NITAG Training Manual

STRENGTHENING THE TECHNICAL CAPACITY OF NATIONAL IMMUNISATION TECHNICAL ADVISORY GROUPS (NITAGs)

SIVAC
Supporting Independent Immunization and Vaccine Advisory Committees

nrc
NITAG Resource Center

EVIPNet

amphpid
HEALTH POLICY AND INSTITUTIONAL DEVELOPMENT

PREFACE

The SIVAC Initiative, implemented by AMP, was established in 2008 with the main objective of supporting national authorities in low- and middle-income countries to set up and strengthen their NITAGs. In 2012, WHO designated the Health Policy and Institutional Development Unit (HPID) of the "Agence de Médecine Préventive" (AMP) as a WHO Collaborating Centre on evidence-informed Immunisation policy-making considering its experience with National Immunisation Technical Advisory Groups (NITAGs).

The SIVAC Initiative has supported the creation and/or strengthening of **16 NITAGs** and organised **OVER 20 TRAINING WORKSHOPS** in collaboration with partners in Africa, South-East Asia, Europe, Eastern Mediterranean and Western Pacific WHO regions, with the aim of building NITAG capacity to function in accordance with WHO guidelines.

Building from this experience, the SIVAC Initiative has developed a training catalogue that describes the project strategy and key interventions to reinforce the NITAGs' capabilities to provide decision-makers with sound technical and evidence-based recommendations. As presented in the catalogue of trainings, the SIVAC capacity building strategy comprises regional and national training programmes with the following goals:

i. For regional trainings:

- To develop local expertise to sustain NITAG capacity building (e.g. training local experts as technical resources and facilitators of future regional and national NITAG trainings)
- To promote a learning-by-experience approach through the sharing of best practices and lessons learned among countries with a similar context

ii. For national trainings:

- To address specific country needs as related to NITAG scope of work or topics of interest

The target groups identified in the training catalogue are:

- National experts as potential future facilitators for NITAG trainings
- NITAG chairs and secretariats
- NITAG members, including core members, liaison members, and ex-officio members

To implement this strategy, the SIVAC Initiative has developed a training manual that comprises four units: three core units and one with optional trainings ("On-demand"). The three core units are: 1) Establishment and mode of operations of an efficient NITAG; 2) Analysis of Immunisation in the context of health systems and the policy decision-making process; 3) Technical and scientific capacities of NITAGs. The "On-demand" training includes the following sections: 1) Informing vaccine decision-making with economic evidence; 2) Socio-anthropological approach to vaccination; 3) Grading of Recommendations, Assessment, Development and Evaluation (GRADE) for NITAGs.

As the number of NITAGs is increasing, it is expected that new and existing NITAGs will need to reinforce their capacities. It is important to ensure that support will be available when needed.

Capacity building is a continuous process; the availability of local technical assistance to NITAGs will help maintain the NITAGs' technical skills.

The objective of this manual is to guide facilitators of capacity building workshops/trainings organised for NITAG members and secretariats. The manual will provide guidance on how to prepare, design and facilitate the training and will provide resources for the facilitation.

The training manual is organised in teaching units and sections. Each teaching unit contains:

- A facilitator's folder which includes for each section: the content (providing an overview of the main points of the section); instructions for course facilitation (giving suggestions on the roll-out of the session); a slide deck to be adapted for the lecture (to be downloaded from the NITAG Resource Center at ***www.nitag-resource.org***)

- Resources for the participants, and for each section: summary of the section; templates; articles and other resources

ACKNOWLEDGMENTS

The manual has been developed by the SIVAC Initiative team in collaboration with the AMP Training Unit and the Evidence-Informed Policy Network (EviPNet) of the World Health Organisation. The team wants to acknowledge the valued contribution of partners (CDC, WHO) for their inputs, and the technical experts listed below for reviewing of the materials:

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CONTENT

TRAINING 1:
ESTABLISHMENT AND MODE OF OPERATIONS OF AN EFFICIENT NITAG

Section A: Role, scope and functions of NITAGs

Section B: NITAG tools

TRAINING 2:
ANALYSIS OF IMMUNISATION IN THE CONTEXT OF HEALTH SYSTEMS AND THE POLICY DECISION-MAKING PROCESS

Section A: The influence of the health system on NITAG recommendations

Section B: Stakeholder analysis and mapping

TRAINING 3:
TECHNICAL AND SCIENTIFIC CAPACITIES OF NITAGS

Section A: Evidence assessment methodologies

Section B: Development of an evidence-based recommendation note

TRAINING 4:
"ON-DEMAND"

- Informing vaccine decision-making with economic evidence
- Socio-anthropological approach to vaccination
- Grading of Recommendations, Assessment, Development and Evaluation (GRADE) for NITAGs

T R A I N I N G 1

ESTABLISHMENT AND MODE OF OPERATIONS OF AN EFFICIENT NITAG

SECTION A

ROLE, SCOPE, AND MODE OF OPERATIONS OF NITAGS

SECTION B

NITAG TOOLS



FOR
FACILITATOR

TABLE OF CONTENTS

INTRODUCTION 5

TARGET AUDIENCE

PREREQUISITE SKILLS/KNOWLEDGE

LEARNING OBJECTIVES

TRAINING MATERIALS

SECTION A

ROLE, SCOPE, AND MODE OF OPERATIONS OF NITAGS

1.ROLE OF A NITAG 7

1.1. DEFINITION

1.2. NITAG CONTRIBUTION TO THE NATIONAL HEALTH SYSTEM

1.2.1. STRENGTHENED DECISION-MAKING PROCESS REGARDING VACCINATION

1.2.2. DECISION ADAPTED TO THE NATIONAL CONTEXT

1.2.3. STRENGTHENED NATIONAL IMMUNISATION PROGRAMMES

2. SCOPE OF ACTION AND MODE OF OPERATIONS 8

2.1. NITAG TERMS OF REFERENCE

2.2. DIFFERENCE BETWEEN A NITAG AND OTHER EXISTING COMMITTEES WITHIN THE FIELD OF VACCINATION

2.2.1. DIFFERENCE WITH THE INTERAGENCY COORDINATION COMMITTEE (ICC)

2.2.2. DIFFERENCE WITH THE NATIONAL REGULATORY AUTHORITY (NRA)

2.2.3. DIFFERENCE WITH WORKING GROUPS FOCUSING ON A SPECIFIC DISEASE

2.3. NITAG METHOD OF WORKING

2.3.1. NITAG COMPOSITION

2.3.2. INDEPENDENT EXPERTISE

2.3.3. MULTIDISCIPLINARY EXPERTISE

2.3.4. A TRANSPARENT MODE OF OPERATION

2.3.5. RESPECT OF CONFIDENTIALITY AGREEMENT

2.3.6. A PERMANENT COMMITTEE

REFERENCES 12

FACILITATOR INSTRUCTIONS 13

SECTION B
NITAG TOOLS

1. THE NITAG INTERNAL PROCEDURES MANUAL 26

1.1. PURPOSE

1.2. HOW TO PREPARE AND VALIDATE THE INTERNAL PROCEDURES MANUAL

1.3. MANUAL CONTENT

1.3.1. OVERVIEW OF THE NITAG

1.3.2. MODE OF OPERATION

1.3.3. FINANCIAL CONSIDERATIONS

2. DEVELOPMENT OF THE NITAG WORK PLAN 30

2.1. PURPOSE

2.2. HOW TO PREPARE THE WORK PLAN

2.3. WORK PLAN PRESENTATION

2.3.1. THE NARRATIVE DESCRIPTION OF ACTIVITIES

2.3.2. ACTIVITY TIMELINES, MILESTONES, AND DELIVERABLES

2.3.3. THE OPERATING BUDGET

2.4. WORK PLAN CONTENT

2.4.1. OBJECTIVE 1: PRODUCING SCIENTIFIC DOCUMENTS

2.4.2. OBJECTIVE 2: STRENGTHENING NITAG CAPACITY

2.4.3. OBJECTIVE 3: ENSURING NITAG FUNCTIONING

2.4.4. OBJECTIVE 4: ASSESSING NITAG PERFORMANCE

REFERENCES 33

FACILITATOR INSTRUCTIONS 34

INTRODUCTION

This training is presented in two sections A and B that are further introduced below.



TARGET AUDIENCE

- Secretariat, chair and members of the NITAG



PREREQUISITE SKILLS/KNOWLEDGE

- There are no prerequisites for Section A. Before training on Section B, participants are advised to go through Section A which covers knowledge of the NITAG's role, scope of action, and mode of operations.



LEARNING OBJECTIVES

Section A's learning objectives are to:

- Understand the role and responsibilities of NITAGs within the national health system
- Understand core principles of NITAG functioning that ensure the credibility of its recommendations (e.g. conflict of interest and confidentiality, recording of meetings and proceedings)

In section B, the learning objectives are:

- Development of a manual for internal procedures, including establishment of working groups that identify and analyse the evidence needed to support a recommendation
- Development of an annual or multi-year action plan that incorporates all national stakeholder perspectives, reflects international recommendations, and includes a monitoring and evaluation plan



TRAINING MATERIAL

- PowerPoint presentation, notes for the facilitator, summary for the participant, templates, examples, and publication resources.

SECTION A

ROLE, SCOPE, AND MODE OF OPERATIONS OF NITAGs



FOR
FACILITATOR

This section defines the role, scope of action, and method of working of National Immunisation Technical Advisory Groups (NITAGs). It explains the fundamental differences between NITAGs and other existing committees in the field of immunisation and highlights the specificities of NITAGs.

The concepts presented are illustrated through interactive group exercises, which also provide an opportunity for participants to identify challenges unique to their contexts.

1. ROLE OF A NITAG

1.1. DEFINITION

National Immunisation Technical Advisory Groups (NITAGs) are national advisory committees made up of experts, in charge of guiding health authorities and leaders of national immunisation programmes in the definition and implementation of national immunisation policies and strategies.

It is important to insist on three essential points of this definition that will be developed later on in this section:

- NITAG composition: independent national experts who sit in the committee on their own capacity
- NITAG mandate: advisory committee, meaning that final decisions are made by national authorities
- NITAG scope of action: covers all aspects relating to vaccination concerning all populations

A number of countries have already set up successful NITAGs: USA (ACIP), Canada (NACI), United Kingdom (JCVI), France (CTV), Australia (ATAGI), Thailand (ACIP), China (EACIP), South Africa (NAGI), Tunisia (CTV), Sri Lanka (ACCD), etc. More recently in Africa, NITAGs have been established in Côte d'Ivoire (CNEIV-CI), Mozambique (CoPI), Senegal (CCVS), Benin (CNCV-Benin) and Kenya (KENITAG).

1.2. NITAG CONTRIBUTION TO THE NATIONAL HEALTH SYSTEM

The field of immunisation is becoming increasingly complex, with a number of newly available vaccines, a diversity of manufacturers, additional target populations that now include not only children but also adolescents and adults, and limited funding for expensive vaccines. Furthermore, there are many concurrent health priorities. The decision-making process in regards to vaccination is thus becoming more and more complicated.

A functional and successful NITAG helps to provide answers to issues relating to the complex immunisation landscape. It allows for a credible, accountable, and independent decision-making process as well as for ownership of vaccination policies and the strengthening of the national immunisation programme.

1.2.1. Strengthened decision-making process regarding vaccination

By virtue of its composition and mandate, a NITAG contributes to strengthening immunisation decision-making processes, supporting credible, accountable, and independent decisions. A NITAG is made up of national experts and issues evidence-based recommendations independently, using a rigorous and systematic method for assessing data quality.

1.2.2. Decisions adapted to the national context

On an international or even regional level, recommendations are issued regarding vaccination and immunisation policies and strategies. These recommendations can be adapted to a country's specific situation.

A NITAG considers the country context and specific features when formulating recommendations submitted to the Minister of Health. By providing national authorities with evidence-based information regarding vaccinations, the committee helps the government make informed decisions and thus resist external pressure. Lastly, by helping authorities make decisions based on evidence and taking into account the local situation, the NITAG promotes increased, sustained, and strengthened trust among the population regarding vaccination.

1.2.3. Strengthened national immunisation programmes

The NITAG's multidisciplinary composition enables it to address immunisation issues through different lenses. In addition, the committee helps to optimise synergy-based decision-making processes, by encouraging consultations with Interagency Coordination Committees (ICCs), National Regulatory Authorities (NRAs), and other ad hoc committees. Lastly, it helps national authorities stay informed about scientific developments in the vast field of immunisation.

The place of a NITAG in the national health system comes from its role in evidence-informed immunisation decision-making. Thanks to its composition, terms of reference, and working methods, it contributes to enhancing the relevance of vaccination policies and programmes. This in turn may lead to additional funding from the government and donors and improve vaccine acceptability among populations.

2. SCOPE OF ACTION AND MODE OF OPERATIONS

A NITAG is an advisory committee that provides guidance in regards to vaccination, either in response to questions from the Minister of Health or to draw attention to a given subject. In both cases, the recommendation provides advice to the Minister of Health about a certain issue in vaccination. In the end, the decision to act on the recommendation is the sole prerogative of the Minister of Health.

2.1. NITAG TERMS OF REFERENCE

The NITAG's scope of action covers all vaccine- and vaccination-related topics for which the Minister of Health requires scientific and technical advice. The NITAG may be required to issue recommendations in the following fields:

- policies and strategies related to vaccination, and vaccines for children and the rest of the population
- the introduction of new vaccines and new technologies, their impact on the health system and immunisation programmes
- updated information on the safety and quality of vaccines and on the fight against new diseases that could be avoided through the use of vaccines
- other issues relating to vaccination and vaccines

The NITAG's terms of reference are specified in the legal document (order, decree) pertaining to the creation of the committee. Each country defines its NITAG's terms of reference according to its own needs and resources. The list suggested above is therefore fairly general and is not necessarily exhaustive.

2.2. DIFFERENCE BETWEEN A NITAG AND OTHER EXISTING COMMITTEES WITHIN THE FIELD OF VACCINATION

Due to its responsibilities, the NITAG holds a specific place within the national health system. Certain precautions are to be taken when establishing a NITAG. It cannot be a coordinating or a regulatory body, and has no executive powers. It is therefore important to distinguish NITAGs from Interagency Coordination Committees (ICCs), National Regulatory Authorities (NRAs), and ad hoc committees.

The NITAG has a special function within the bodies, structures, and institutions that participate in the decision-making process concerning vaccination policies and strategies.

2.2.1. Difference with the Interagency Coordination Committee (ICC)

- **Scope of action**

The NITAG gathers, circulates, and analyses evidence to help make informed decisions for all issues related to vaccination.

The ICC coordinates the actions led by the agencies represented in the committee regarding the implementation of a national vaccination decision. It deals with the operational side of national immunisation programme activities such as financial management and resource mobilisation.

- **Mandate**

The NITAG is a technical advisory committee. It is responsible for helping the Minister of Health make decisions. It makes recommendations to national authorities regarding policies and strategies.

The ICC's role comes in the implementation of these decisions.

- **Members**

Key NITAG members include national experts who have the right to vote. Other governmental services and technical partners take part in NITAG activities as non-core members, also referred to as ex-officio and liaison members.

The ICC is generally chaired by the Minister of Health. Technical partner representatives and committee members take part in the decisions. Local experts are not widely represented.

Ultimately, in comparison to the ICC, the NITAG is neither a coordination committee, an implementation unit, nor an executive committee. It is instead a technical advisory committee that does not make any operational decisions. The NITAG has multidisciplinary expertise and covers a much wider scope of activities than the ICC.

2.2.2. Difference with the National Regulatory Authority (NRA)

A NITAG has no regulatory powers. Unlike the National Regulatory Authority (NRA), a NITAG is not responsible for the following: authorisation and inspection of clinical tests, certifications, quality control, and post-marketing monitoring of vaccination products.

2.2.3. Difference with working groups focusing on a specific disease

A NITAG is not an ad hoc committee that focuses on a specific topic within a set time frame, such as poliomyelitis, measles, or hepatitis committees.
A NITAG is based on multidisciplinary expertise, and its services can be required to answer any questions relating to vaccination and vaccines. It is part of the health system and constitutes a permanent step in the decision-making process regarding vaccination and vaccines.

2.3. NITAG METHOD OF WORKING

To outline the NITAG method of working, it is first important to know the committee's composition, then to specify its fundamental operating principles, which include: independent expertise, multidisciplinary expertise, transparent operation, respected confidentiality, and ensured sustainability.

2.3.1. NITAG composition

There is no absolute rule concerning the number of core members required to form a NITAG. Nonetheless, it is important not to create a NITAG with very few members as absences may have significant consequences on the committee's activities. Similarly, a group made up of a large number of experts is trickier to manage. Experience has shown the following best practice rule: effective committees operate with a group of **10 to 15 core members,** with different skill sets. Lastly, it is preferable for the NITAG to be made up of an odd number of experts to make the voting process easier.
The NITAG is made up of **core members** (or full members) and **non-core members** (ex-officio and liaison members). A distinction between these two categories is essential during the NITAG's decision-making process. Core members alone participate in the deliberations and voting on the recommendations to be issued.

- **Core members (or full members)**

Full members are national experts who are **well-renowned in their field**. They sit on the committee in **their own capacity**, as experts and not as representatives of a group, organisation, or institution. Full members are **the only committee members authorised to vote.**

- **Non-core members: ex-officio members**

Ex-officio members **represent the various governmental services** involved in the field of vaccination:

immunisation programme leaders, other departments or programmes within the Ministry of Health, NRAs, national vaccination control laboratories, Ministry of Education officials, Ministry of Finance officials, etc.

- **Non-core members: liaison members**

Liaison members are convened as representatives of knowledgeable groups, professional associations in the health sector, national advisory committees, non-governmental organisations (NGOs), and **technical partners** such as WHO and UNICEF.
Non-core members, i.e. ex-officio and liaison members, participate in NITAG meetings to provide technical information on behalf of their organisations, but do not contribute to the final issuing of recommendations.

- **The executive secretariat**

The executive secretariat provides **technical and administrative support** to ensure the proper operation of the NITAG. This function is most often fulfilled by the Ministry of Health and is usually hosted by the national immunisation programme. It may be held as well by an academic institute. The NITAG's secretariat provides committee members with any preparatory documents, coordinates the preparation of the agenda, including identification of priority questions to be put in the agenda, prepares the logistical and administrative aspects of meetings, supports working groups activities, and archives all the documentation relating to the daily operation of the NITAG, such as meeting reports.

2.3.2. Independent expertise

The experts are members appointed on an individual basis for their expertise. They do not represent an institution or interest group. To guarantee their independence, it is important to specify that this function within the committee is held on a voluntary basis and that experts do not receive a salary for their activities within the NITAG. The Chairperson of the NITAG must not be under the direct authority of the Minister of Health.
Furthermore, the NITAG's independence is reflected in the process used to issue a recommendation: experts will base their conclusion on a transparent and systematic method to collect and review the best available evidence on the topic. This method will be introduced in the 3rd training.

2.3.3. Multidisciplinary expertise

The committee's multidisciplinary nature makes it possible to address the complex array of vaccination issues through a comprehensive and integrated approach. The full members represent a wide range of disciplines: paediatrics, public health, epidemiology, immunology, health economics, vaccinology, social sciences, etc. These skills may however be limited in certain countries. Experts should belong to at least five different fields of expertise. Collective expertise should reflect the specific responsibilities attributed to the NITAG. Regarding the NITAG's composition, other elements such as male/female equity can also be taken into consideration.
Core members are to fulfil their responsibilities and commitment to the NITAG in order to ensure its correct operation.

2.3.4. A transparent mode of operation

The NITAG has internal procedure documents that detail the mode of operation. The document is validated and signed by all full members that sit on the committee. Section B of this training course will provide further information on these guidelines.

The conflict of interest declaration procedure, set out in the procedures manual, contributes to the transparency of all decisions made within the NITAG. Full members are required to fill out an interest declaration after their appointment to identify any possible conflicts of interest. This declaration is renewed on a yearly basis. Prior to each NITAG meeting, the declaration must, if necessary, be updated according to the agenda.

2.3.5. Respect of confidentiality agreement

NITAG members are also required to respect a confidentiality policy. Before each meeting, all participants, including external resources must fill out a confidentiality agreement that guarantees the confidential nature of any information subject to property rights, should such information be presented during the meeting. This procedure is also detailed in the procedures guidelines.

