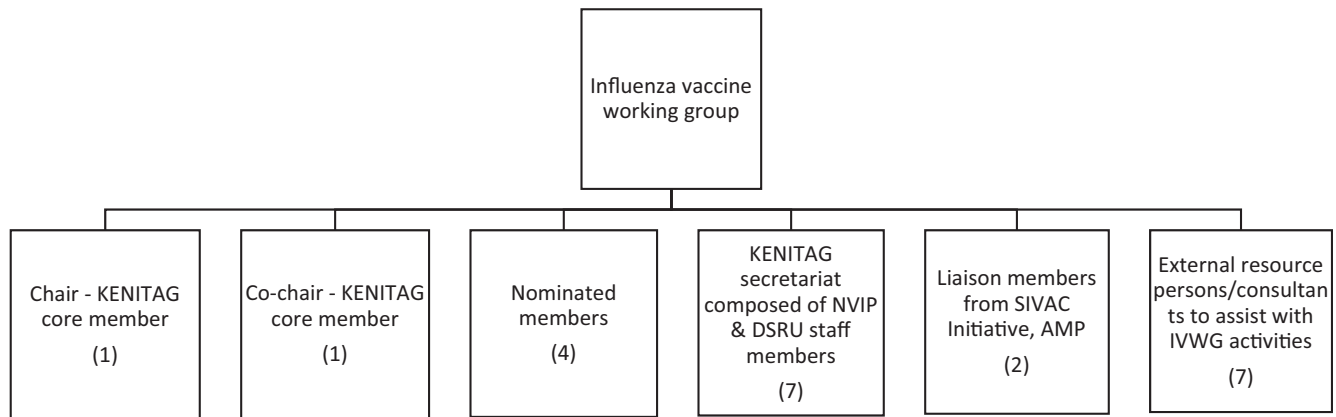


Fig. 2. Composition and number of individuals in influenza vaccine working group. AMP - Agency of Preventive Medicine; DSRU - Disease Surveillance Response Unit; IVWG - Influenza Vaccine Working Group; KENITAG - Kenya National Immunization Technical Advisory Group; NVIP - National Vaccines Immunization Program; SIVAC Initiative - Supporting Independent Immunization and Vaccine Advisory Committees Initiative.

- iii. collect, review and summarize evidence on specific data elements of the recommendation framework and document the process in the manner prescribed in the KENITAG internal procedures manual.

3.4. Defining the recommendation framework and ranking by level of importance the data to consider in making the recommendation

The first meeting of the IVWG took place in February 2015. As per their terms of reference, the IVWG developed a work plan and recommendation framework (refer to [Table 2](#)) to guide the

compilation of evidence. The recommendation framework which ranked the importance of data was approved by core KENITAG members in the February 2015 quarterly meeting. Following core members' approval, the WG members oversaw the collection and compilation of the evidence around the data elements.

3.5. Finding the evidence, keeping a record of search methods and outputs, and assessing the quality of data

The search process focussed on Kenyan studies. Where these were not available, the search was widened to include studies from

Table 2

Assessment of data obtained as per the recommendation framework.

Issue	Element	Specific data requested by KENITAG	Ranking of the importance of the data*	Summary of the outcome of the literature search
1. Disease	Burden of disease	Local data on the morbidity in general population, data from surveillance sites (total number infected, infection rate of influenza), hospital based surveillance data, position in priority disease list, circulating strains, seasonality and mortality curve, correlation with lower respiratory tract infections, epidemiology over time/trends over time (5 to 10 years)	Critical	Most local studies presented findings on children <5 years of age. No local studies on the epidemiology of influenza in the elderly, health care workers, and pregnant women . Limited local data on co-morbidities as risk factors for influenza
	Use and costs of health care	Local data health facility attendance, increased workload for health care worker, admissions	Important	Local data on use of health care available, especially for children <5 years of age. No local data on costs.
		Drug use (e.g. inappropriate use of antibiotics and anti malarials)	Important	Local data available, especially for children <5 years of age
	Social impact of disease	School and work absenteeism	Important	No Kenyan data available. Used studies from outside Kenya
		Indirect costs to patients and families	Important	No Kenyan data available. Used studies from outside Kenya
		Productivity losses	Important	No Kenyan data available. Used studies from outside Kenya
	Alternative preventive and control measures	Drugs, hygiene/hand washing, vitamin supplements (A, D)	Important	No Kenyan data available. Used studies from outside Kenya
2. Vaccine and immunization characteristics	Vaccine characteristics	Vaccine presentation and formulation	Important	Sufficient data obtained
		Dosage and route of administration	Important	Sufficient data obtained
		Administration schedule and possibility of co-administration with other vaccines and drugs	Important	Sufficient data obtained
		Flexibility of vaccination schedules	Important	Sufficient data obtained
	Vaccine indirect effects	Impact on antibiotic use	Important	No Kenyan or African studies obtained.
		School/work absenteeism	Important	No Kenyan or African studies obtained.

(continued on next page)

	Safety	Type, consequences and frequency of short and long-term adverse events following vaccination including adverse effects on foetus and new born, and Guillian Barre Syndrome	Critical	No Kenyan data available. Used studies from outside Kenya
		Risk groups or risk factors for adverse events	Critical	No Kenyan data available. Used studies from outside Kenya
		Contraindications	Critical	No Kenyan data available. Used studies from outside Kenya
	Efficacy and effectiveness	Efficacy worldwide	Critical	Used data from Kenya and Africa studies.
		Efficacy against strains circulating in Kenya	Critical	Used data from Kenya and Africa studies.
		Duration of protection and waning of immunity in general and risk groups	Critical	Used data from Kenya and Africa studies.
		Impact on incidence of severe pneumonia, admissions, outpatient attendance, mortality	Critical	Used data from Kenya and Africa studies.
3. Economic and operational considerations	Vaccine related costs and resource use	Local data on the direct and indirect costs to administer the vaccine as they compare to those of other existing vaccines or other prevention or control measures	Important	No data obtained
	Vaccine availability	Local data on cost to the government	Important	No data obtained
		Local data on sources of funding	Critical	No data obtained
		Availability in private sector	Non - critical	No data obtained
	Economic impact of intervention on immunization program as well as health sector	Cost benefit, cost effectiveness, DALY, QALY,	Important	No Kenyan data available. Used studies from outside Kenya
4. Health policy and programmatic issues	Feasibility	Local data on accessibility of target population and risk groups, no. of individuals in target pop and risk groups	Important	No local data obtained
		Local data on human, technical and financial requirements i.e. cold chain, supply chain requirements	Important	No local data obtained
		Local data on possibility of inclusion into regular immunization schedule	Important	No local data obtained
		Reliability and sustainability of surveillance system for disease	Critical	Local data available
	Ability to evaluate	Adverse events following immunization (AEFI) monitoring	Critical	No local data obtained
		Local data on availability of information systems to measure coverage and vaccine utilization	Important	No local data obtained
	Acceptability	Perception of the public and medical community about the flu and the vaccine	Critical	Some local data available
		Health seeking behaviour	Critical	Some local data available
	Equity	Accessibility for all the inhabitants in the country	Important	No local data obtained

*Ranking of the importance of the data: **Critical data elements** (shaded red) are essential for any recommendation to be made, while **important data elements** (shaded orange) would be beneficial to the process of making the recommendation but not to the same degree as critical data elements. Information on **non-critical data elements** (shaded green) is not mandatory for the recommendation.

the rest of Africa. Where African studies were deficient, the search was expanded to include studies from other low- and middle-income countries and finally high income countries (Fig. 3). Systematic reviews were the preferred source of information for data on vaccine effectiveness and safety, however where these were absent, individual studies were collected (Supplementary Table 1).

The quality of studies to be included in the report was assessed using the Critical Appraisal Skills Programme (CASP) tool. The CASP tool is a set of checklists that are used to review the methods used in different types of studies, as well as the credibility and relevance of results to local decision making [16]. Studies that scored less than half of the total score were not considered. The steps of the search process and outputs, and the summary and grading of studies were documented in the form of tables.

Two residential 10 day workshops with a team of 7 consultants (external resource persons drawn from other departments within MoH), liaison members and secretariat members were held to complete the literature search process and prepare the draft of the influenza vaccine technical report in January and March 2016. During these workshops, members had access to reliable internet connection, printing facilities and published articles. Unfortunately, programmatic data held by the NVIP, MoH required

by the IVWG were not made available during these workshops. Secretariat members from NVIP did not have time to compile the programmatic data required, and in fact were unable to attend the residential workshops due to ongoing vaccination campaigns.

Additional experts in systematic literature searches were invited to support the working group as external resource persons, however no private sector manufacturers or experts from other partners were invited to speak to the working group.