2.3.6. A permanent committee

NITAGs are officially created by ministerial decree or by any other administrative act in accordance with the national administrative and legal system in force. It is an important procedure, as it ensures that the NITAG is officially recognised by the Minister of Health and government authorities and is a legally established committee. This also serves to formally integrate the NITAG into the national health system and guarantee its sustainability.

The elements listed below make up the criteria for measuring a NITAG's compliance with standards:

a. committee's legal and administrative basis;
b. existence of an official written mandate;
c. systematic conflict of interest declaration;
d. multidisciplinary nature (at least five fields of expertise represented: paediatrics, public health, infectious diseases, epidemiology, immunology);
e. at least one scheduled meeting and
f. agenda and preparatory documents circulated to members at least one week prior to meetings.

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2. M. Bryson, ***A global look at National Immunisation Technical Advisory Groups,*** Vaccine 28S (2010) A13-A17
3. B. Gessner, ***Informing decision makers: Experience and process of 15 National Immunisation Technical Advisory Groups,*** Vaccine 28S (2010) A1-A5
4. ACIP Website (Advisory Committee on Immunisation Practices in the USA): http://www.cdc.gov/vaccines/acip/



FACILITATOR INSTRUCTIONS

IMPORTANT NOTES:

This training explains the principles adopted by NITAGs and presents relevant concepts. It is important for participants to familiarise themselves with these concepts.

It is essential for trainees to actively participate. Create as many opportunities as possible to ask questions and gather feedback during the session.

An example of an interactive exercise is provided. Facilitators should feel free to modify or prepare a different one according to the context. The cards for this exercise should be prepared and sorted in advance.

A video will be shown; it's an edited excerpt from an ACIP session to illustrate some of the concepts presented: statement on the conduct of the session, request for conflict of interest declarations, organisation of a working group, and decision-making procedures.



Knowledge objectives

At the end of this section, participants will be able to :

- Understand the role and responsibilities of NITAGs within the national health systems
- Understand core principles of NITAG functioning that ensure the credibility of its recommendations



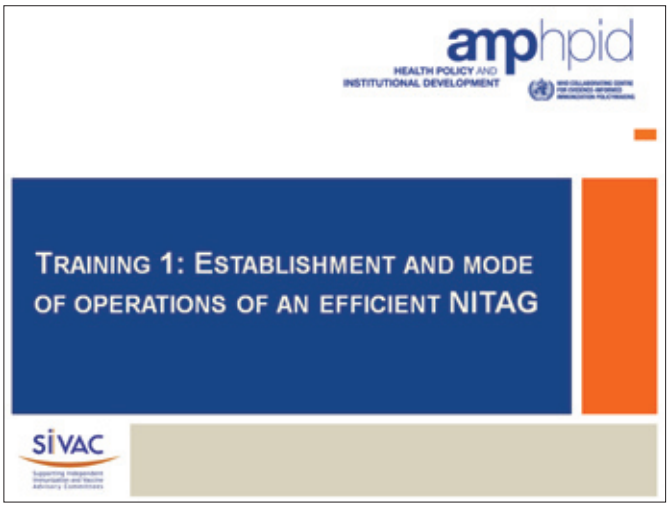
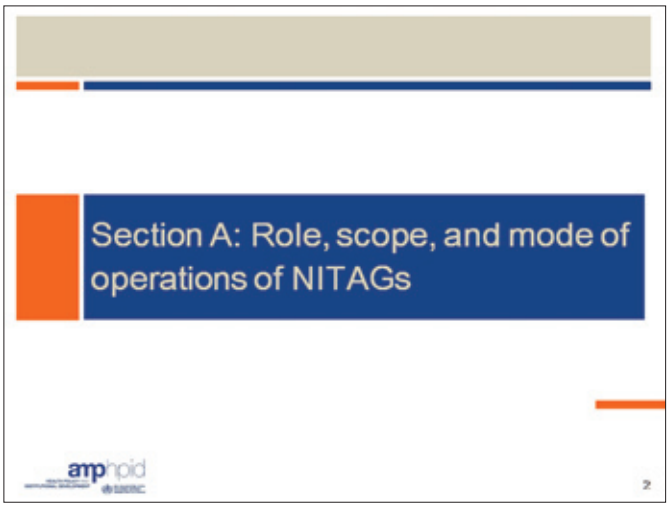
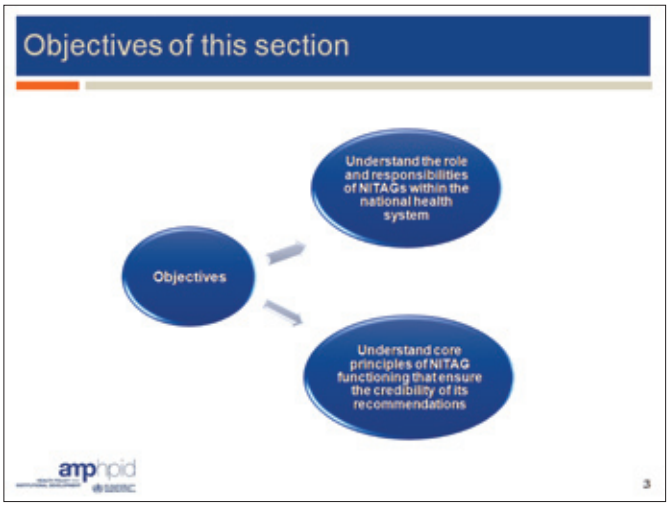
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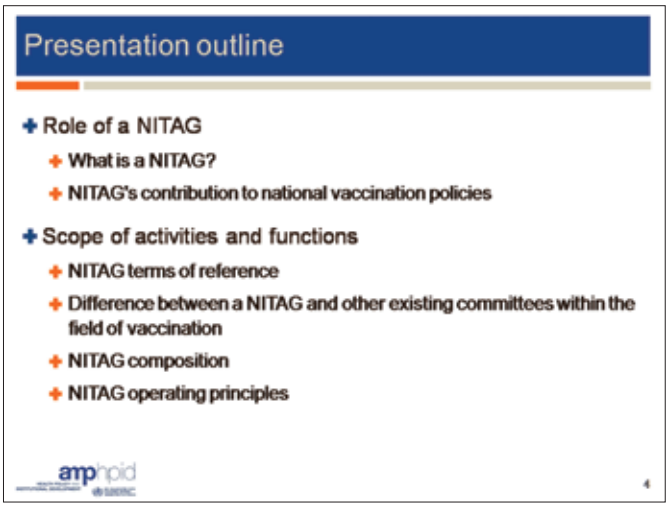
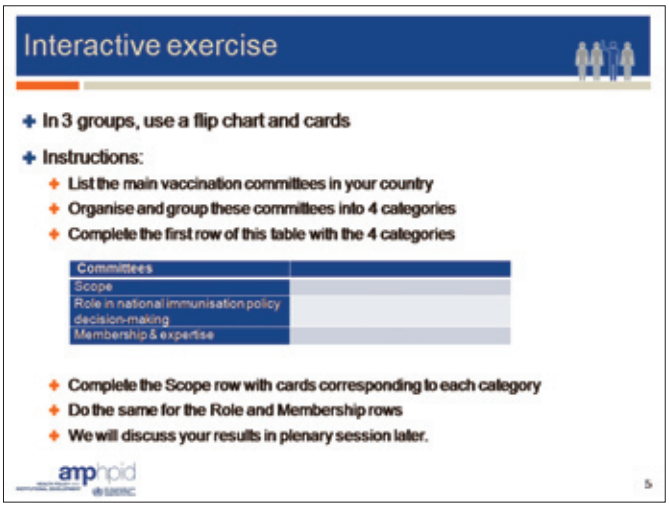
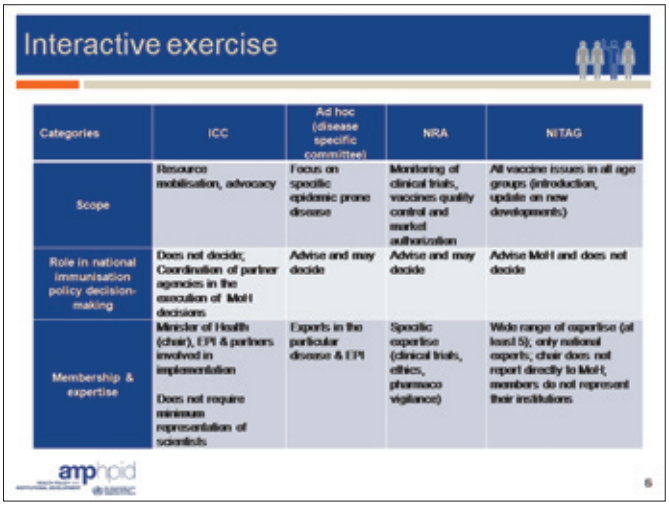
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STEP 3	PRESENTATION 6-16	46'
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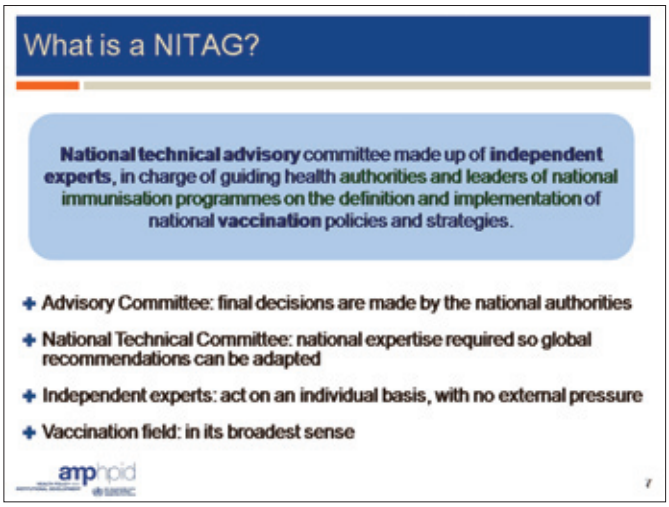
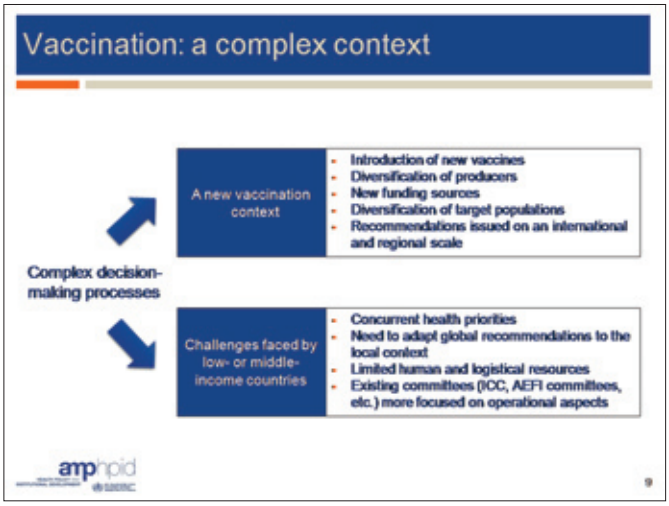


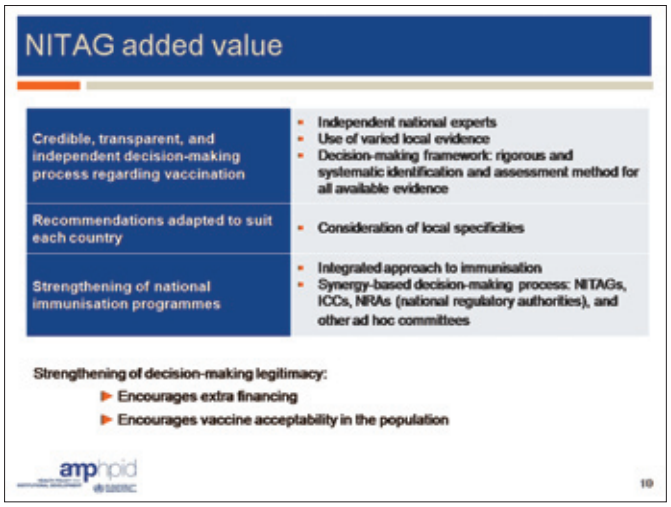
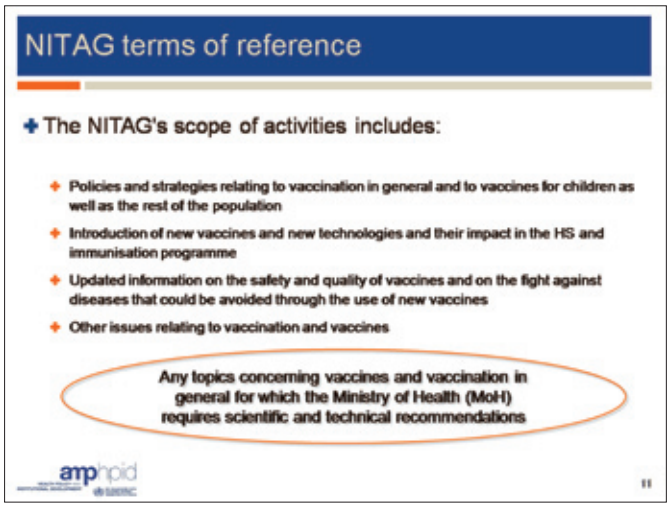
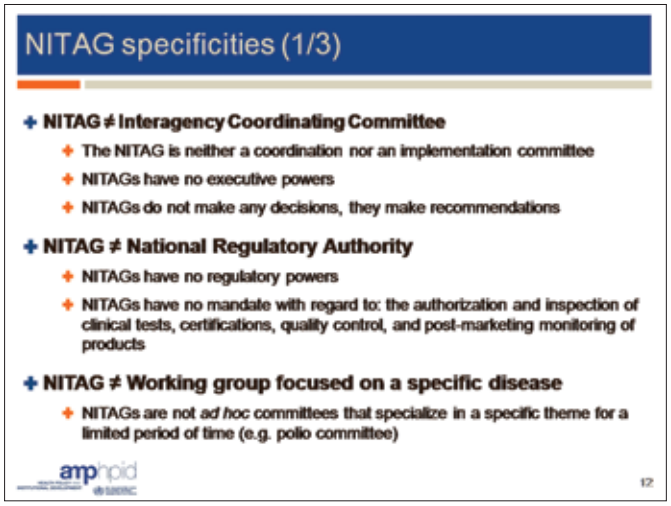
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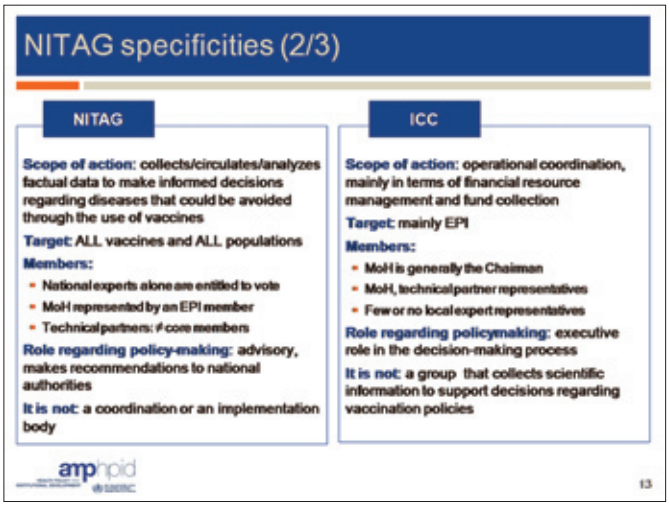
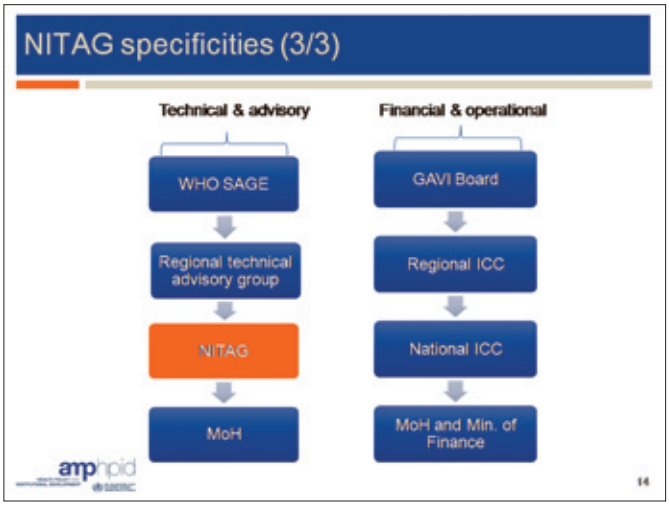
- PowerPoint presentation
- Content document and facilitator instructions
- 10 printed presentations with space for participant comments
- 3 sets of cards for the activity (end of document)
- 3 flip charts
- 10 coloured markers
- Repositionable tape or gum
- Scissors
- Download video from www.nitag-resource.org

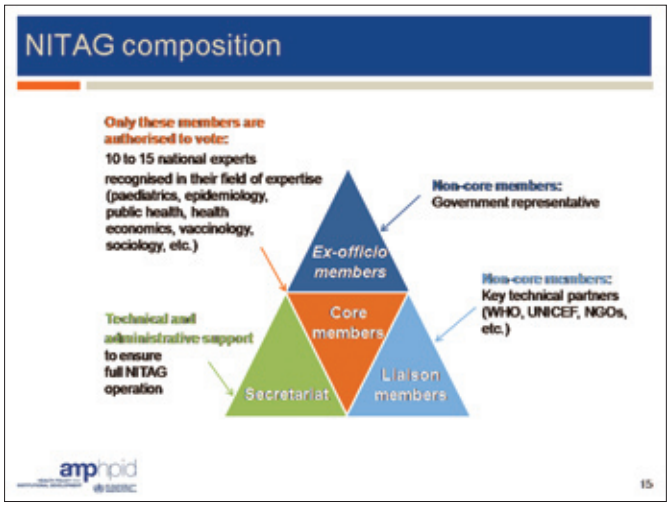
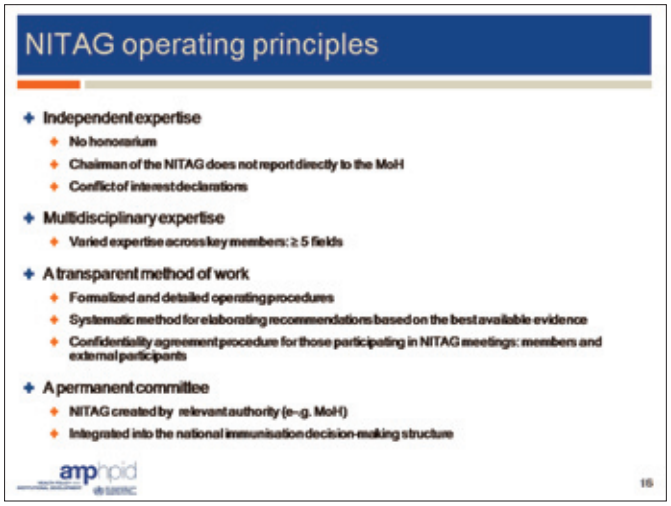
Slides	Facilitation methods
	**Presentation:** This training explains the principles adopted by NITAGs and presents relevant concepts. It is important for participants to familiarise themselves with these concepts. 2'
	
	**Presentation:** Present the objectives. 5'

Slides	Facilitation methods
	**Presentation:** Read out the presentation outline. 5'
 	**Interactive exercise:** *The aim of this exercise is to show participants the specificities of the NITAGs as they compare to other immunisation committees.* 60' 1. Organise participants in 3 groups and give to each : - a flip chart - markers, tape/gum, scissors - a set of cards (5') 2. Ask participants to list on their flip chart the main vaccination committees in their country (expected names include ICC, polio / measles committee, National Regulatory Authority (NRA), NITAGs). (10') 3. Ask them to organise and group these committees in 4 categories (10') 4. Ask them to reproduce the table on slide 5 onto their flipchart and to complete the first line with the 4 categories found. (5') 5. Ask them to take the Scope cards and to try to bring together categories and corresponding Scope cards. (5') 6. Ask them to take the Role cards and to try to bring together categories and corresponding Role cards. (5') 7. Ask them to take the Membership cards and to try to bring together categories and corresponding Membership cards. (5') 8. Ask each group to present briefly on the exercise. (15' and 5' per group) 9. Present a synthesis of the table with slide 6 (5')