3.6. Preparation of the technical report

All those involved in developing the technical report were oriented to the KENITAG procedure on issuing evidence-based recommendations. For KENITAG members this included a 4-day workshop on NITAG functions and mode of operations, members' roles, and the principles and methodology for issuing evidence-based recommendations. This included defining the search question, conducting a literature search, grading the quality of evidence and documenting the processes undertaken. External consultants and IVWG members not part of the main KENITAG team were provided with a 1-day orientation. During the process of developing the technical report, core KENITAG members were kept abreast

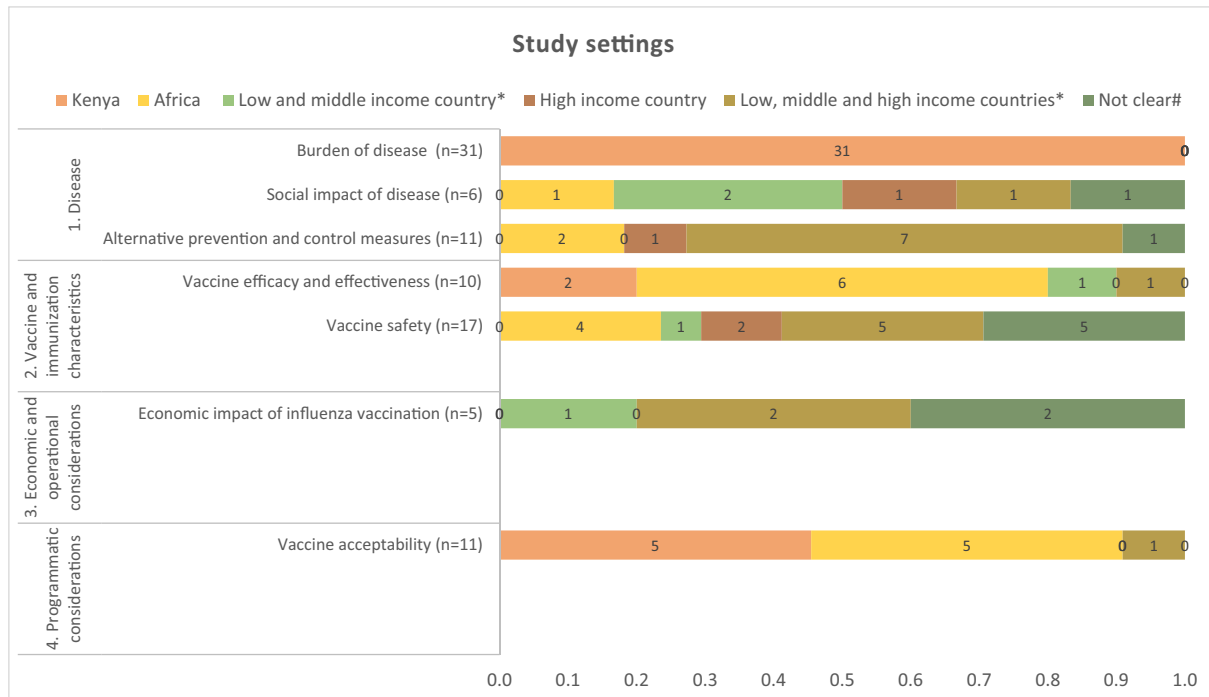


Fig. 3. Distribution of study settings of research articles used to inform KENITAG recommendation. * This category also includes studies from African countries. # In these studies the authors did not clearly indicate the location of studies included in the systematic review. This figure only includes elements of the recommendation framework that required evidence from published studies.

of the progress and outputs of the IVWG during quarterly KENITAG meetings. Following the completion of compilation of evidence, the technical report was presented by the chair of the IVWG during a KENITAG meeting in May 2016.

3.7. Preparation of the recommendation note

During the KENITAG meeting of May 2016 the IVWG technical report was deliberated on, and KENITAG members developed their recommendations after voting. The final recommendation note issued by KENITAG provided the contextual information regarding the influenza vaccine decision, the method applied to collect, select and analyse data, the method used to reach the recommendation, and the recommendation itself.