Slides	Facilitation methods
	**Presentation:** Run through the first part. **Question:** 1. Ask participants to comment on the words in bold. 2. Then, run through the second part that explains the key words. 3'
	**Q&A:** 1. Ask participants what is changing in the immunisation context and what the challenges are. 2. Ask participants who have several years' experience in decision-making processes how they feel about the current situation of the immunisation programmes. 5'
	**Presentation:** 5'

Slides	Facilitation methods
	**Presentation:** Use the points raised by participants in the previous slide to show how NITAGs can help overcome challenges in the field of vaccination. 5'
	**Presentation:** Give the following key message: ToRs for NITAGs and other committees are not the same. 3'
	**Presentation:** 5'

Slides	Facilitation methods
	Presentation: 5'
	Presentation: Highlight the place NITAGs hold in decision-making and implementation processes regarding global and national policies. 5'

Slides	Facilitation methods
	Presentation: Question & Answers: Ask for any question for clarification on the type and roles of each category of membership 5'
	Presentation: 5'

CARDS FOR THE INTERACTIVE EXERCISE:

GROUP 1

Scope card	Scope card	Scope card	Scope card
Resource mobilisation; advocacy	Focus on specific epidemic-prone disease	Monitoring of clinical trials, vaccine quality control and market authorisation	All vaccine issues in all age groups; vaccine introduction; update on new developments
Role card	**Role card**	**Role card**	**Role card**
Do not decide; Coordinate partner agencies in the execution of the MoH decision	Advise and may decide	Advise and may decide	Advise MoH and do not decide
Membership card	**Membership card**	**Membership card**	**Membership card**
Minister of health (Chair); EPI & Partners involved in implementation; Do not require minimum representation of scientists	Experts in the particular disease & EPI	Specific expertise in clinical trials, ethics, pharmacovigilance	Wide range of expertise (at least 5); only national experts; Chair does not report directly to MoH; members do not represent their institutions



GROUP 2

Scope card	Scope card	Scope card	Scope card
Resource mobilisation; advocacy	Focus on specific epidemic-prone disease	Monitoring of clinical trials, vaccine quality control and market authorisation	All vaccine issues in all age groups; vaccine introduction, update on new developments
Role card	**Role card**	**Role card**	**Role card**
Do not decide; Coordinate partner agencies in the execution of the MoH decision	Advise and may decide	Advise and may decide	Advise MoH and do not decide
Membership card	**Membership card**	**Membership card**	**Membership card**
Minister of health (Chair); EPI & Partners involved in implementation; Do not require minimum representation of scientists	Experts in the particular disease & EPI	Specific expertise in clinical trials, ethics, pharmacovigilance	Wide range of expertise (at least 5); only national experts; Chair does not report directly to MoH; members do not represent their institutions

GROUP 3

Scope card	Scope card	Scope card	Scope card
Resource mobilisation; advocacy	Focus on specific epidemic-prone disease	Monitoring of clinical trials, vaccine quality control and market authorisation	All vaccine issues in all age groups; vaccine introduction, update on new developments
Role card	**Role card**	**Role card**	**Role card**
Do not decide; Coordinate partner agencies in the execution of the MoH decision	Advise and may decide	Advise and may decide	Advise MoH and do not decide
Membership card	**Membership card**	**Membership card**	**Membership card**
Minister of health (Chair); EPI & Partners involved in implementation; Do not require minimum representation of scientists	Experts in the particular disease & EPI	Specific expertise in clinical trials, ethics, pharmacovigilance	Wide range of expertise (at least 5); only national experts; Chair does not report directly to MoH; members do not represent their institutions



SECTION B

NITAG TOOLS



FOR

FACILITATOR

This section presents the tools available to efficiently run a NITAG. The session focuses on two key documents for an efficient NITAG: the NITAG internal procedures manual and the NITAG work plan. It presents the steps that should be followed for drawing up and validating these two NITAG documents. It also suggests key elements of the content.

1.THE NITAG INTERNAL PROCEDURES MANUAL

1.1. PURPOSE

The internal procedures manual describes all the rules and procedures applicable to the NITAG for its establishment and functioning. It clarifies the mode of operations, thus contributing to transparency in the decision-making process.

1.2. HOW TO PREPARE AND VALIDATE THE INTERNAL PROCEDURES MANUAL

The Executive Secretariat drafts the internal procedures manual based on the official document (decree, administrative act) that established the NITAG. The secretariat can use manuals from other countries and the WHO guidelines (P Duclos, 2008) to fill in the different sections of the document. Then, the NITAG's core members should validate the manual. Finally, each core member must sign the internal procedures manual by the first committee meeting.

1.3. WHICH CONTENT?

The internal procedures manual might include three main sections: an overview of the NITAG's definition; a description of the NITAG's mode of operation; and procedures and funding mechanisms.

1.3.1. Overview of the NITAG

The internal procedures manual must include an overview of the NITAG's definition and terms of reference, as stated in the official document establishing the NITAG.

- **NITAG's definition (refer to the official document on NITAG establishment)**

The NITAG's definition should include a basic introduction: name of the NITAG with its acronym, nature, date and reference of the official document (decree, order, or ministerial note). Then, the manual clarifies the NITAG's mission and describes its relationship to other existing committees. Finally, it specifies the NITAG's composition and definition of the different types of members: core members, ex-officio members (representatives from government entities), liaison members (representatives from technical partners, organisations, NGOs), observers, and the organisation hosting the NITAG's scientific and technical secretariat.

- **NITAG's terms of references (refer to the official document on NITAG establishment)**
  - Members' roles and duties

    The manual specifies roles, prerogatives (e.g. voting), and duties for each member category: core members, ex-officio members, liaison members, scientific and technical secretariat, and Chairperson.

    This part must specifically explain who is responsible for the following activities: convening meetings, proceedings of the meetings, preparing meeting agendas and logistics, drafting reports and minutes, sending reports and minutes, archiving documents including declarations of interest and confidentiality agreements, coordinating the work of sub-groups, preparing annual technical and financial reports, submitting reports to the authorities, communicating with the authorities and the public, updating the website, etc.

    Regarding the secretariat responsibilities these can be: providing support for the organisation of meetings (layout of decision documents and reports); keeping NITAG archives up to date; preparing annual technical reports; monitoring expenses; and preparing financial reports.
  - Members' terms

    This part indicates the nomination procedure (appointment by the MoH), term of office, number of terms, and Chairperson rotation schedule. Usually, the core members' term is for three (3) or four (4) years, with or without the possibility for a second term. The NITAG membership renewal procedure should be described. The procedure should try to maintain some stability by avoiding a renewal of all core members at the same period of time.

    The document clarifies circumstances and procedures for excluding members, for example a number of unexcused absences at meetings or an absence of conflict of interest declaration.

    Finally, the manual indicates the measures to be taken in the event that the Chairperson is away for a long period of time (with details about the duration).

1.3.2. Mode of operation

This section describes the procedures for drawing up the work plans, holding meetings, drafting and finalising the minutes, preparing recommendations and decision-making, and submitting reports to the authorities.

- **Drawing up the NITAG work plan**

The consultation process for identifying priority issues to be addressed by the committee in the current or following years is described here. The methods used for drawing up and finalising the work plan are also mentioned. The manual states the circumstances in which review of the work plan takes place. It specifies the monitoring and evaluation framework, indicates how to determine indicators, and stipulates the periodicity of external review. The latter part of the training will focus on the development of the work plan.

- **Holding meetings**
  - Convocation

    The manual specifies how meetings are convened (it may be by the technical and scientific secretariat, upon the Chairperson's request) and the required timelines ahead of the meeting for sending notifications, agendas, and the reference documents to be discussed. As recommended in the WHO Guidelines, the NITAG secretariat should send these preparatory documents within a reasonable period of time (at least one week before) allowing members sufficient time to prepare for discussions.

- Nature of the meetings
  This part specifies when meetings are closed or open to other members and the public. Open meetings have the advantage of strengthening a transparent decision-making process (e.g. ACIP in the USA where the public can join meetings via internet or physically), and the disadvantage of slowing the process and intimidating some experts.
  The manual specifies the procedures for when the committee invites external persons.
- Frequency of meetings
  A schedule of regular meetings must be set in advance. A NITAG should meet at least once a year in a plenary session. It is desirable that it should meet at least twice a year. Country experiences show some variation in the number of annual meetings. E.g. some NITAGs organise three or four plenary meetings per year such as the NACI in Canada, the ACIP in the US, the JCVI in the UK, the ACCD in Sri Lanka, and the CCVS in Senegal. Other NITAGs schedule meetings less often such as the ACIP of Thailand, the CNCV-Benin, and the NAGI in South Africa, with one or two regular meetings per year. There are also some NITAGs that schedule more plenary sessions such as the CTV in France with at least eight meetings per year.
  NITAGs may also meet in extraordinary sessions based on the importance or urgency of an issue. The manual indicates the procedures for extraordinary meetings.

- **Conflict of interest declaration and confidentiality agreement**
  - Conflict of interest declaration
    This section clarifies the management of conflicts of interest in the NITAG. A conflict of interest designates a conflict between the public functions and private interests of a person that could adversely affect the performance of their official duties. The declaration of conflict of interest from members will help avoid situations in which specific interests could affect their impartiality. Core members should not represent the interests of a particular group or interested party. They should refrain from advocating policies, opinions, and products of the organisation for which they work. The declaration of conflict of interest will help prevent potential conflicts both in a transparent and ethical way. The type of conflict of interest will be clarified: when financial, it will be clarified whether the interests are personal (i.e. payment to a member) or non-personal (i.e. payment for the benefit of a department run by a member, but not to the member personally) and whether they are specific or non-specific to the topic or product considered by the committee. It will also be clarified whether there are other non-financial factors that could affect their impartiality in the NITAG work.
    The manual specifies when conflict of interest forms are submitted and updated; usually, each core member completes the annual conflict of interest declaration form at the time of committee launch and at the beginning of each year. In addition, before each committee meeting (plenary session, extraordinary session) or working group sessions, members complete an updated declaration form in case of a change related to specific topics on the agenda.
  - Confidentiality agreement
    The internal procedures manual states also whether committee members and external parties are bound to the confidentiality of recommendations. In any case it is advised that members follow rules of precautionary principles with regards to external communication.
    The manual clarifies who is entitled to share information on behalf of the committee

(usually it is the Chairperson or a duly authorised representative).
A confidentiality agreement must be filled in by all the participants, including external invitees, when the presenter deems the information presented and discussed during the meeting confidential.

- **Drafting, finalising, and distribution of the minutes**

The section indicates who is responsible for drafting the minutes of the meetings (it may be the secretariat or the committee's rapporteur).
The manual specifies: timelines for submitting draft minutes to members; timelines for finalising reports, whether they are disclosed to the public and by which medium (for example on the NITAG Resource Center); whether a period of embargo prior to publication applies and, if so, what defines the lifting of the embargo. If a website is available, the manual specifies how documents are posted and accessed (e.g. an exclusive link for members could be created to provide access to confidential documents).

- **Preparing recommendations and decision-making**
  - First steps for preparing a discussion on a recommendation
    The manual states the process for preparing discussions on a recommendation. Usually, a working group is established. The procedures manual will clarify the following points (and a guidance document providing more details on the development of working group terms of reference will be attached to the manual).
  - Organisation of a working group
    The purpose of establishing a working group is to prepare the technical dossier on the topic under consideration. The working group collects evidence on the different thematic areas that will inform the recommendation. It is advisable to set up a working group on a specific topic as soon as the annual work plan is defined so that the group has time to provide sufficient information for meaningful future discussions.
  - Working group establishment
    The manual describes the procedure for the working group establishment and the responsibilities of the NITAG Executive Secretariat and NITAG Chair. These working groups are appointed for a set period of time.
    The NITAG Secretariat and Chair select a working group Chair among NITAG core members based on his/her specific expertise, and a working group Secretariat. Then, they send an appointment letter describing the working group terms of reference, the list of questions to be addressed, the timelines, and deliverables to the working group Chair and Secretariat.
  - Working group composition
    The manual clarifies the procedures for selection. The working group Chair and working group Secretariat identify relevant independent experts in the field of interest in collaboration with the NITAG Executive Secretariat. It is made up of core members according to their expertise with regards to the terms of reference of the working group. External experts can be included in the groups, including consultants and members of existing disease-specific committees, when relevant. In most cases, working group membership consists of: at least one NITAG core member; a rapporteur; possibly non-core members (ex-officio / liaison members); and possibly external experts (consultants or existing disease-specific committee members).
  - Working group functioning

The manual gives indications on the working group functioning rules, and specifically on the coordination, management of conflicts of interest, recruitment of external experts and reporting. Usually, the working groups are coordinated by the NITAG Secretariat. This means that there are regular meetings between the NITAG Secretariat and the working group Chair to review progress and provide assistance if needed.

- Decision-making process
  The manual specifies periods and systems for disseminating working group reports to the committee members. The decision process chosen to adopt a recommendation should be indicated, e.g. voting procedures by majority vote or unanimous consensus.

- **Submission of approved recommendations to national authorities**
  The manual indicates submission timelines and method; provides a detailed description of the position of the person receiving the recommendation; and indicates the monitoring system.

1.3.3. Financial considerations

A budget is drawn up for the NITAG's functioning. The manual indicates items that should be covered by the budget and sources of funding.

- **Budget sections**

This part lists the different costs that should be included in the NITAG operating budget. These sections could be costs related to activities related to: producing scientific documents, strengthening NITAG capacities, ensuring NITAG functioning, and assessing NITAG performance.

- **Sources of funding**

The financial part of the manual clarifies all available and potential sources of funding: Ministry of Health and partners (details on duration of partner supports, agreement, and terms of reference). It also indicates the activities that ensure the financial viability that should be included in the work plan.

2. DEVELOPMENT OF THE NITAG WORK PLAN

2.1. PURPOSE

The work plan describes all the activities of the NITAG and its Executive Secretariat, and should include more than the activities supported by partners such as the SIVAC Initiative. It should be an annual work plan.

The purpose of the work plan is to establish a road map with clear milestones and deliverables to ensure the development of high quality, evidence-informed recommendations and to monitor activities aiming to achieve the NITAG's mission. It should be noted that the annual work plan can still be revised depending on new developments.

2.2. HOW TO PREPARE THE WORK PLAN

The work plan should be developed by a relevant team representing the NITAG and its Executive Secretariat (e.g. the Secretariat and a sample of NITAG members, with participation from the Chairperson). At the end, it should be validated by the NITAG's core members.

The preparation of the work plan requires the identification of national immunisation priorities in consultation with the Ministry of Health. The work plan encompasses 3 parts: a narrative description of activities, a timeline with milestones and deliverables, and the budget (see templates).

2.3. WORK PLAN PRESENTATION

2.3.1. The narrative description of activities

The suggestion is to group NITAG activities that serve the same objective. In an objective, a range of information should be provided for each activity: description of the activity (objective, context, details about implementation, expected results), timelines, persons in charge, and technical and financial provisional resources (national and partner support).

2.3.2. Activity timelines, milestones, and deliverables

On the basis of the narrative document, the summary timeline is presented in the form of a Gantt chart and highlights the expected deadlines for each activity. It can be completed to indicate actual completion dates. Key milestones and deliverables are highlighted.

2.3.3. The operating budget

The operating budget describes the cost of the different activities and the different funding sources (e.g. national budget and partner support such as direct financial support provided by the SIVAC Initiative).

2.4. WORK PLAN CONTENT

Based on NITAG terms of reference and experiences, a series of objectives and NITAG activities is suggested.

2.4.1. Objective 1: Producing scientific documents

This objective covers the core activities of the NITAG and its Secretariat.

- **General information**

This section states the priorities selected for the annual NITAG agenda, in accordance with the topics submitted by the MoH and EPI to the NITAG. The terms of reference for each topic are presented to the NITAG members at the plenary sessions. This section indicates the number of plenary sessions per year.

- **Recommendation(s)**

The specific process for preparing and issuing each recommendation is described, taking into account the required time and resources. Tasks include: terms of reference preparation and presentation; working group member selection; recruitment of consultants if needed; working group establishment; conducting of specific studies if necessary; development of a working group work

plan; number of working group sessions; preparation of background documents and technical documents; drafting the recommendation; presentation to the plenary session; discussion and validation of the recommendation; submission to the MoH; follow-up of the submission.
For each activity, it is important to specify the details about the activities, the timelines, the person responsible, and the provisional budget.

2.4.2. Objective 2: Strengthening NITAG capacity

This section describes all activities that build the capacity of the NITAG Secretariat and members, such as:

- **Orientation workshop for NITAG members**

The orientation workshop for NITAG members is crucial. It is the opportunity to explain to NITAG members their roles and responsibilities. Such training is required for NITAG establishment and for membership renewal.

- **Training on the development of evidence-based recommendations**

The method for developing an evidence-based recommendation is essential because it is the core activity of a NITAG. Thus, it is crucial to plan a training session for the NITAG Secretariat and some members on identifying, collecting and assessing evidence, and producing an evidence-based recommendation.

- **Study visits to other NITAGs**

Capacity building includes the organisation of study visits to other existing and well-established NITAGs in order to attend a committee meeting, learn about its functioning, present its work about a specific recommendation, and share experiences. A debriefing session is planned to present the lessons learned from the study visit to all NITAG members.
Another type of study visit could also be organised to share experiences between several NITAGs in the same region about the same topic. It could create and/or strengthen a NITAG regional network.

- **Other trainings needed**

Other specific trainings could be identified according to local specificities and study topics.

2.4.3. Objective 3: Ensuring NITAG functioning

- **NITAG Secretariat office equipment and installation**

The objective is to provide the NITAG's Secretariat with a dedicated office and the necessary equipment so as to conduct all its activities (organisational and scientific). The office is equipped with telecommunication facilities: telephone line and internet connection.

- **Development of tools and documents for NITAG functioning**

This section draws a list of all documents that should be prepared and validated and, persons in charge of these tools: i.e. the internal procedures manual, conflict of interest declaration, confidentiality agreement, work plan with timelines and budget.

- **Logistic and administrative organisation of the NITAG meeting (statutory and extraordinary meetings)**

All the logistic and administrative aspects for holding meetings should be described and planned: preparation of background documents; notes for the meeting in advance; required materials; booking of a meeting room; recording documents (list of participants, report).

2.4.4. Objective 4: Assessing NITAG performance

- **Expense monitoring**

Expense monitoring is important for the development of a financial sustainability plan.

- **Advocacy for resource mobilisation**

Advocacy activities for resource mobilisation must be identified and planned.

- **Monitoring and evaluation of the NITAG**

Monitoring of the development and implementation of the work plan for the next year must be planned. This includes the definition of monitoring objectives and the identification of measurement indicators. Three categories of indicators should measure processes, outcomes, and impact of the committee. They may be selected from the list suggested by WHO and the SIVAC Initiative (J. Blau et al., *Indicators to Assess National Immunisation Technical Advisory Groups*).
An external review should also be planned according to the intervals indicated in the internal procedures manual. It is important to determine the periodicity of the external evaluation.

REFERENCES

1. P. Duclos, ***National Immunisation Technical Advisory Groups (NITAGs): Guidance for their establishment and strengthening,*** Vaccine 28S (2010) A18-A25.
2. K. Senouci et al, ***The Supporting Independent Immunisation and Vaccine Advisory Committees (SIVAC) Initiative: A country-driven, multi-partner programme to support evidence-based decision making***, Vaccine 28S (2010) A26-A30
3. M. Bryson, ***A global look at National Immunisation Technical Advisory Groups,*** Vaccine 28S (2010) A13-A17
4. B. Gessner, ***Informing decision makers: Experience and process of 15 National Immunisation Technical Advisory Groups,*** Vaccine 28S (2010) A1-A5
5. J. Blau et al. ***Indicators to Assess National Immunisation Technical Advisory Groups***, Vaccine, 31 (2013) 2653-57
6. Alex Adjagba et al. ***Supporting countries in establishing and strengthening NITAGs: Lessons learned from 5 years of the SIVAC Initiative***. Vaccine 33 (2015) 588-595

FACILITATOR INSTRUCTIONS

IMPORTANT NOTES:

During the session, participants are invited to read and discuss the documents. The various documents relating to the topics covered should be provided to the participants prior to the start of the training.

If there are NITAGs participating in the training who are in the process of developing their internal procedures manuals or work plan, they can be given the opportunity to get inputs from the other participants on these. If not, the facilitator will use the examples provided in the resources folder. They must be informed in advance. This is best organised in small group discussion.

Knowledge objectives

At the end of this section, participants will be able to:

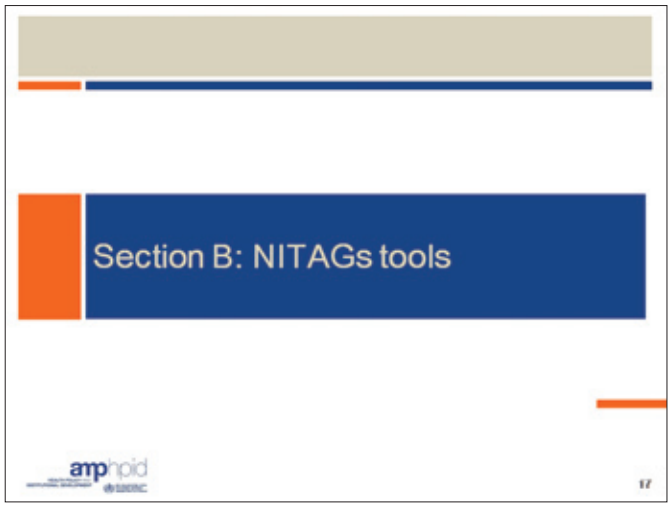
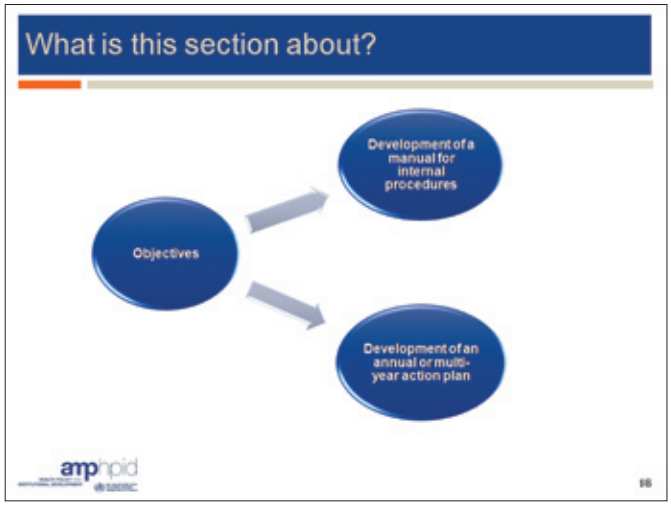
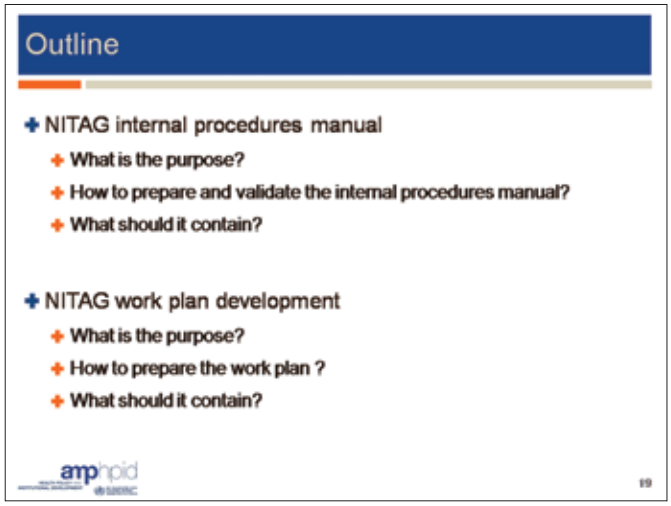
- Understand the role and responsibilities of NITAGs within the national health systems
- Understand core principles of NITAG functioning that guarantee the credibility of its recommendations

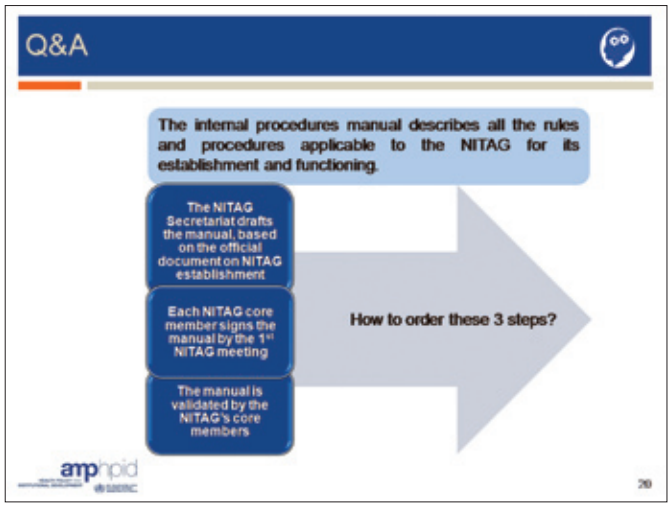
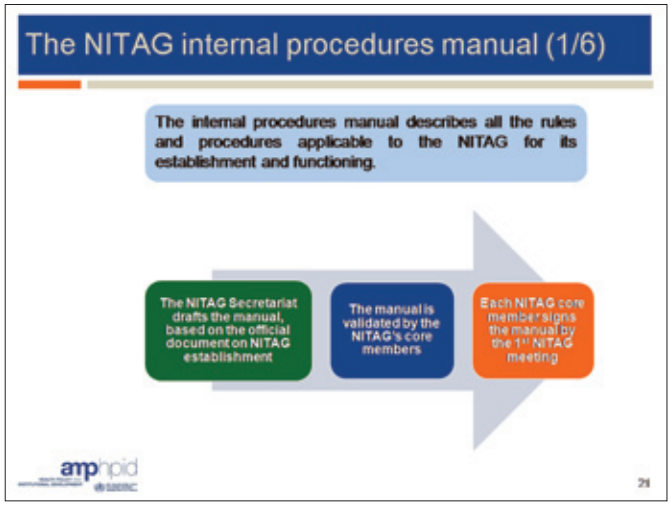
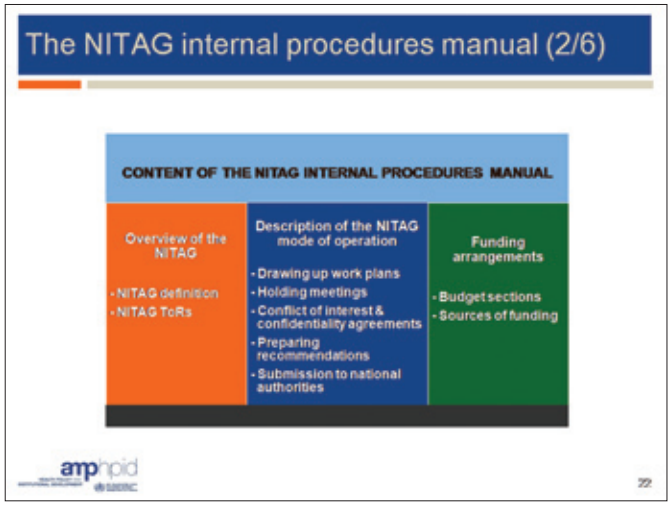
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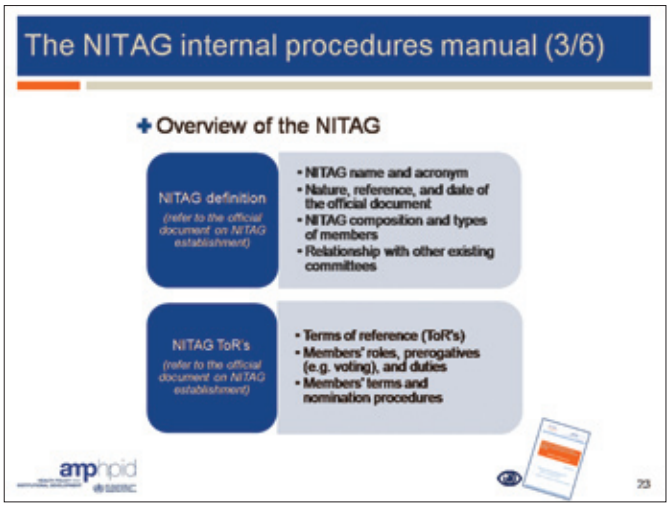
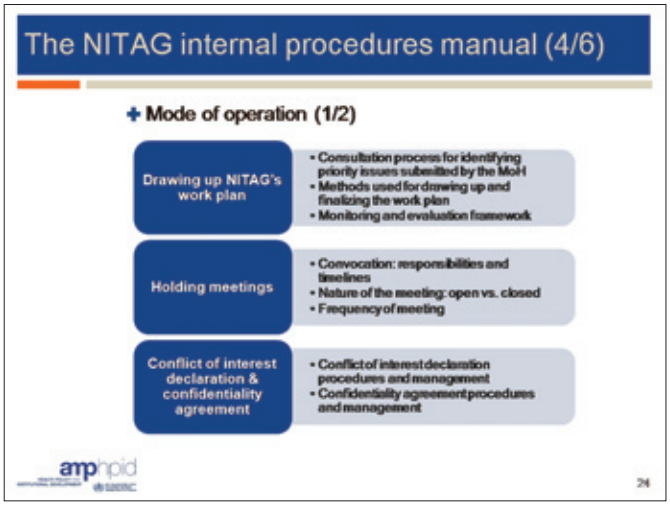
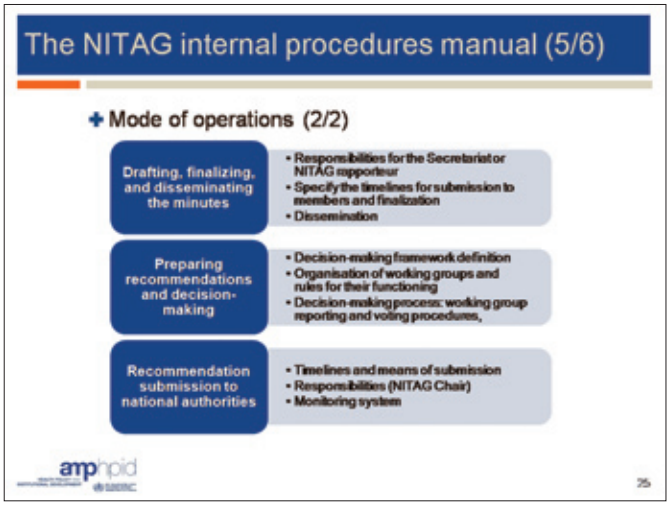
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STEP 1	PRESENTATION & Q&A SLIDES 4-11	60'
STEP 2	BRAINSTORMING SLIDE 13	10'
STEP 3	PRESENTATION	30'
STEP 4	GROUP WORK SLIDE 19	120'

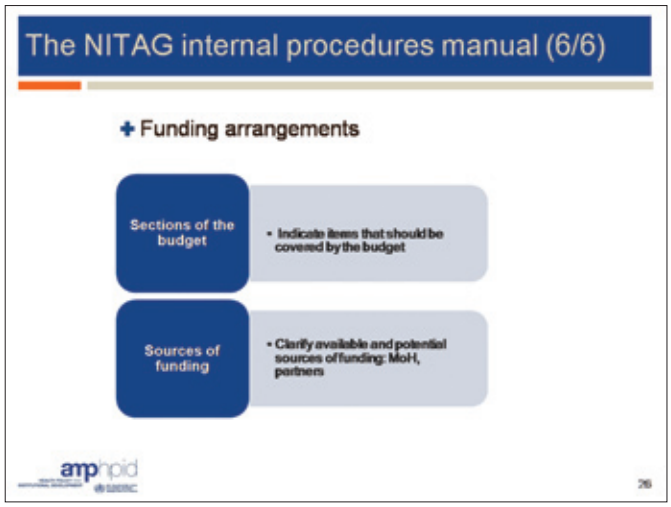
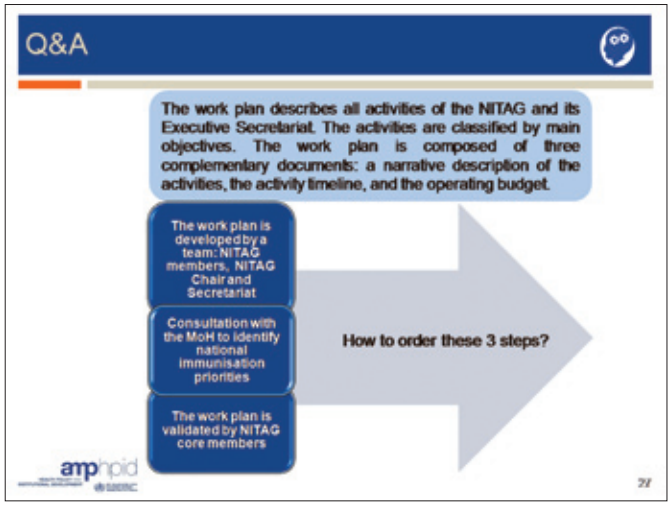
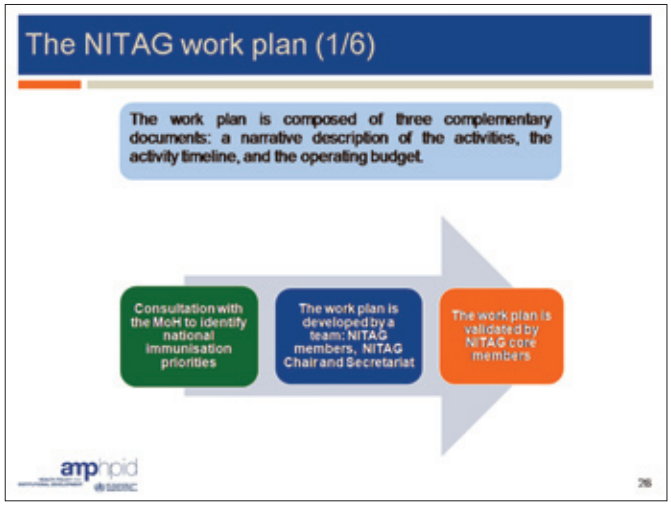
Training material

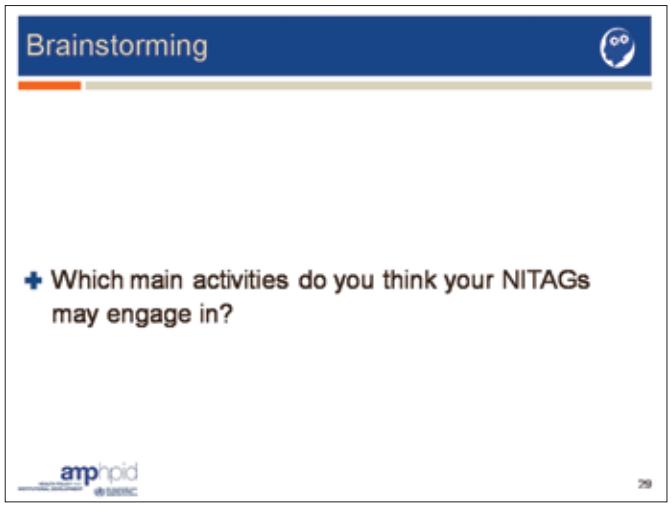
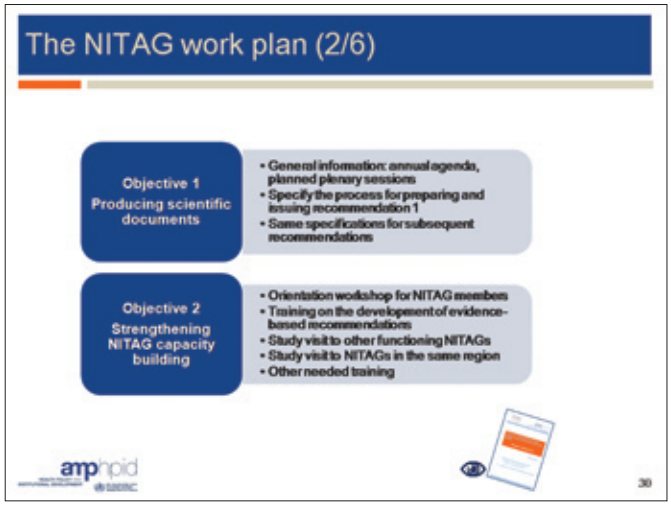
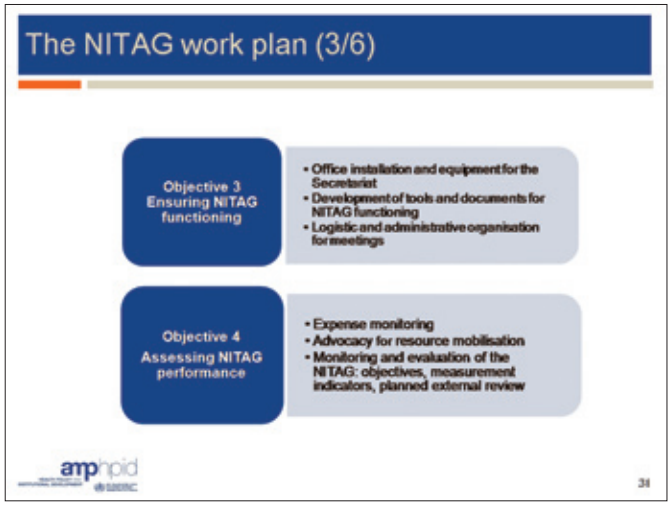
- PowerPoint presentation
- Content document and facilitator instructions
- Summary
- 1 flip chart
- 1 coloured marker

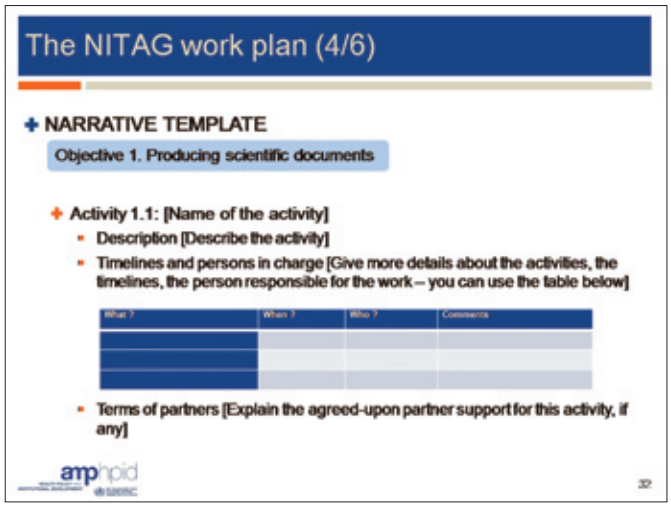
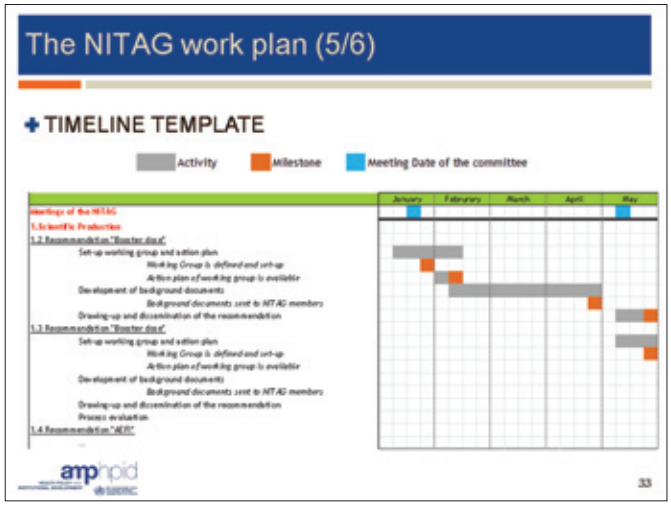
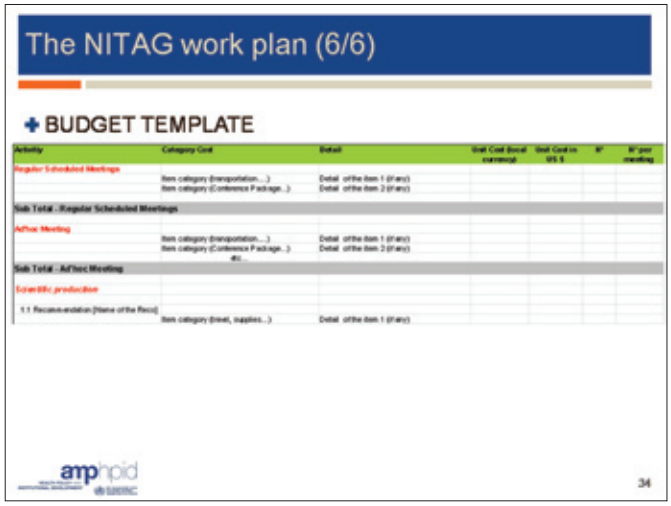
Slides	Facilitation methods
	**Presentation:** This section presents the NITAG tools such as the internal procedures manual, and the work plan 2'
	**Presentation:** 3'
	**Presentation:** 5'