Data on most of the critical elements listed in the recommendation framework had been obtained (Table 2). However, it was noted that most Kenyan studies describing the burden of influenza disease focused on young children less than 5 years of age. There were significant gaps in knowledge regarding the local burden of disease among pregnant women, individuals with co-morbidities, the elderly and health care workers. Only two other data items described as critical, – information on the sources of funding and ability to conduct surveillance for adverse events following immunization (AEFI) were not made available to KENITAG.

Despite these gaps in data, KENITAG concluded it had sufficient evidence of significant burden of disease among children less than 5 years of age. Given limited resources available for vaccine preventable diseases in Kenya, KENITAG recommended prioritization of children 6 to 23 months of age for annual vaccination with the inactivated influenza vaccine as this is a group at risk for severe disease. However, because of limited experience with influenza vaccination in Kenya, KENITAG further recommended that the policy should be adopted only after conducting a pilot vaccine demonstration project. The pilot study would be used to fill some of the gaps in local knowledge by providing an economic evaluation of

the vaccination program targeting children 6 to 23 months including cost-effectiveness analysis of different vaccination strategies (e.g. year round versus time bound vaccination periods); determining the actual programmatic requirements of the vaccination program such as additional cold chain use and human resource requirements; and assessing vaccine uptake within the target group. This data would be useful in preparing for nationwide introduction of the seasonal influenza vaccine should the government adopt the recommendation.

As there was insufficient local data to support recommendations for other risk groups, KENITAG also recommended that additional local epidemiological studies among pregnant women, individuals with co-morbidities, the elderly and health care workers should be conducted before expanding the current recommendation. The recommendation note was shared with the MoH in June 2016.

3.8. Progress post recommendation

In November 2016 the MoH sent out a communication to all influenza partners and stakeholders in the country to assist with actualizing the recommendation for a pilot study put forward by KENITAG and addressing the knowledge gaps identified [17]. The pilot study of influenza vaccination among children 6–23 months of age had not commenced by 2018. However, in response to the gaps highlighted by KENITAG, the Kenya Medical Research Institute (KEMRI) and the Centers for Disease Control and Prevention (CDC), are undertaking an epidemiological study on the burden of influenza among pregnant women and their newborn children. Researchers from the University of Nairobi, the CDC, the London School of Hygiene and Tropical Medicine, United Kingdom and the KEMRI-Wellcome Trust organization, are undertaking a modelling study on the cost-effectiveness of different influenza vaccination timing schedules given the lack of clearly defined influenza seasonality in Kenya. CDC will also work towards imple-

menting a pilot vaccine demonstration project to answer the programmatic questions posed by KENITAG. These studies are of significant relevance as the Kenyan government works towards attaining universal health coverage for its citizens [18] and considers the possibility of expanding their immunization program.

3.9. External support for KENITAG activities during the seasonal influenza vaccine recommendation process

During the vaccine recommendation process, the SIVAC Initiative trained KENITAG members on their roles and provided framework documents to guide the development of KENITAG's own documents. In addition, the SIVAC initiative provided a consultant to support secretariat activities and provided financial support for KENITAG meetings up to mid-2015. Thereafter, CDC, provided funding for KENITAG and IVWG meetings up to 2016 through a cooperative agreement with the Government of Kenya that was channelled through the MoH, aside from facilitating access to scientific articles that were utilised in the technical report. Financial support for meetings was used to book meeting venues, provide per diem payments to meeting attendees, print meeting documents, communicate with meeting attendees, and pay for accommodation during overnight meetings.

A summary of KENITAG activities from June 2014 through June 2016 is provided in [Supplementary Table 2](#).

3.10. Summary of the main challenges during the seasonal influenza vaccine recommendation process

There was insufficient local data for KENITAG to make recommendations on seasonal influenza vaccination among pregnant women, individuals with co-morbidities, the elderly and health care workers, despite the WHO recommendation to vaccinate these groups [12]. KENITAG did not consider evidence of disease burden from neighbouring countries, or other LMICs in its assessment of disease burden ([Fig. 3](#)).

The secretariat was unable to adequately take up its role in preparing the background documents and technical report that were used as the basis of KENITAG deliberations due to insufficient personnel time. While this challenge was partially addressed by the incorporation of external resource persons (i.e., persons contracted by external partners), programmatic data in the custody of MoH were not provided to KENITAG because of unavailability of personnel to compile and present the data. Lack of time to conduct KENITAG activities also contributed to delays in scheduling meetings and enlisting members to the IVWG.