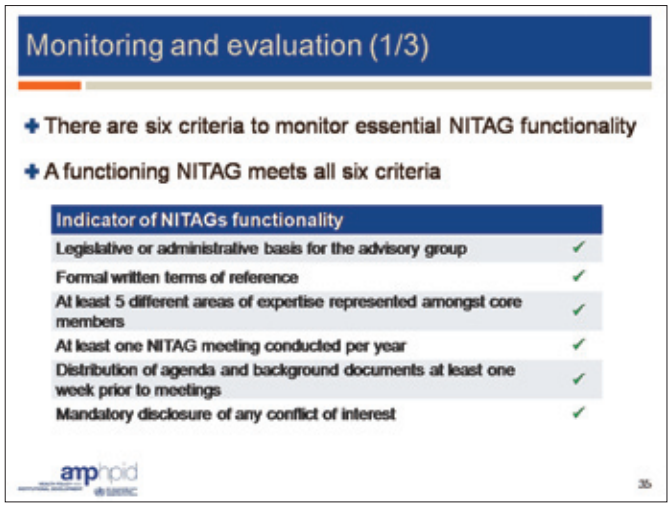
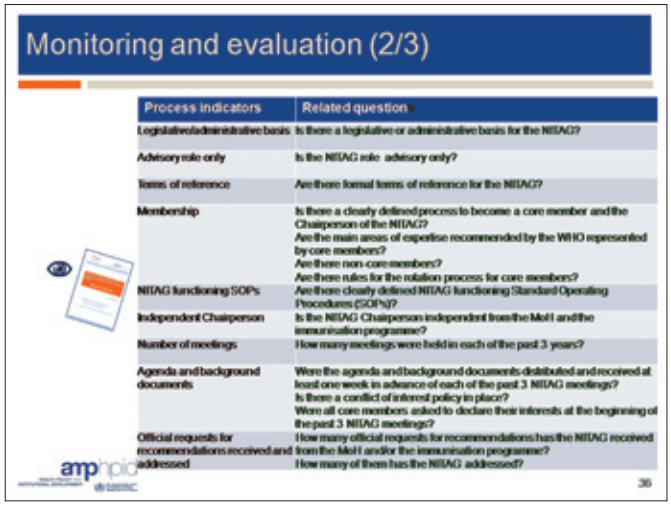
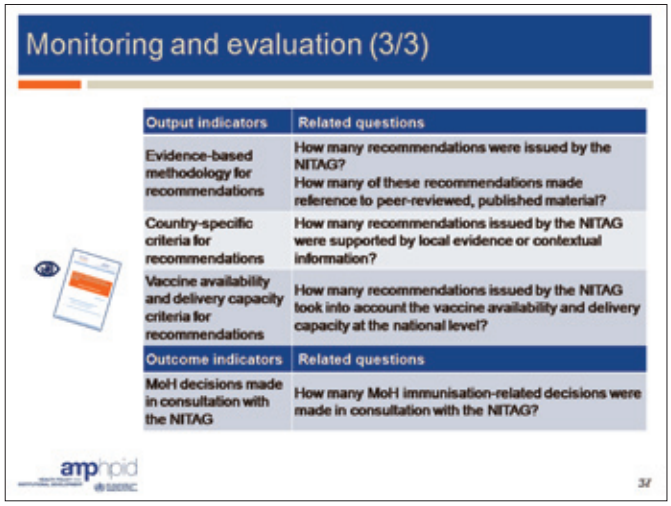
Slides	Facilitation methods
	**Q&A** 1. Present the first part: The internal procedures manual describes all the rules and procedures applicable to the NITAG for its establishment and functioning. 2. Ask the participants to place these 3 steps in order. 5'
	**Presentation:** 5'
	**Presentation:** 5'

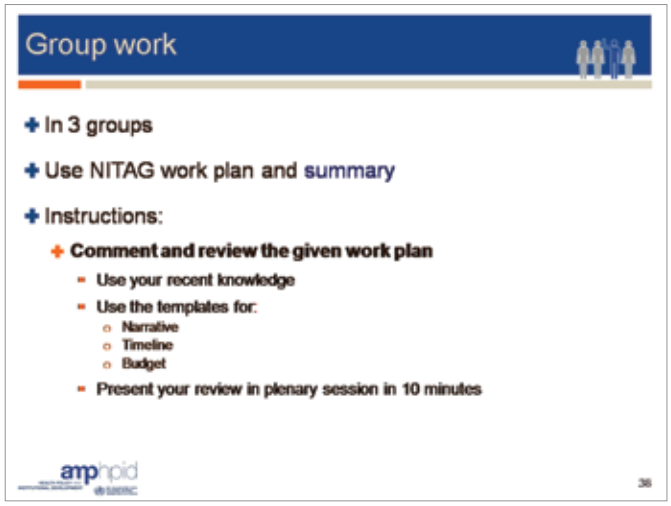
Slides	Facilitation methods
	**Presentation:** Invite participants to follow the slide presentation on the manual content using the hard copy of the summary 5'
	**Presentation:** 1. Emphasise the procedures for the conflict of interest declaration and the confidentiality agreement, and explain why they guarantee transparency and independence. 2. Invite participants to have a look at the templates for both declarations. **Q&A:** 3. Ask participants to give examples of what could generate conflicts of interest. 10'
	**Presentation:** 1. Stress the roles and responsibilities of the NITAG Secretary, NITAG Chair, and the working group. 2. Explain in particular the working group functioning. 5'

Slides	Facilitation methods
	**Presentation:** **Q&A** 5'
	**Q&A** 1. Present to participants: The work plan describes all activities of the NITAG and its Executive Secretariat. The activities are classified by main objectives. The work plan is composed of three complementary documents: a narrative description of the activities, the activity timeline, and the operating budget. 2. Ask the participants to place these 3 steps in order. 5'
	**Presentation:** Stress the roles and responsibilities of the MoH, NITAG Chair, NITAG Secretariat, and core members. 5'

Slides	Facilitation methods
	**Brainstorming:** Which main activities do you think your NITAGs may engage in? 1. Invite participants to suggest activities 2. Write on the flip chart all suggested activities 10'
	**Presentation:** Then present the main suggested categories of activities. 5'
	**Presentation:** 5'

Slides	Facilitation methods
	**Presentation:** of the 3 key documents of the work plan: 1. The narrative template 5'
	**Presentation:** of the 3 key documents of the work plan: 2. The timelines template 5'
	**Presentation:** of the 3 key documents of the work plan: 3. The budget template Emphasise the complementarity and consistency between the three documents: narrative, timeline, and budget. **Q&A** 10'

Slides	Facilitation methods
	Presentation: 5'
	Presentation: Invite participants to read Annex 5 of the summary 3'
	Presentation: Invite participants to read Annex 5 of the summary 2'

Slides	Facilitation methods
 *Objective: the aim of this exercise is to review and comment on a NITAG work plan from country X or one from participating countries, using the template provided as a guideline, in 3 small groups.*	**Group work:** 1. Organise participants in 3 groups and give to each: - an existing work plan (from country X or one from participating countries) - a flip chart - markers (5') 2. Ask participants to review and comment on the given work plan using their recent knowledge and templates provided as a guideline. 3. Highlight the points which are well addressed in the manual and the missing points for the: - Narrative plan (30') - Timeline (30') - Budget (30') 4. Prepare 3 slides or 3 flip chart sheets to present well addressed points and the missing points for 1) the narrative plan, 2) the timeline, and 3) the budget 5. 3 participants from each group report back in plenary with slide or sheet supports. (30' or 10' per group) 120'



Supporting Independent
Immunization and Vaccine
Advisory Committees



T R A I N I N G 1

ESTABLISHMENT AND MODE OF OPERATIONS OF AN EFFICIENT NITAG

SUMMARY



FOR
PARTICIPANT

TABLE OF CONTENTS

NITAG TOOLS

SUMMARY FOR PARTICIPANT 6

TARGET AUDIENCE

PURPOSE

NOTE

1. NITAG OVERVIEW 7

2. MODE OF OPERATION 8

3. FINANCIAL CONSIDERATIONS 10

APPENDIX 1: CONFLICT OF INTEREST DECLARATION 11

APPENDIX 2: CONFIDENTIALITY AGREEMENT 18

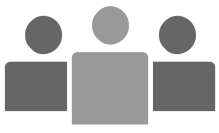
APPENDIX 3. GUIDANCE FOR DEVELOPMENT OF THE NITAG ANNUAL WORK PLAN 20

APPENDIX 4: GUIDANCE FOR DEVELOPING WORKING GROUP TOR 24

APPENDIX 5: NITAG MONITORING AND EVALUATION 26

Templates for developing an internal procedures manual and the work plan can be downloaded from the NITAG Resource Center: www.nitag-resource.org

NITAG TOOLS



FOR

PARTICIPANT

DRAWING UP THE NITAG'S INTERNAL PROCEDURES MANUAL

TARGET AUDIENCE

NITAG technical and scientific secretariat

PURPOSE

- Assist the technical and scientific secretariat in drawing up the NITAG's internal procedures manual

NOTE

- The internal procedures manual sets forth the rules and procedures applicable to the NITAG for its establishment and operations
- The secretariat can use this document as a framework, making the necessary amendments in line with the specific national context
- The internal procedures manual must include the NITAG's terms of reference, as stated in the official document establishing the NITAG
- Each NITAG core member must sign the internal procedures manual prior to the launch of the NITAG

The manual will include the following sections:

- NITAG overview
- Mode of operation
- Financial considerations
- Appendices

The following table lists items that should be described in each section.

1. NITAG OVERVIEW

LIST OF ITEMS TO CONSIDER IN DEVELOPING THIS SECTION	COMMENTS
SECTION 1.1 NITAG'S DEFINITION (REFER TO THE DECREE, ORDER, OR MINISTERIAL NOTE)	
• Name of the NITAG, NITAG acronym • Nature, date, and reference of the official document on the NITAG establishment • NITAG's mission • Relationship/situation with respect to other committees • Nature, date, and reference of the official document on member appointment • NITAG's composition and definition of the different types of members: > Core members > Ex-officio members (representatives of government entities) > Liaison members (representatives of technical partners, organisations, NGOs) > Observers > Organisation hosting the NITAG's scientific and technical secretariat	
SECTION 1.2 NITAG'S TERMS OF REFERENCE (REFER TO THE DECREE, ORDER, OR MINISTERIAL NOTE)	
• Members' roles and duties > Roles, prerogatives, and duties for each category of members in running the committee (right to vote, duty of active participation of all members): core members, ex-officio members, liaison members, scientific and technical secretariat, Chairperson • Members' term > The nomination procedure (appointment by the MoH) > Term of office > Number of terms > Whether full members may be appointed again after serving for the maximum number of years and terms > Chairmanship rotation schedule > Membership renewal procedure (try to maintain some stability) > List of the circumstances for excluding members > Measure in the event that the Chairperson is away for a long period of time (specify period)	This section must specifically explain who is responsible for: • Convening meetings • Preparing meeting proceedings • Preparing meeting agendas and logistics • Drafting reports and minutes • Sending reports and minutes • Archiving documents, including declarations of interest and confidentiality agreements • Coordinating working groups • Preparing annual technical and financial reports • Submitting reports to the authorities • Communicating with the authorities and the public • Updating website

2. MODE OF OPERATION

LIST OF ITEMS TO CONSIDER IN DEVELOPING THIS SECTION	COMMENTS
SECTION 2.1 DRAWING UP THE NITAG WORK PLAN	
• The consultation process for identifying priority issues to be addressed by the committee in the current year or in the following years • Sections of the work plan • Method for drafting and finalising the work plan • Circumstances for reviewing the work plan • The monitoring and evaluation framework > Determination of the indicator selection and measurement system > Determination of assessment/external review intervals, system for drawing up the review's terms of reference > Annual reports may include a section referring to certain process indicators	• The plan can be either annual or multiannual. • The work plan will be backed up with an activity monitoring and assessment plan. The indicators must allow for the assessment of the process, results, and impact of the committee. The indicators may be selected from the list proposed by WHO.
SECTION 2.2 HOLDING MEETINGS	
• **Convocation** > Procedure > Required timelines ahead of the meeting for sending notifications, agendas, and reference documents • **Nature of the meeting** > Open vs closed meetings > Procedure for when the committee invites external persons • **Frequency of meetings** > Number of scheduled plenary meetings per year > Procedures for extraordinary meetings	• The preparatory documents should be sent at least one week in advance by the NITAG secretariat. • Meetings should be held at least once a year, but it is highly recommended to meet at least twice a year.
SECTION 2.3 CONFLICT OF INTEREST DECLARATION AND CONFIDENTIALITY AGREEMENT	
• **Conflict of interest declaration** > Times of year when the annual conflict of interest (CoI) declaration form is to be signed > Procedures for updating this declaration • **Confidentiality agreement** > Members are expected to follow rules of precautionary principle > Procedures for signing the confidentiality agreement before a meeting if necessary	• It is advised that CoI forms be signed at the appointment of the committee and at the beginning of each year and updated. before each meeting if necessary • For more details on the conflict of interest declaration and templates, please refer to Appendix 1. • Refer to Appendix 2.

LIST OF ITEMS TO CONSIDER IN DEVELOPING THIS SECTION	COMMENTS
SECTION 2.4 DRAFTING, FINALISING, AND DISTRIBUTING THE MINUTES	
• Person in charge of the draft: secretariat or committee's rapporteur • Timelines for submitting draft minutes to members • Timelines for finalisation • Whether the reports are disclosed to the public and by which medium • Whether a period of embargo prior to dissemination to the public applies and, if so, what defines the lifting of the embargo • If a website is available, an exclusive link for members could be created for access to confidential documents • Responsibilities of the secretariat: > Providing administrative support in organising the meetings > Keeping NITAG archives up to date > Preparing annual technical reports > Monitoring expenses and preparing financial reports	
SECTION 2.5 PREPARING RECOMMENDATIONS AND DECISION-MAKING	
• Process for the preparation of discussions on a recommendation > Responsibilities of the secretariat and the Chairperson : develop framework and research questions > Validation of the framework and research questions in a plenary session • Organisation of a working group (WG) > WG appointment period: appointed for a set period of time > Procedures for WG establishment and responsibilities of the secretariat and the Chairperson in the elaboration of the WG terms of reference (ToRs) > Appointment letter to the WG Chair and secretariat: ToRs, list of questions to be addressed, timelines, and deliverables > WG composition and selection procedures: a Chair selected from NITAG core members, a secretariat, at least one NITAG core member, a rapporteur, possibly non-core members and external experts > WG coordination: by the scientific and technical secretariat • Decision-making process > Periods and systems for distributing the WG's reports to NITAG members > Voting procedure: majority vs unanimous consensus	• The purpose of establishing a working group is to prepare the technical dossier on the topic under consideration. The working groups collect evidence on the different thematic areas that will inform the recommendation. • Refer to Appendix 4 *"Guidance for developing WG ToR"*.

LIST OF ITEMS TO CONSIDER IN DEVELOPING THIS SECTION	COMMENTS
SECTION 2.6 SUBMISSION OF APPROVED RECOMMENDATIONS TO NATIONAL AUTHORITIES	
• Submission timelines and channel • Responsibilities of the NITAG Chairperson for submission to national authorities • Description of the position of the recipient of the recommendation at the MoH • Monitoring system	

3. FINANCIAL CONSIDERATIONS

LIST OF ITEMS TO CONSIDER IN DEVELOPING THIS SECTION	COMMENTS
SECTION 3.1 BUDGET SECTIONS	
• List the different costs included in the NITAG operating budget • The costs are grouped into sections such as: > Producing scientific documents: activities for preparing and issuing recommendations, resources needed > Strengthening NITAG capacities: orientation workshop, training programmes, study visits > Ensuring NITAG functioning: appointment, equipment for the secretariat, development of tools and documents, logistics and administrative organisation of NITAG meetings > Assessing NITAG performance: expense monitoring, advocacy for resource mobilisation, monitoring and evaluation	
SECTION 3.2 SOURCES OF FUNDING	
• Available and potential sources of funding > MoH > Partners: duration of support, agreement, ToRs • Activities ensuring financial viability included in the work plan	

APPENDIX 1: CONFLICT OF INTEREST DECLARATION

REPUBLIC OF ... *(MENTION COUNTRY NAME)*
(FULL NAME OF MINISTRY OF HEALTH OF THE COUNTRY)
(ADD MINISTRY OF HEALTH'S LOGO)
(FULL NITAG TITLE, FOLLOWED BY ITS ACRONYM)

1. INTRODUCTION

To ensure integrity and trust by the authorities and the scientific community, ... *(specify NITAG acronym)* requires that its members, as well as any invited resource persons (to plenary sessions, extraordinary sessions, working groups, etc.), declare their connection with any entity or organisation, public or private, whose field of expertise or intervention may create a conflict of interest with the expertise of the committee.

A conflict of interest designates a conflict between the public functions and private interests of an official which could adversely affect the performance of his/her official duties[1]. The declaration of conflict of interest from members of .... *(specify NITAG acronym)* will help avoid situations in which specific interests could affect their impartiality. Core members should not represent the interests of a particular group or of an interested party. They should refrain from advocating policies, opinions and products of the organisation in which they work.

Independence from government is defined by the absence of direct or indirect links of supervision in the immunisation programme or preferably more widely within the programme of the Ministry of Health. Members should feel free and encouraged to express their opinions even if they are in conflict with those of the immunisation programme's officials or the policy of the Ministry of Health.

Some critical information for the committee's work can only be obtained by establishing contact with vaccine producers. In addition, leading national experts in the field of vaccines and immunisation often have links with various interest groups, such as industry, professional associations and governments[2].

This search for conflicts of interest requires a certain level of rigour to distinguish between a potential bias caused by a conflict of interest and the need for expertise in vaccinology. The goal of such work is not only to identify people without any conflict of interest, but also to prevent potential conflicts both in a transparent and ethical way.

[1] *Bertok J, Managing conflict of interest in public service: OECD guidelines and Country Experiences, Organization for Economic Cooperation and Development (OECD) publications, Paris, 2003*

[2] *P. Duclos, National Immunisation Technical Advisory Goups (NITAGs): Guidance for their establishment and strengthening, Vaccine 28S (2010) A18-A25.*

2. TYPES OF CONFLICTS OF INTEREST

a. Personal interests

"Personal interests" involve payment to a member. The main examples are:

- **Consultancy:** any consultancy, directorship, position in or work for the industry, which attracts regular or occasional payments in cash or kind.
- **Fee-paid work:** any work commissioned by the industry for which the member is paid in cash or kind.
- **Shareholdings:** any shareholding or other beneficial interest in shares of the industry. This does not include shareholdings through unit trusts or similar arrangements where the member has no influence on financial management.

b. Non-personal interests

"Non-personal interests" involve payment for the benefit of a department run by a member, but not to the member personally. The main examples are:

- **Fellowships:** the holding of a fellowship endowed by the industry.
- **Support by the industry:** any payment, other support or sponsorship by the industry which does not convey any pecuniary or material benefit to the member personally but which does benefit their position or department, for example:
  - A grant from a company for the running of a unit or department for which the member is responsible;
  - A grant or fellowship or other payment to sponsor a post or a member of staff in the unit for which the member is responsible. This does not include financial assistance for students;
  - The commissioning of research or other work by, or advice from, staff who work in a unit for which the member is responsible.

Members are required to declare their interests in relation with the committee's agenda. They must state whether the interests are personal or non-personal and whether they are specific or non-specific to the topic or product considered by the committee. Interests are considered "relevant" if they occurred within the twelve (12) months preceding the inauguration of the new members and existing members. Any members who have doubts about the statement of interest or the procedure are required to inform the Chairperson for review.

3. CONFLICT OF INTEREST DECLARATION PROCEDURE

This declaration is made through a form which all committee members complete prior to the *... (specify NITAG acronym)*'s establishment and update annually. It is sent to *.... (Full name of Ministry of Health of the country)* and released as needed.

Before each committee meeting (plenary session, extraordinary session) and when the working groups are appointed, an updated declaration is prepared by the Secretariat of *.... (specify NITAG acronym)* based on potential changes related to items on the agenda. NITAG members have to complete this updated declaration if necessary.



Members of .... *(specify NITAG acronym)* who did not complete a conflict of interest declaration must withdraw from the committee or its working groups.
Any reported interests may be revealed during the meeting, possibly published succinctly online and/or made available to the public upon request.

Affirmative answers to the questions on the form will not lead to the de facto exclusion or limitation of participation in committee meetings of the member involved. The Chair of .... *(specify NITAG acronym)* is responsible for the analysis of the completed forms to determine the potential existence of a conflict of interest.
After examining the contents of the conflict of interest declaration form, the Chair may decide whether or not a conflict of interest applies and whether this is a minor or major conflict.

If a conflict of interest is reported, the Chair applies one or a combination of the following three options:

- The member may be invited to attend meetings or work on condition that his/her interest is publicly disclosed;
- The member may be asked not to take part in a portion of the meeting, discussions or work in relation to his/her interest or not to participate in related decision-making;
- The member may be asked not to take part in the meeting or work.

The usual procedure is as follows:

- Members with a specific personal interest will be asked to leave the room for the discussion and decision-making.
- Members with a non-specific personal interest may participate in discussions but may not take part in the decision-making.
- Members with specific non-personal interests may answer direct questions from the Chair but may not take part in the decision-making.
- Members with non-specific non-personal interest may take part in the discussions and the decision-making.

Any conflict of interest is publicly disclosed to other participants at the beginning of activities and in the report or any other document produced at the end.

In an audit or further examination, the contents of a member's conflict of interest declaration form could be made available to persons who are not part of .... *(specify NITAG acronym)* if the member's objectivity is disputed and the Chair of .... *(specify NITAG acronym)* considers revelation as a major concern for their credibility.

By completing the attached form the member hereby agrees to these terms.

4. ANNUAL CONFLICT OF INTEREST DECLARATION FORM TEMPLATE

(To be filled in by each member at the appointment of the committee and at the beginning of each year)

First names & last name: .....

Inauguration date of ***... (specify the NITAG's acronym):*** .....

List of topics on the annual work plan of ***... (specify the NITAG's acronym):***

1. .....
2. .....
3. .....
4. .....

1. Are there any factors that can affect your impartiality in the work relating to the items on the agenda?

Yes ❑ No ❑

If so, which ones?

.....
.....
.....
.....
.....

2. Could the findings of this work positively or negatively affect the interests of persons with whom you are personally or professionally related (child over the age of majority, siblings, colleagues, etc.)?

Yes ❑ No ❑

If so, explain:

.....
.....
.....
.....
.....

3. Do you have any financial participation (shares, bonds or equity instruments) in the company (or in the direct competitor) producing or marketing a product in relation with one of the topics on (specify the NITAG's acronym) agenda?

Yes ❑ No ❑

4. Have you been in the last three (3) years owner, manager, partner, employee, member of a decision-making body of the company (or of the direct competitor) producing or marketing a product in relation with one of the topics on (specify the NITAG's acronym) agenda?

Yes ❑ No ❑

5. Have you been involved in the last three (3) years in any other types of regular activities for the company (or for the direct competitor) producing or marketing a product in relation with one of the topics on (specify the NITAG's acronym) agenda?

Yes ❑ No ❑

6. Have you been involved in the last three (3) years in any scientific work (tests, studies, evaluation, etc.) with the company (or with the direct competitor) producing or marketing in relation with one of the topics on (specify the NITAG's acronym) agenda?

Yes ❑ No ❑

If so, in what capacity?

- Epidemiological studies related to the disease under study ❑
- Clinical trials ❑
- Other (specify) ❑

Are these studies paid?

- Yes ❑
- No ❑

7. Have you attended in the past three (3) years a meeting (conference, symposium, training, etc.) organised by the company (or by the direct competitor) producing or marketing a product in relation with one of the topics on (specify the NITAG's acronym) agenda?

Yes ❑ No ❑

If so, in what context?

- Speaker ❑
- Participant ❑
- Member of the organising/scientific committee ❑
- Other (specify) ❑

Under what conditions?

- Travel and accommodation expenses covered by the company ❑
- Fees paid by the company ❑
- Other (specify) ❑

8. Have you received in the past three (3) years financial support from a partner (organisation, institution, foundation, etc.) for conducting an activity that might have a link with the topics on the agenda?

Yes ❑ No ❑

9. Are any of your relatives employed by the company (or by the direct competitor) producing or marketing a product in relation with one of the topics on (specify the NITAG's acronym) agenda?

Yes ❑ No ❑

If yes,

- Spouse ❑
- Child ❑
- Other (specify) ❑

Comments:

.....

.....

.....

.....

.....

.....

I declare on my word of honour that the information provided above is true and complete. I also undertake to inform the Secretariat of ***... (specify the NITAG's acronym)*** of any subsequent changes and complete a new form to describe any applicable changes.

Date and signature:

5. UPDATED CONFLICT OF INTEREST DECLARATION FORM TEMPLATE

(To be filled in by members in case of a change related to specific topics on the agenda)

First names & last name: .....

Meeting date of .... *(specify the NITAG's acronym):* .....

....

List of items of the agenda of .... *(specify the NITAG's acronym):*

1. .....
2. .....
3. .....
4. .....

Describe the type of conflict of interest:

.....

.....

.....

.....

I declare on my word of honour that the information provided above is true and complete.

Date and signature:

APPENDIX 2: CONFIDENTIALITY AGREEMENT

Members of the National Immunisation Technical Advisory Group (NITAG) may use this template for the preparation of the Confidentiality Agreement to be filled in by members prior to any meeting and by experts invited occasionally, to safeguard the confidentiality of the information covered by rights of property.

This template stems from that of the Strategic Advisory Group of Experts (SAGE) available online at: http://who.int/immunization/sage/Full_SAGE_TORs.pdf

Countries are invited to use this document as a template, which they should however adapt to their needs, in line with the special characteristics or circumstances applicable to them.

1. TERMS

1. Commercial companies, university research centres, hereinafter referred to as "institutions", as well as scientists (individuals), regularly provide or present elements relating to the research, products, and processes, hereinafter referred to as "information", to the NITAG. Such information is considered by said commercial companies, research centres, and individuals as their property. To guarantee suitable use of such information by the NITAG, whilst safeguarding the rights of property of the institutions or individuals, the Undersigned hereby undertakes to maintain the confidentiality of this information.

2. The information provided by such institutions or individuals, partners such as AMP/SIVAC, or other committees during meetings, via online collaborative work platforms, during conference calls, or other channels, is to be considered by the Undersigned as confidential, unless otherwise specified by the institution or individual in question.

3. The Undersigned hereby undertakes to handle such confidential information as information covered by rights of property and undertakes not to make any copies or disclose such information, either partially or in full.

4. The Undersigned undertakes to return any information considered as confidential to the institution/individual upon request thereof.

5. The Undersigned will not be bound to secrecy if he/she is able to prove:

a) that he/she had the information before the discussion disclosing all or part of the confidential information owned by the institution/individual;

b) that the information was under public domain at the time it was disclosed by the institution or individual;

c) that the information has fallen into public domain by no fault of the Undersigned; or

d) that the Undersigned was given access to the information by a third party, in compliance with the legal and confidential obligations of the institution/individual.

6. This confidentiality agreement is applicable throughout the period during which the Undersigned is involved in the group or committee activities, irrespective of form, and for a period of five (5) years running from the end of their term of office, unless otherwise specified by the institution/individual.

2. DESCRIPTION

Topic and source of information:

.....
.....
.....
.....
.....
.....
.....
.....
.....
.....

Name, title and position of the Undersigned:

.....
.....
.....

Date and signature:

APPENDIX 3: GUIDANCE FOR DEVELOPMENT OF THE NITAG ANNUAL WORK PLAN

TARGET AUDIENCE

NITAG Executive Secretariat and NITAG members

PURPOSE

- The purpose of the document is to present some guidance for the development of the work plan of the NITAG and its Executive Secretariat.

COMMENT

- The work plan should include all activities and aspects of work of the NITAG and its Secretariat.
- The initial work plan covers the activity for the first year of the NITAG, and a yearly work plan will be developed for the following years.



1. DEVELOPMENT OF THE WORK PLAN

The work plan describes all activities of the NITAG. Usually, it is recommended to have a yearly work plan.

The purpose of the work plan is to establish a road map with clear milestones and deliverables to ensure the development of high quality, evidence-informed recommendations and to monitor activities aimed at achieving the NITAG's mission.

The work plan should be developed by a relevant team representing the NITAG and its Executive Secretariat (e.g. the Secretariat and a sample of NITAG members, with participation from the Chairperson).

2. DOCUMENTS TO BUILD AND PRESENT THE WORK PLAN

The work plan is complete when the activities are described with relevant information on related timelines and budget.

The three following templates are provided:

- Template for narrative description of activities
- Template for the budget
- Template for the timeline summary

2.1. NARRATIVE DOCUMENT TEMPLATE

Group the activities into at least four main objectives; each objective can then contain one or several activities (this can be modified depending on experience and needs of the NITAG):

1. **Producing scientific documents, core activity of the NITAG**
2. **Strengthening NITAG through capacity building of the Secretariat and NITAG members**
3. **Ensuring NITAG functioning**
4. **Assessing NITAG performance**

How to use the narrative template:

For each activity, the following information should be provided:

- Description of the activity (objective, context, details about implementation, etc.)
- Timelines and persons in charge. This can be written in a table with the following information:
  - List of activities/expected results
  - Timelines
  - Persons responsible for the activity (additional persons can be involved in conducting the activity)

Producing scientific documents

Activity 1.1: **(Name of the activity)**

Description: (Describe the activity)

Timelines and persons in charge: (Give details about the activities, the timelines, the person responsible for the work – you can use the table below)

What?	When?	Who?	Comment

Terms of partners' support: (Explain the agreed upon support from partners for this activity, if any)

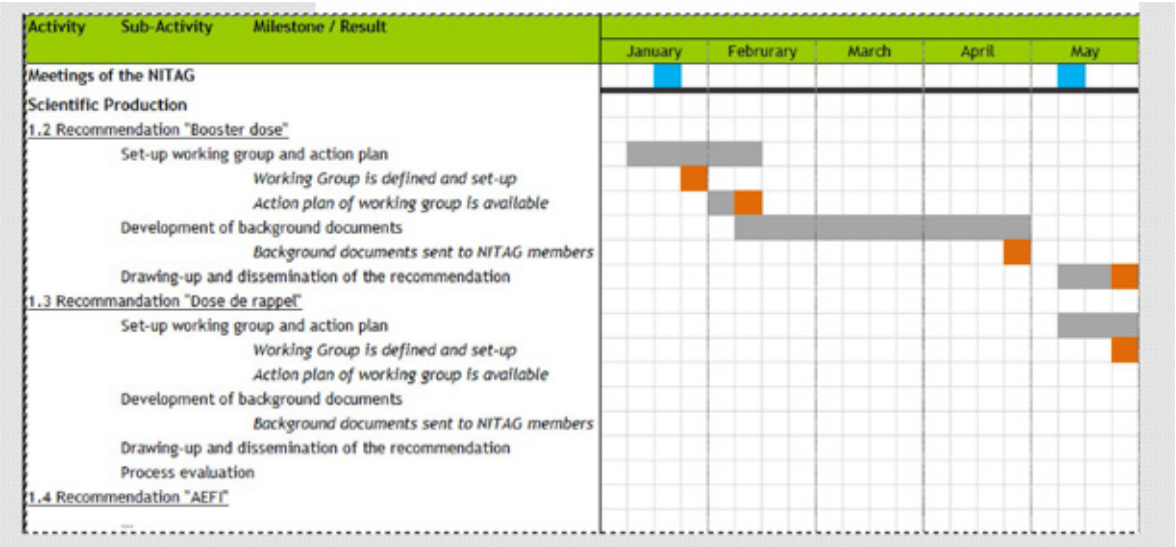
2.2. TIMELINE TEMPLATE

On the basis of the narrative document, the "Timeline summary" Excel sheet can be completed.

How to use the timeline summary template:

The basic principle is to take the same identification for each component/activity, and to colour the activities (for their whole expected duration) and the expected deliverables. The proposed template enables the identification of activities/results in months and weeks. Name the component/activities as they are in the narrative document.

- If relevant, split the activity into sub-activities
- Indicate expected results
- Colour in blue the expected dates for NITAG meetings at the top of the document
- Colour in grey the duration of each activity (sub-activity)
- Colour in orange the date when results are expected



2.3. BUDGET TEMPLATE

The objective here is to develop an operating budget in accordance with the narrative and timeline.

How to use the budget template:

- The budget should be linked to the activities, with a direct reference to the activities described in the narrative document
- Exchange rate between the local currency and US$ (or €) should be provided
- For each activity, write the description of the item and the unit cost
- There are two possibilities for the calculation of the total amount per line:
  - > Some expenses depend on the number of meetings (e.g. catering for participants): use the two columns "nb per meeting" and "nb meetings"
  - > Some expenses do not depend on the number of meetings: use only the column "nb"

Activitiy	Category Cost	Detail	Unit Cost (local currency)	Unit Cost in US $	Nb	Nb per meeting	Nb meetings	Total budget (US $)	National resources (US $)	partners funding (US $)	Comments
Scientific production											
1.1 Recommendation [Name of the Reco]											
	Item category (travel, supplies…)	Detail of the item 1 (if any)									
	Item category (travel, supplies…)	Detail of the item 2 (if any)									
1.2 Recommendation [Name of the Reco]											
	Item category (travel, supplies…)	Detail of the item 1 (if any)									
	Item category (travel, supplies…)	Detail of the item 2 (if any)									
1.3 Recommendation [Name of the Reco]											
Sub Total - Support for scientific production								-			
Capacity strengthening component											
2.1 [Name of Activity]											
	Item category (travel, supplies…)	Detail of the item 1 (if any)									
	Item category (travel, supplies…)	Detail of the item 2 (if any)									
2.1 [Name of Activity]											
	Item category (travel, supplies…)	Detail of the item 1 (if any)									
	Item category (travel, supplies…)	Detail of the item 2 (if any)									
Sub Total - Technical / Scientific capacity building								-			

APPENDIX 4: GUIDANCE FOR DEVELOPING WORKING GROUP ToR

1. BACKGROUND

Provide background information on the NITAG, how it was established and its purpose.

2. DECISION TO ESTABLISH NITAG WORKING GROUP AND ITS PURPOSE

- Provide the justification for establishing Working Groups (WGs) and explain how they are intended to contribute towards NITAG deliberations and operations. Refer to the NITAG meeting where decision to establish the WG was taken.
- Describe how WGs are to be established
- When issuing specific Terms of Reference (TOR) to a WG, provide information on how that particular WG was formed

3. TERMS OF REFERENCE OF THE WORKING GROUP

- The following information, specific to each WG, should be provided:
  - A background of the issue referred to the WG
  - The question examined by the NITAG and a general outline of the issues to be deliberated on by the WG
  - The name of the WG Chairperson
  - The expected duration of the WG
- Outline the timeframe for the WG to submit their work plan, timelines and recommendation framework following establishment of the WG.

4. WORKING GROUP COMPOSITION AND SELECTION OF MEMBERSHIP

- Describe how the Chairperson of the Working Group (WG) is appointed
- Provide a description of the WG composition and size
- Describe who is responsible for nominating members to the WG, what specific expertise is required and the time frame in which nomination of members to the WG is to be concluded following receipt of the WG ToRs
- Describe the process of vetting and final approval of nominated members
- Describe the role of the WG Chair, WG secretary and WG members in the functioning of the WG

5. MODUS OPERANDI

5.1. SETTING UP WORKING GROUP OPERATIONS

- Describe the need, frequency and process for signing confidentiality agreements and conflict of interest forms
- Describe how conflicts of interest are recorded/declared during WG meetings/ operations



- Explain how WG meetings will take place and who will be responsible for facilitating preparations for WG meetings
- Describe how meeting reports are generated and shared and the persons responsible for the generation and sharing of reports
- Outline who should be provided with meeting reports

5.2. DEVELOPMENT OF WORKING GROUP TECHNICAL REPORTS

Briefly describe each of the stages to be followed in the development of a technical report, i.e.:

- Review of the issue for discussion
- Development of a work plan and timelines
- Formation of the recommendation framework
- Submission of the WG work plan, timelines and recommendation framework to NITAG for review and approval
- Collection, review, and synthesis of evidence
- Documentation of the process
- Assessing the quality of evidence
- Documentation of the outcome
- Preparation of a technical report

It is essential to provide a detailed description of how to define a recommendation framework, collect and synthesise evidence, and develop an evidence-based technical report. This information may be presented as an appendix to the ToRs. Alternatively, reference may be made to the NITAG internal procedures manual or another reference manual containing this information. An outline of the technical report will be provided in the appendices.

5.3. SUBMISSION OF WORKING GROUP TECHNICAL REPORTS

- Explain the process for submitting WG technical reports to the NITAG
- Describe who is permitted to issue statements on behalf of the NITAG to the relevant government authority or the public

5.4. PAYMENT

- Define who is eligible for reimbursement/payment and which expenses are permissible
- Outline whether external consultants will be paid and the person responsible for facilitating payment

5.5. MANAGEMENT OF CONFLICT OF INTEREST/UNDUE INFLUENCE

- Describe how conflicts of interest are to be documented and managed
- Outline the restrictions in WG participation and/or decision-making applicable to individuals with identified conflicts of interest
- Describe the discretionary authority of the NITAG Chairperson and/or the WG Chairperson in making judgements on conflicts of interest or undue influence cases in order to preserve public trust in the integrity of NITAG operations

APPENDIX 5: NITAG MONITORING AND EVALUATION

There are 6 criteria for monitoring essential NITAG functionality; a properly functioning NITAG meets all 6 criteria.

INDICATORS OF NITAG FUNCTIONALITY	
Legislative or administrative basis for the advisory group	☑
Formal written terms of reference	☑
At least 5 different areas of expertise represented amongst core members	☑
At least one NITAG meeting conducted per year	☑
Distribution of agenda and background documents at least one week prior to meetings	☑
Mandatory disclosure of any conflict of interest	☑

PROCESS INDICATORS	RELATED QUESTION
Legislative/ administrative basis	Is there a legislative or administrative basis for the NITAG?
Advisory role only	Is the NITAG's role solely technical advisory?
Terms of reference	Are there formal terms of reference for the NITAG?
Membership	Is there a clearly defined process to become a core member and the Chairperson of the NITAG? Are the main areas of expertise recommended by WHO represented by core members? Are there non-core members? Are there rules for the core member rotation process?
NITAG functioning SOPs	Are there clearly defined NITAG functioning Standard Operating Procedures (SOPs)?
Independent Chairperson	Is the NITAG Chairperson independent from the MoH and the immunisation programme?

PROCESS INDICATORS	RELATED QUESTION
Number of meetings	How many meetings were held in each of the past 3 years?
Agenda and background documents	Were the agendas and background documents distributed and received at least one week in advance of each of the past 3 NITAG meetings? Is there a conflict of interest policy in place? Were all core members asked to declare their interests at the beginning of the past 3 NITAG meetings?
Official requests for recommendations received and addressed	How many official requests for recommendations has the NITAG received from the MoH and/or the immunisation programme? How many of them has the NITAG addressed?

OUTPUT INDICATORS	RELATED QUESTION
Evidence-based methodology for recommendations	How many recommendations were issued by the NITAG? How many of these recommendations made reference to peer-reviewed, published material?
Country-specific criteria for recommendations	How many recommendations issued by the NITAG were supported by local evidence or contextual information?
Vaccine availability and delivery capacity criteria for recommendations	How many recommendations issued by the NITAG took into account the vaccine availability and delivery capacity at the national level?

OUTCOME INDICATORS	RELATED QUESTION
MoH decisions made in consultation with the NITAG	How many MoH immunisation-related decisions were made in consultation with the NITAG?