KENITAG and IVWG meetings did not take place as per the work plan. During the 2014 to 2016 period, the MoH did not provide financial resources to support the activities of KENITAG or the IVWG. As a result, KENITAG meetings and activities that required funding were dependent on external partners for support. When renewal agreements with partners were delayed or funds were depleted, KENITAG activities were temporarily halted ([Supplementary Table 2](#)).

4. Discussion

This report describes KENITAG's seasonal influenza vaccine recommendation and highlights the major challenges encountered by the committee which included lack of comprehensive local data, workforce constraints, and scarce financial resources. Moreover, KENITAG was only able to issue a provisional recommendation for the use of influenza vaccine in Kenya with the caveat that, for actual implementation, missing data on programmatic costs and delivery strategies should be gathered through a vaccine demon-

stration project. Similar challenges are likely to be encountered in other newly established NITAGs in LMICs. It is important to have an understanding of the practical challenges that are likely to disrupt NITAGs and to identify sustainable alternatives when considering new (or changes to) vaccination programs.

The process of deriving the Kenyan seasonal influenza vaccine recommendation was at par with international guidelines [15,19], nonetheless, reliance on local disease burden data greatly limited the scope of KENITAG's recommendation. Although WHO recommends the prioritization of pregnant women and other at risk populations for influenza vaccination, the committee's assessment was that there were insufficient data in Kenya to evaluate those risk groups. Contextualizing global recommendations to local settings requires that policy decisions are grounded in local evidence. However, in some cases, NITAGs could consider burden of disease data from other countries where disease epidemiology is expected to be similar.

The determination of which elements of the recommendation framework requires local data is country specific and is ultimately guided by the judgement of NITAG members and views of country policy makers. Of the data elements that were considered, it was clearly evident that data on local disease burden was a critical factor in Kenya. Similarly, all 21 NITAGs surveyed in Europe in 2013 reported that local disease burden was a key factor to consider when making a vaccine recommendation, and only 30% considered disease burden in neighbouring countries as a proxy [20]. In 6 low-and-middle-income countries surveyed in 2017, NITAG members cited a preference for local data but were open to using what was available [21]. In accordance with NITAG's guidance [19], the process by which data from other countries with similar disease epidemiology is weighted and ultimately influences local vaccine recommendations should occur in a systematic, transparent and reproducible manner. The process of utilizing burden of disease data from other countries to build confidence among national decision makers and substantiate local policy recommendations is an area that requires further discussions.

Remarkably, cost-effectiveness of influenza vaccination programs, i.e., how much it would cost to prevent one case of influenza and related complications, was considered an important but not critical element for KENITAG deliberations. This is despite the fact that the re-classification of Kenya from a low income country to a lower-middle income country in 2015 [22] means that the country is expected to transition away from Gavi support and rely on domestic funds for its NIP. Newer vaccines are less consistently cost-effective when compared to traditional vaccines (e.g. measles, diphtheria, pertussis and tetanus vaccines), further emphasising the need to consider the outputs of properly conducted economic evaluations in deciding whether a vaccine should be introduced instead of adopting other public health measures that also prevent illness and death [23]. Cost effective analyses are often underutilised in NITAGs around the world, in spite of their proven utility [20,21]. However, such considerations will likely increase in importance over time, especially in resource limited settings where choosing the most appropriate health interventions for competing health priorities is undertaken in the context of scarce resources.

Our experience underscores the need to provide sufficient human capacity and financial support when establishing and maintaining NITAGs. While it is recommended that the secretariat functions of KENITAG are provided by NIP staff [19], the additional work load placed on these individuals on top of their primary duties, means that secretariat functions cannot be effectively carried out if additional human resources are not provided. By hosting the secretariat within the NVIP, it was expected that programmatic data would be more easily accessed and recommendations more easily taken up by the MoH because government staff would be more intimately involved in the process of deriving the recommen-

dation from the available data. The limited capacity of the secretariat led to the engagement of a team of external resource persons to assist with compiling the evidence and generating the technical report, leading to a more expensive process. The NITAG secretariat should be adequately staffed with individuals who are facilitated to devote enough time to their role.

Limited funding for NITAG operations is likely to remain a challenge for newly established groups in developing countries [21]. In order to consistently hold meetings, make per diem payments to members, and facilitate the evidence search process, NITAGs will undoubtedly require a dedicated budget line within the national health budget. However, formal recognition by MoH doesn't always guarantee domestic funding for NITAG activities [21,24]. It would be important for NITAGs from LMICs to explore supplementary sources of funding and support from outside the Ministry should government funding be limited or absent. Though this should be cognizant of the potential for conflicts of interest to arise should NITAGs be funded by entities who stand to directly gain or lose by their recommendations.