SIVAC

Supporting Independent
Immunization and Vaccine
Advisory Committees

amphpid

HEALTH POLICY AND
INSTITUTIONAL DEVELOPMENT

WHO COLLABORATING CENTRE
FOR EVIDENCE-INFORMED
IMMUNIZATION POLICYMAKING

T R A I N I N G 2

ANALYSIS OF IMMUNISATION IN THE CONTEXT OF HEALTH SYSTEMS AND THE POLICY DECISION-MAKING PROCESS

SECTION A

THE INFLUENCE OF THE HEALTH SYSTEM ON NITAG RECOMMENDATIONS

SECTION B

STAKEHOLDER ANALYSIS AND MAPPING



FOR
FACILITATOR

TABLE OF CONTENTS

INTRODUCTION 5

TARGET AUDIENCE

PREREQUISITE SKILLS/KNOWLEDGE

TRAINING MATERIALS

SECTION A
THE INFLUENCE OF THE HEALTH SYSTEM ON NITAG RECOMMENDATIONS

PRESENTATION OF THE SECTION 7

LEARNING OBJECTIVES

1. HEALTH SYSTEMS AND HEALTH SYSTEM ANALYSIS 8

1.1. THE HEALTH SYSTEM FRAMEWORK

1.2. THE HEALTH SYSTEM BUILDINGS BLOCKS

1.2.1. OVERALL OUTCOME

1.2.2. KEY HEALTH SYSTEM ATTRIBUTES

1.3. THE IMMUNISATION SYSTEM WITHIN THE HEALTH SYSTEM

1.4. HEALTH SYSTEM STRENGTHENING OR VERTICAL APPROACH

1.5. THE CONCEPT OF UNIVERSAL HEALTH COVERAGE (UHC)

2. THE ROLE OF THE NITAG 16

2.1. ANALYSIS OF HEALTH SYSTEM CHALLENGES

2.2. POLICY ADVICE INTERACTING WITH DIFFERENT KEY STAKEHOLDERS

REFERENCES 17

FACILITATOR INSTRUCTIONS 18

ANNEX 1: TABLE OF CONSTRAINTS 25

SECTION B
STAKEHOLDER ANALYSIS AND MAPPING

PRESENTATION OF THE SECTION 28

LEARNING OBJECTIVES

1. THE STAKEHOLDER ANALYSIS 29

1.1. PURPOSE

1.2. THE MAPPING & ANALYSIS TOOLS

1.2.1. IDENTIFICATION OF STAKEHOLDERS

1.2.2. PRIORITISATION

1.2.3. DATA COLLECTION

1.2.4. ANALYSIS

1.2.5. ENGAGEMENT STRATEGIES

2. STAKEHOLDER ANALYSIS IN THE CONTEXT OF IMMUNISATION 34

2.1. IMPLEMENTATION OF ENGAGEMENT STRATEGIES

2.2. RESOURCES NEEDED TO CONDUCT A STAKEHOLDER ANALYSIS

REFERENCES 35

FACILITATOR INSTRUCTIONS 36

ANNEX 1: POWER/INTEREST GRID 43

ANNEX 2: TABLE OF STAKEHOLDERS 44

INTRODUCTION

This training is presented in two sections A and B that are further introduced below.



TARGET AUDIENCE

- The secretariat, the Chair and members of the NITAG.



PREREQUISITE SKILLS/KNOWLEDGE

- Knowledge of NITAG mode of operations (sections A&B of Training 1) on NITAG establishment and operations



TRAINING MATERIAL

- PowerPoint presentation, instructions for the facilitator, summary for participant, templates and article references

SECTION A

THE INFLUENCE OF THE HEALTH SYSTEM ON NITAG RECOMMENDATIONS



FOR
FACILITATOR

PRESENTATION OF THE SECTION

This is an introduction to the concept of the health system and its building blocks; to understand how these influence immunisation programmes and how to use them in formulating NITAG recommendations. It explains the links between health systems and barriers to immunisation and the contextual factors related to policy advice to address these barriers.

The section includes a group exercise.



LEARNING OBJECTIVES

Knowledge and understanding of:

- The immunisation programme in the broader context of the health system;
- The structural environment within which immunisation-related decisions are being made and implemented;

And

- Improved capacity within NITAG to formulate relevant and influential recommendations, based on health system analysis.

1. HEALTH SYSTEMS AND HEALTH SYSTEM ANALYSIS

This section explains the concept of health system, its structure, and how the system works and how it contributes to health outcomes. To better understand the health system and its different parts the health system is usually broken down into "building blocks". The building blocks have been defined by WHO. The different building blocks are also explained in more detail. Together these building blocks constitute the "health system" (in a country, region, or district). The interrelationship of the building blocks is explained in more detail in this section. The deconstruction of the health system into building blocks helps to explain decision-making and the decision-making process in the system.

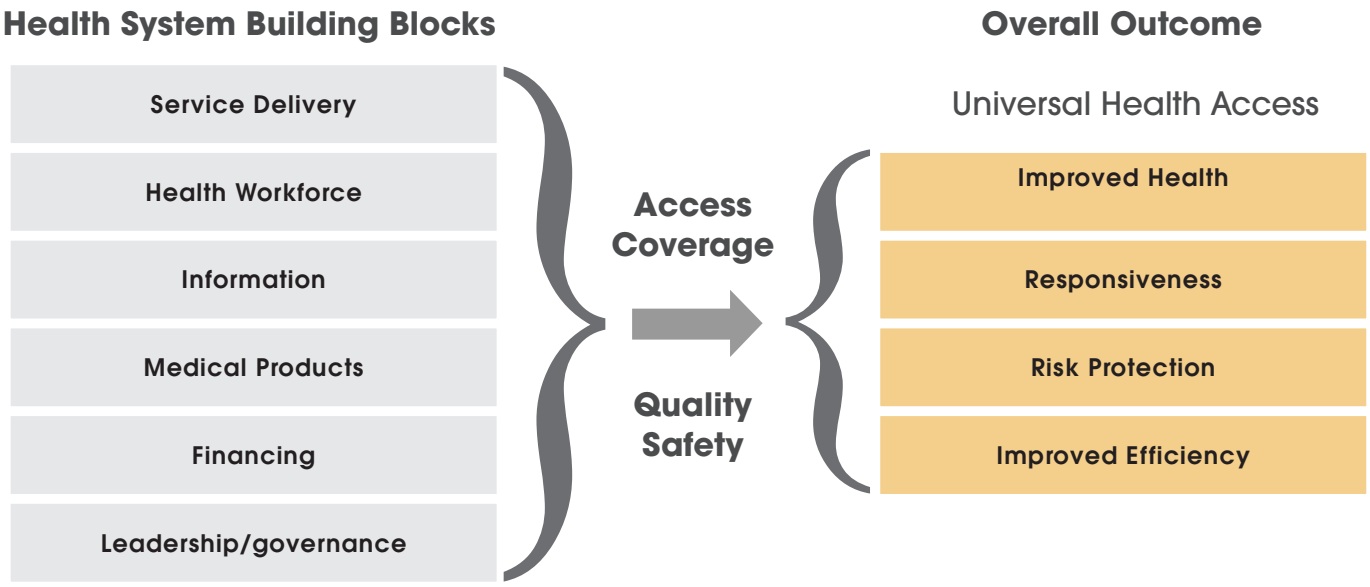
The health system constitutes the structural environment within which health policies are being formulated and health services are being delivered. It is important to understand this structure and how it works in order to be able to make credible recommendations for delivery of health services and more specifically to address and lift barriers to immunisation.

Furthermore it is important for a NITAG to be able to identify and analyse policy issues and how these are embedded in a health system structure cutting across different building blocks and impacting on outcome. Equity for example cuts across health system building blocks, but the level will be specific to each country context. Equity in financing of health services and equity in access to health services are major barriers to immunisation in low income countries. NITAGs need to know how to make this analysis and use that knowledge to make a relevant policy recommendation.

1.1. THE HEALTH SYSTEM FRAMEWORK

A health system is not an end in and of itself; it is instead a means to achieve health outcomes in a population. Health systems should be a vehicle for accelerating progress on health-related goals, but as a vehicle it is subject to constraints impeding progress. A health system framework helps policy-makers, including NITAG, to identify challenges and make relevant recommendations with the aim of achieving better health in the population.
The health system framework includes an input side (the building blocks) and an output/outcome side (the expected impact of the health system on a population).

THE WHO HEALTH SYSTEM FRAMEWORK



The building blocks are the combined input. The inputs have to be combined so that access, coverage, quality and safety are maximised, in order to reach the overall outcome and goals:

- Improved health of individuals, families and communities
- Responsiveness to health threats
- Protection against financial consequences of ill-health
- Improved efficiency ensuring best use of resources available

The aim is to address inequitable health outcome in society by moving towards universal health coverage.

1.2. THE HEALTH SYSTEM BUILDINGS BLOCKS

Service delivery

This building block describes the component of service delivery in the health system. For services to be provided there needs to be:

- Networks of health facilities, organised in health districts or local area networks with the back-up of specialised and hospital services, responsible for defined populations;
- Provision of a range of packages (basic package of care) with a comprehensive and integrated range of clinical and public health interventions, which responds to the needs of the population;
- Standards, norms, and guidance to ensure access and essential dimensions of quality: safety, effectiveness, integration, continuity, and people-centredness;
- Mechanisms to hold providers accountable for access and quality and to ensure consumer voice.

Human resources for health

This building block describes the component of health workforce in the health system. A properly performing workforce is one that is responsive to the needs and expectations of people, is fair and efficient to achieve the best outcomes possible given available resources and circumstances. Countries are at different stages of development of their health workforce but common concerns include improving recruitment, education, training, and distribution; enhancing productivity and performance; and improving retention. This requires:

- Arrangements for achieving sufficient numbers of the right mix (numbers, diversity, and competencies);
- Payment systems that produce the right kind of incentives;
- Regulatory mechanisms to ensure system-wide deployment and distribution in accordance with needs;
- Establishment of job-related norms, deployment of support systems and enabling work environments.

Health information systems

This building block describes the component of health information in the health system. Good governance requires good and reliable information on health outcome and health challenges. This specifically includes timely intelligence on:

- Progress in meeting health targets, which includes household surveys, civil registration systems and epidemiological surveillance, coverage surveys, etc.;
- Health financing data such as National Health Accounts (NHA) and an analysis of financial and other barriers to health services for the poor and vulnerable;
- Trends and needs for health workforce; on consumption of and access to pharmaceuticals and vaccines; on appropriateness and cost of technology; on distribution and adequacy of infrastructure, including cold chain equipment and capacity;
- Arrangements to make information accessible to all involved, including communities, civil society, health professionals, and politicians.

Essential medical products and technologies

This building block describes the component of medical products and technologies in the health system. Economically, medical products are the second largest component of most health budgets (after salaries) and the largest component of private health expenditure in low- and middle-income countries. Key components of a functioning system are:

- A medical products regulatory system for marketing authorisation and safety monitoring, supported by relevant legislation, enforcement mechanisms, an inspectorate and access to a medical product quality control laboratory;
- National lists of essential medical products, national diagnostic and treatment protocols, and standardised equipment per levels of care;
- A supply and distribution system to ensure universal access to essential medical products and health technologies through public and private channels, with focus on the poor and disadvantaged;
- A national medical product availability and price monitoring system;
- A national programme to promote rational prescribing.

Health financing

This building block describes the component of financing in the health system. Health financing can be a key policy instrument to improve health and reduce health inequalities if its primary objective is to facilitate universal coverage by removing financial barriers to access and preventing financial hardship and catastrophic expenditure. The following can facilitate these outcomes:

- A system to raise sufficient funds for health fairly, including through taxes, user fees, donor funds;
- A system to pool financial resources across population groups to share financial risks;
- A financing governance system supported by relevant legislation, financial audit and public expenditure reviews, and clear operational rules to ensure efficient use of funds.

Leadership and governance

This building block describes the governance component in the health system. Leadership and governance are context-specific, but common "good practices" in leadership and governance can be identified. These include:

- Ensuring that health authorities take responsibility for steering the entire health sector. Health and health challenges should not be left ungoverned;
- Defining, through transparent and inclusive processes, national health policies, strategies, and plans that set a clear direction for the health sector;
- Effective regulation through a combination of guidelines, mandates, and incentives, backed up by legal measures and enforcement mechanisms;
- Effective policy dialogue with other sectors;
- Mechanisms and institutional arrangements to channel donor funding and align it to country priorities.

1.2.1. Overall outcome

Health systems have multiple goals. The World health report 2000 (WHO) defined overall health system outcomes or goals as:

- Improved health for the population;
- Responsiveness to people's needs;
- Social and financial risk protection;
- Improved efficiency

There are also important intermediate goals: the route from inputs to health outcomes is through achieving greater access to and coverage for effective health interventions, without compromising efforts to ensure provider quality and safety.

1.2.2. Key health system attributes

Irrespective of how a health system is organised, there are some desired attributes for each building block that hold true across all systems.

- **Multiple, dynamic relationships**

A health system, like any other system, is a set of inter-connected parts that must function together to be effective. Changes in one area have repercussions elsewhere. Improvements in one area cannot be achieved without contributions from the others. Interaction between building blocks is essential for achieving better health outcomes.

- **Health system strengthening**

Health System Strengthening (HSS) is defined as improving the six health system building blocks and managing their interactions in ways that achieve more equitable and sustained improvements across health services and health outcomes. It requires both technical and political knowledge and action.

- **Is progress being made?**

A key concern of governments and others who invest in health systems is how to tell whether and when the desired improvements in health system performance are being achieved. Convincing indicators that can detect changes on the ground are needed.

1.3. THE IMMUNISATION SYSTEM WITHIN THE HEALTH SYSTEM

The immunisation system is embedded within the larger health system and has links to all the health system components. It is important to understand how the immunisation system is linked to the broader health system and its components and how decisions on broader issues also affect the immunisation system. For example: policy recommendations on health workforce can have a huge impact on immunisation services by affecting supply and training (quality) of health workers at facility level. Another example is policy recommendations on health financing which can impact access to funding for outreach services by health facilities, or supportive supervision carried out by the District Health Team. A third example is policy recommendations on integration of services (basic package, integrated child health services, etc.) which can lead to more resources for immunisation. The purpose of the analysis (by NITAG) is to understand the links, identify the policy areas, and make relevant recommendations with the aim of lifting barriers to Immunisation.

Health system barriers to immunisation

In order to better understand how the immunisation system is embedded in the larger health system, it is useful to look at examples of how poor health systems undermine the performance of immunisation programmes in developing countries. Some of these examples include:

- Unavailability of staff, transport and funds for immunisation activities at district level to provide outreach services (relevant building blocks: Service delivery, Health workforce, and Medical Products);
- Poor cold-chain maintenance (Relevant building blocks: Health workforce, Medical products);
- Failure to mobilise communities to ensure high demand for immunisation (Relevant building blocks: Service delivery, Health workforce, Governance);
- Failure to track available data on district immunisation coverage and vaccine stock levels (Relevant building blocks: Information, Governance);
- Failure to procure and stock vaccines and devices (Relevant building blocks: Financing, Medical products, Governance);
- Lack of health infrastructure (Relevant building blocks: Service Delivery, Medical Products, Governance).

1.4. HEALTH SYSTEM STRENGTHENING OR VERTICAL APPROACH

There is a lively debate about the merits of investing in health system strengthening (global approach) as opposed to having a vertical approach (invest in the immunisation system directly). International organisations such as Gavi The Vaccine Alliance and The Global Fund to Fight AIDS Tuberculosis and Malaria have swung back and forth between these two approaches.

Examples: During 2010-2012, Gavi The Vaccine Alliance, The Global Fund, and World Bank tried to set up the Health System Funding Platform to promote a global approach to health system strengthening and coordinate their support to health system strengthening. The effort proved to be difficult to implement in practice and when it failed both Gavi and the Global Fund went back to a more vertical approach of their cash-based support. Lately, the Ebola outbreak in Sierra Leone and Liberia has pushed donors and governments to return to a global approach to health system strengthening again.

What are the differences between a global approach and a more vertical approach?

A vertical approach can be better tailored to the objective of the support, such as supporting in-service training for vaccinators, or recruiting surge capacity. A global approach will on the other hand be more sustainable and provide a more stable infrastructure within which the immunisation system can function.

In the table below, some examples of health system strengthening interventions using a vertical or global approach are given.

HEALTH SYSTEM BUILDING BLOCKS	VERTICAL APPROACH	GLOBAL APPROACH
Service Delivery	Through separate project facilities and/or specific facilities	Through general facilities under government supervision
Health workforce	Temporary employee hired by the project	Government employee on the payroll
Information	Separate reporting through the project	Reporting through national Health Monitoring Information System (HMIS)
Medical products	Separate disease-specific channels	Through government channels
Financing	Project budget	Government budget
Governance	Separate project not part of NHSP	Part of National Health Strategic Plan (NHSP)

1.5. THE CONCEPT OF UNIVERSAL HEALTH COVERAGE (UHC)

The aim of health system strengthening is to address inequitable health outcomes in society by moving towards universal access to fair and responsive health services with social health protection. Universal health coverage (UHC), in respect to services and their financing, means that all people receive the health services they need without suffering financial hardship when paying for them. The full spectrum of essential, quality health services should be covered including health promotion, prevention and treatment, rehabilitation and palliative care.

Health financing for UHC is conceptualised in three dimensions.

These are:

- Population covered: What percentage of the population is covered by the services provided, and who are those not covered? In the case of immunisation, certain population groups in a country can be excluded (even if coverage is high).
- Cost of services covered: What percentage of the services is prepaid as opposed to paid out of pocket? Out-of-pocket payments push people into poverty and need to be reduced as much as possible. Prepayment protects people from catastrophic health expenditures. In the case of immunisation, most services are free of charge or prepaid. But people can still be exposed to expenditures if they have to travel long distances to access the services and if they have to buy the vaccines or devices themselves.
- Services included: What percentage of interventions offered are being included in the UHC package? Is it only basic services or does the package also include other services such as treatment, rehabilitation, etc.? In the case of immunisation, services are often included but services can still be unavailable if vaccines are out of stock or populations are not reached by the services.

Moving towards UHC is necessary but difficult. Tough political decisions need to be taken and new policies need to be implemented. UHC cannot be achieved in all countries overnight, but all countries can take actions to move more rapidly towards it. In countries where health services have traditionally been accessible and affordable, a growing middle class with changing habits makes it increasingly difficult for governments to respond to the ever-growing health needs of populations, and the increasing costs of health services. In other countries, the high burden of communicable diseases or recurrent epidemics is the major challenge.

Key factors in determining which services are prioritised by countries are: epidemiological context, health systems, level of socio-economic development and people's expectations.

Moving towards UHC requires strengthening health systems. An important component of UHC is health financing where attention needs to be paid to raising sufficient funds, minimising out-of-pocket payments through prepayment and pooling, and using available funds (including donor funding where relevant) efficiently and equitably.

Countries must also have a health workforce that can support an affordable, efficient, well-run health system that meets priority health needs through quality, people-centred, integrated care. Good governance, sound systems of procurement and supply of medicines and health technologies, and well-functioning health information systems are other critical elements.

UHC emphasises not only what services are covered, but also how they are covered through focusing on people-centred healthcare and integration of care. A shift in health service delivery is necessary to better tailor services to the individuals of the population they serve. Health systems should be organised around the needs and expectations of people in terms of holistic long-term health to help them better understand their own healthcare needs.

2. THE ROLE OF THE NITAG

2.1. ANALYSIS OF HEALTH SYSTEM CHALLENGES

The NITAG needs to be able to assess health system challenges and the need for reform in order to improve the effectiveness and efficiency of the health system, especially with regard to immunisation. Key challenges need to be identified and policy options developed.

Therefore the NITAG needs to have a clear understanding of the health system in the country, the strengths and weaknesses of the health system building blocks and their components, and the impact of health system policies on immunisation outcome. The knowledge of the policies and the policy process will help the NITAG to make relevant recommendations.

2.2. POLICY ADVICE INTERACTING WITH DIFFERENT KEY STAKEHOLDERS

Policy advice by the NITAG should be framed around the needs and expectations of people and institutions in the country to help them understand the needs and approaches for sustained and continuously improving immunisation programme performance. The people and institutions in the country are in this context referred to as stakeholders in the immunisation programme. The NITAG then needs to be able to identify and assess the perceptions, needs and expectations of stakeholders in order to align policy advice to drivers and barriers to the immunisation programme with the aim of sustaining and continuously improving immunisation programme performance.

Policy advice should include:

- Advice on global or vertical approach to intervention;
- Identification of cross-cutting issues;
- Support and engagement in strategic planning processes;
- Support and strengthening of planning infrastructure (Country Coordination Mechanism, Inter Agency Coordination Committee, others);
- Facilitation of engagement with Civil Society Organisations.