External support may take several forms. NITAGs may make use of regional or international collaborative efforts in making recommendations [25]. Of the published data used by KENITAG, it was only the burden of disease data where KENITAG relied solely on local data. The preference for local data regarding burden of disease was important in making sure the vaccine recommendation was responsive to national health priorities. For most other data elements that required the use of scientific research findings, data from African countries was considered sufficient (e.g. vaccine effectiveness and acceptability), and where this was lacking, data from outside the African region was used (e.g. social impact of the disease, alternative prevention and control measures, vaccine safety, and economic impact of the vaccination program). If a regional collaboration could provide non-country specific data on elements that are unlikely to change across countries in an inclusive process at par with NITAG procedures for evidence collection, it would reduce the workload on individual NITAGs and time spent in compiling evidence. NITAGs could then focus on collecting critical country specific data on local disease burden and vaccine program considerations that would be necessary for most national policy decisions. A similar strategy has been suggested for countries in Europe in order to avoid unnecessary duplication of efforts [20], however this is most likely to be useful when initiated at countries' request. External support may also take the form of collaborations with local research and academic institutions that may provide experts to answer research questions posed by NITAGs or assist in the compilation of evidence [24].

There were a few additional improvements that could have been made to the process of making the seasonal influenza vaccine recommendation. The process of recruiting external members to the IVWG took approximately 5 months. It has been previously recommended that when a NITAG is first established a mapping exercise should take place in order to identify local experts and their fields of expertise [24]. These individuals are then sensitized to the role of NITAGs so that they may be called on to join as core members. Based on the Kenyan experience we further recommend that this database be updated yearly in line with the topics for discussion listed in the annual NITAG work plan in order to provide a pool of experts who could be called on to join specific working groups. This would lead to faster recruitment of nominated members and external resource persons into working groups and avoid unnecessary delays. In addition, local experts from research organizations and the pharmaceutical industry could have been invited to speak to the IVWG during the process to further enrich KENITAG deliberations. Lastly, the adoption of electronic means of collaboration through video or audio conferencing would have reduced the cost of IVWG meetings.

There were several factors that facilitated the decision making process. The existence of a national influenza surveillance system since 2007 [26] had generated awareness among stakeholders within the MoH of the presence and burden of influenza in Kenya. This created an enabling environment to discuss the seasonal influenza vaccine. Furthermore, at the time of making the recommendation, training on the roles and functions of NITAGs and the process of issuing evidence-based recommendations was made available to KENITAG through the SIVAC Initiative, AMP. Moreover, funding for NITAG activities was also available from the SIVAC Initiative and CDC. Finally, because the question posed to KENITAG originated from the MoH they were willing to move forward the recommendations provided by KENITAG [17]. However, the extent to which the MoH will adopt the influenza vaccine recommendation can only be gauged after several years. Although a final recommendation by KENITAG for a nationwide rollout of a seasonal influenza vaccination program among children 6 to 23 months of age is contingent upon a vaccine demonstration project that will gather missing data on programmatic costs and the impact of the new program on the regular immunization schedule in the country, ultimate adoption of the vaccine recommendation into the NIP is dependent on the Ministry of Health.

5. Conclusion

In order to establish an effective NITAG, the issues of work force and financing for activities need to be adequately addressed. Where local disease burden data are lacking, there is need to develop and adopt new methods of utilizing findings from other countries to accurately inform local decisions in a manner that is useful, valid and acceptable to decision makers. Furthermore, considerations of programmatic costs and the cost-effectiveness of the vaccination program may need to be appropriately addressed to inform governments of the program's sustainability.

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Contributorship

RK, EAnyango, DM, PM, CT, MM, EAmukoye, FW and KENITAG co-authors played a role in developing the concept and design of the report. All authors contributed to the acquisition, analysis and interpretation of data. JD, SSC and ABN developed the first draft of the article. EAmukoye, PM, FW and SSC revised the document critically for important intellectual content. All co-authors

gave final approval for the manuscript to be submitted for publication.

Disclosure

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Agency for Preventive Medicine or Centers for Disease Control and Prevention.

Declarations of interest

None.

Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.vaccine.2018.11.062>.

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