REFERENCES

1. Table of constraints (Annex 1)
2. WHO (2010); ***Key components of a well-functioning health system*** http://www.who.int/healthsystems/EN_HSSkeycomponents.pdf
3. WHO (2007); ***Everybody's business: Strengthening health systems to improve health outcomes: WHO framework for action***. WHO ISBN 978 92 4 159607 7:
4. Burchett E D H et al (2014); ***The impact of introducing new vaccines on the health system: Case studies from six low-income countries.*** Vaccine; 32(2014): 6505-6512
5. Favin M et al (2012); ***Why children are not vaccinated: a review of the grey literature.*** Int Health 2012
6. WHO ***Questions and Answers on Universal Health Coverage***

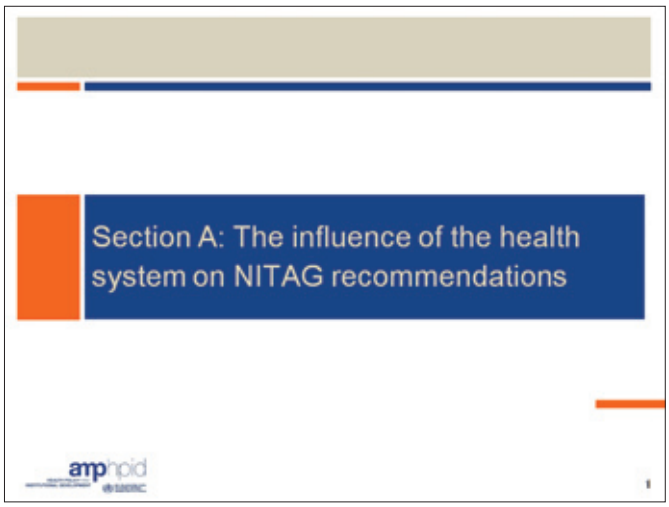
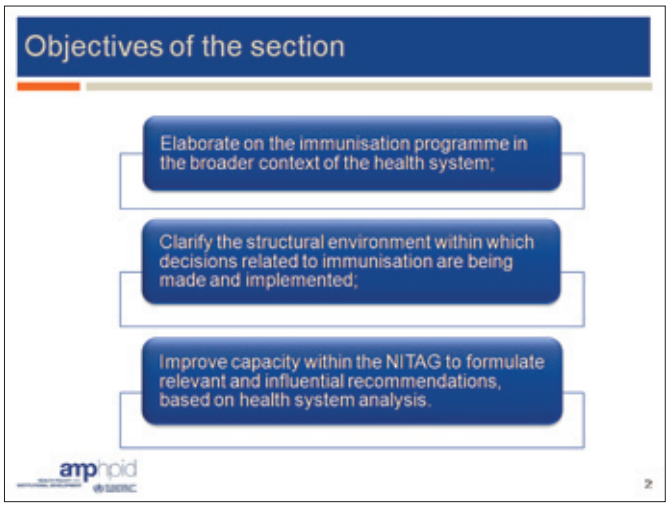
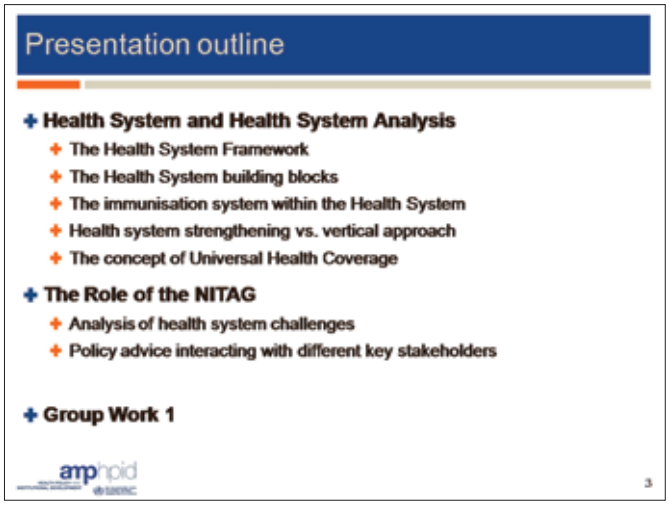
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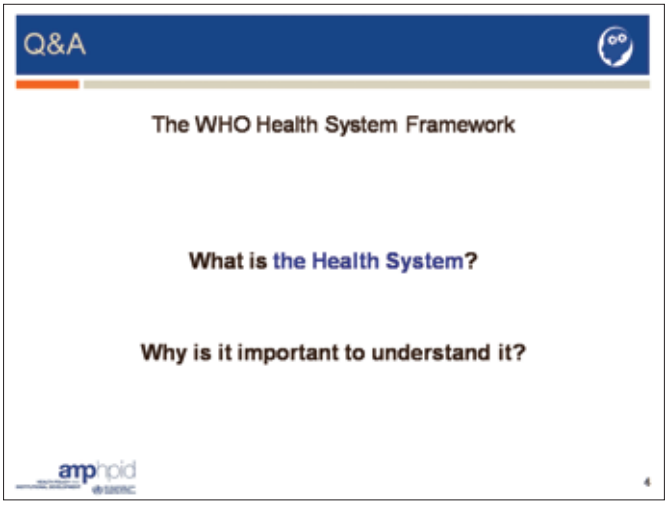
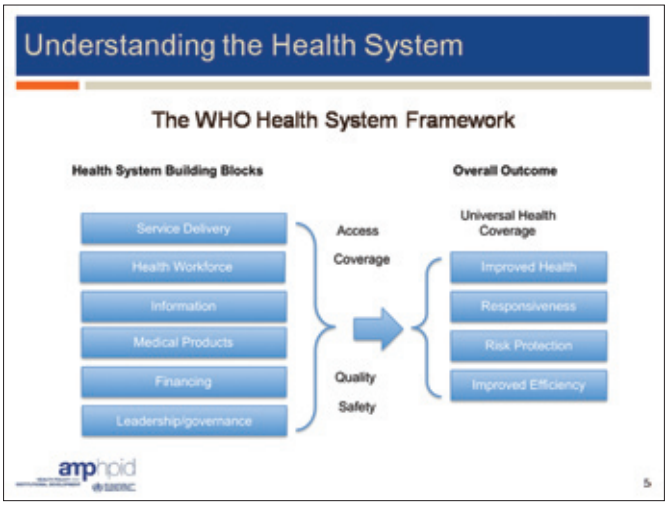
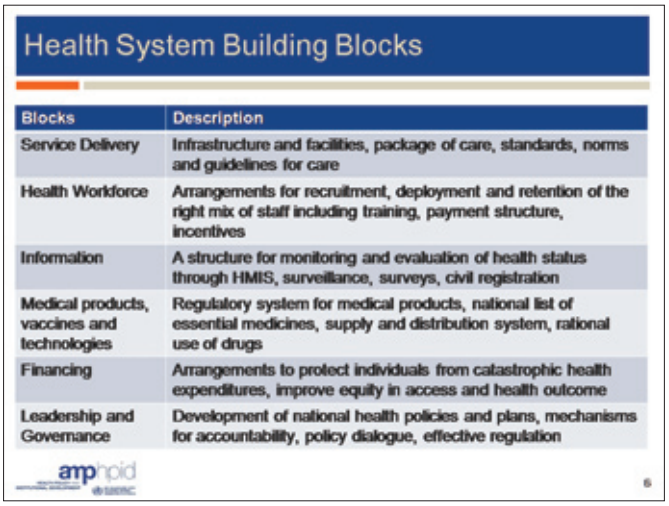
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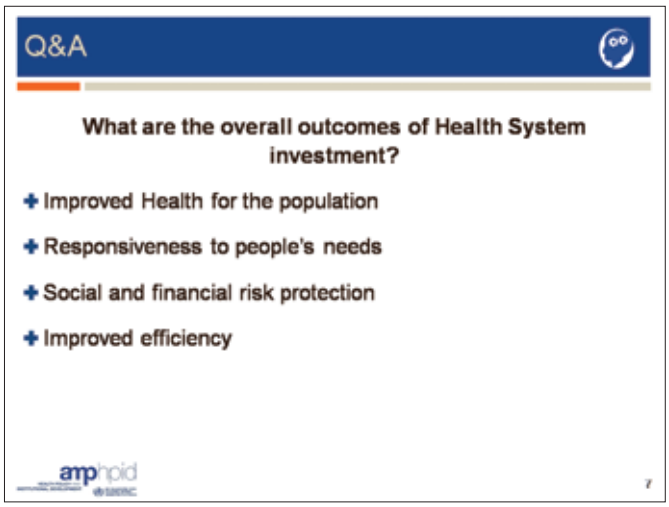
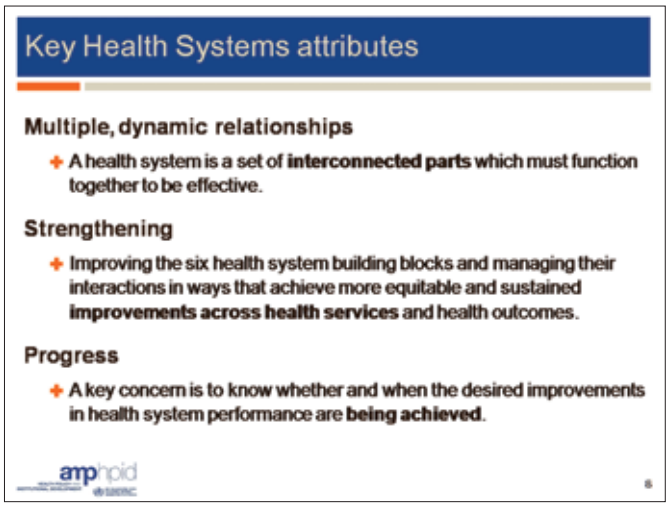
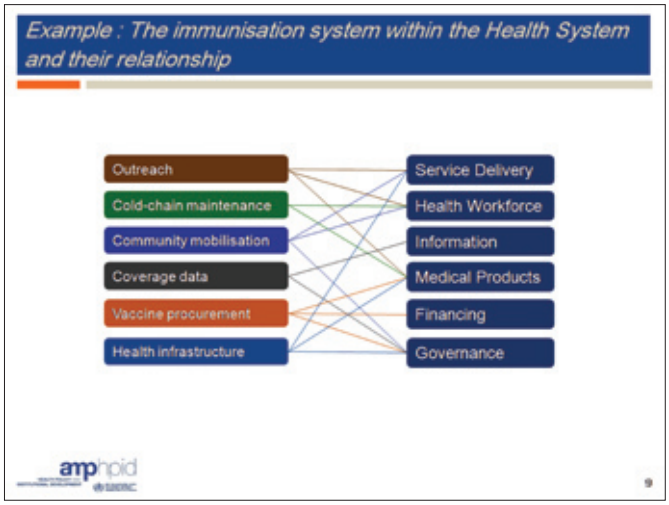
The facilitator will ensure participants have correctly understood the concepts presented in section A, especially the concept of the health system and its components, how health system policies impact on and affect the outcome of Immunisation, and that the purpose of the recommendations of the NITAG is to lift barriers to immunisation.

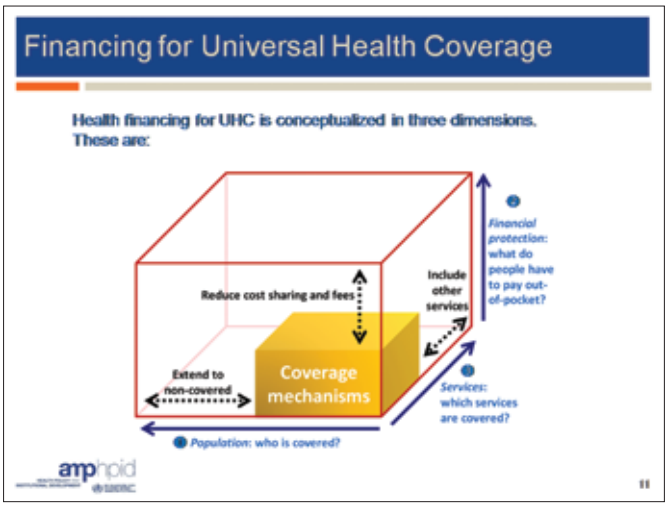
For the group exercise it is important to facilitate an open discussion and link the questions to the presentation. Examples of recommendations are provided.

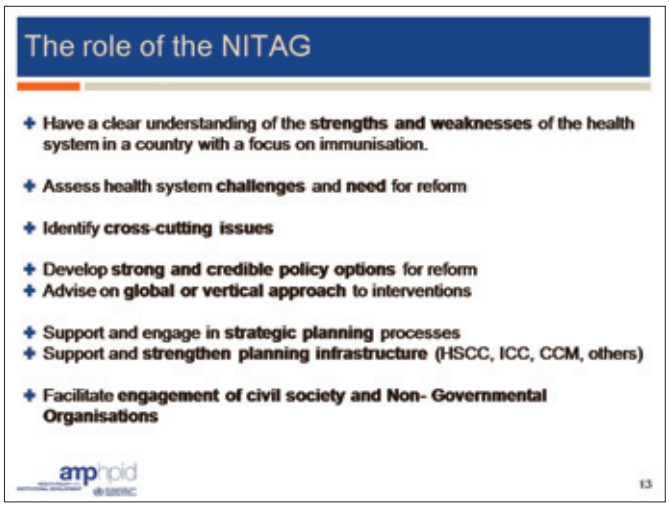
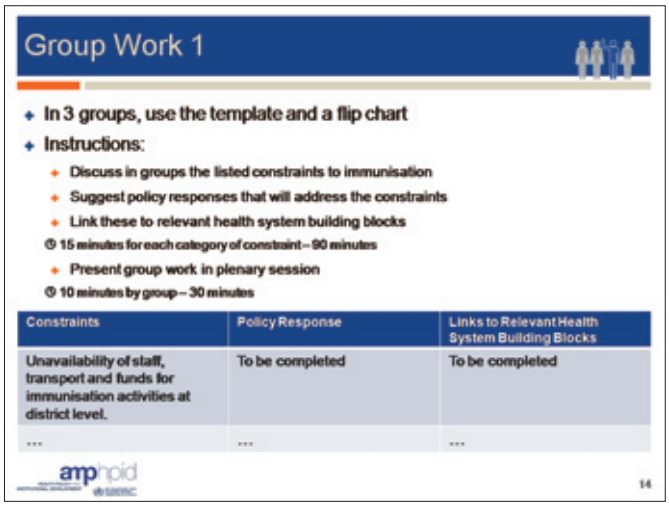
Soft copies of the resources for the group exercises can be downloaded from the NITAG Resource Center www.nitag-resource.org

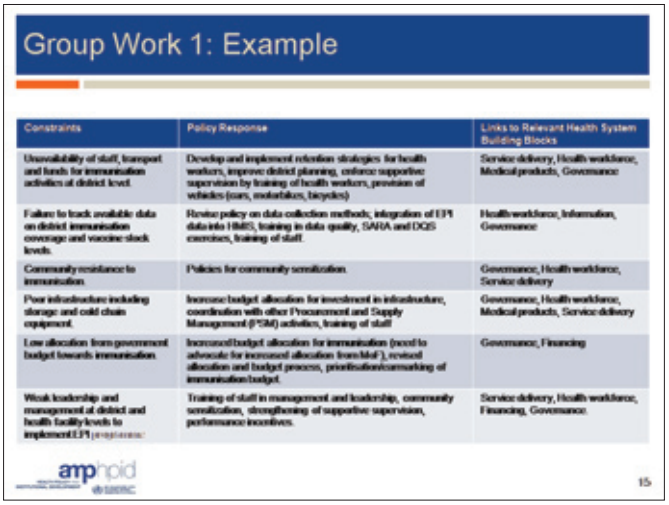
Slides	Facilitation methods
	Presentation:
	Presentation:
	Presentation:

Slides	Facilitation methods
	Q&A:
	**Presentation:** Insist on the following key points: • A strong health system is needed to deliver and scale up new vaccines and to improve immunisation coverage and equity. • Building blocks are specific but interrelated, one cannot function well without the other. • A positive outcome is dependent on all building blocks functioning. • Keeping health systems on track requires a strong sense of direction, and coherent investment in the various building blocks of the health system, so as to provide the kind of services that produce results.
	**Presentation:** Table presented with animation Explain each block of the table

Slides	Facilitation methods
	Questions and answers: Ask participants to list the outcomes of HS investment then show the answers
	Presentation: Animation
	Presentation:

Slides	Facilitation methods
	Presentation: Animation
	Presentation:
	Presentation:

Slides	Facilitation methods
	Presentation:
	Group Work 1: Objective: Understand how policy advice addressing barriers or drivers to immunisation links to health system building blocks and its components for overall attainment of positive health outcomes. 1. Organise participants in 3 small groups (4-5 in each group). 2. Give the following instructions: - Hand out the table that the group should complete (See resources). - Discuss the listed barriers to immunisation. - Suggest policy responses, which will address the barriers. - Link these to relevant health system building blocks. - You have about 90 minutes to do the entire exercise (15 min per constraint). - Then all the groups will present their results in plenary session, with the flip chart. - We will end with a general discussion.

Slides	Facilitation methods
	**Presentation :** To be presented during plenary after group work to facilitate further discussion.



ANNEX 1: TABLE OF CONSTRAINTS

CONSTRAINT	PROPOSED POLICY RESPONSE	LINKS TO RELEVANT HEALTH SYSTEM BUILDING BLOCKS
Unavailability of staff, transport and funds for immunisation activities at district level		
Failure to track available data on district immunisation coverage and vaccine stock levels		
Community resistance to immunisation		
Poor infrastructure, including storage and cold chain equipment		
Low allocation from government budget towards immunisation		
Weak leadership and management at district and health facility levels to implement EPI programme		

SECTION B

STAKEHOLDER ANALYSIS AND MAPPING



FOR
FACILITATOR

PRESENTATION OF THE SECTION

Policy advice by the NITAG should be framed around the needs and expectations of people and institutions in the country to help them understand the needs and approaches for sustained and continuously improving immunisation programme performance. The people and institutions in the country are in this context referred to as stakeholders in the immunisation programme. The NITAG then needs to be able to identify and assess the perceptions, needs, and expectations of stakeholders in order to align policy advice to drivers and barriers to the immunisation programme with the aim of sustaining and continuously improving immunisation programme performance.

This section therefore is an introduction to stakeholder analysis and mapping. It introduces stakeholder analysis methods step by step and suggests how the result of the stakeholder analysis should be used in a decision-making process by the NITAG. The exercise ends with a practical example from a real case study.



LEARNING OBJECTIVES

Develop an understanding of:

- Basic stakeholder analysis and mapping tools;
- How to use stakeholder analysis and mapping in a decision-making process;
- How to describe stakeholders' roles and influences in a diagram form;
- How to prepare engagement strategies.

Gain capacity to:

- Map all institutions, organisations and stakeholders involved in immunisation programme decision-making processes, including identification of those who will be impacted by NITAG recommendations;
- Conduct gap analysis.

1.THE STAKEHOLDER ANALYSIS

1.1. PURPOSE

The purpose of a stakeholder analysis is to identify people or organisations with a keen interest in the policy area of NITAG and who could "make or break" the success of the policy decision/ recommendation by NITAG, and how to deal with these actors. The actors can be winners or losers, they can be included or excluded from the decision-making process, they can be users of results and outcomes of the decisions, and/or participants in the process. The stakeholder analysis is the identification of a project's key stakeholders, an assessment of their interests in the project and the ways in which these interests may affect a project.

The reason for performing a stakeholder analysis is to help the NITAG identify:

- which individuals or organisations to include in your coalition
- what roles they could play and at which stage
- whom to build and nurture relationships with
- whom to inform and consult about a policy decision

To perform a stakeholder analysis is to systematically gather and analyse information about actors who might influence decisions in the field of immunisation. Actors refer to organisations or individuals who have a vested interest in the field of immunisation. Some of these will be obvious stakeholders, such as the Ministry of Health, the EPI programme, donor organisations etc., while others might not be obvious actors and/or only influence decisions indirectly. Examples of these are the media, community leaders (religious and/or political leaders), or pharmaceutical companies such as local pharmacies and vendors of medicines and drugs.

The important thing is to systematically collect and analyse information about these actors and find out what role they play, what it means for the decision-making process, and to advise on how to interact with these stakeholders to ensure support for a policy decision. This analysis should carefully examine characteristics such as knowledge of the area of immunisation, interests, positions (for or against), identifications of known and unknown externalities of a certain position and agenda by an actor, potential alliances, and ability to influence decision-making and policy development in terms of power and leadership.

By knowing who the key actors are, their knowledge, interests, positions, alliances, and importance related to immunisation, the NITAG can guide on how to interact more effectively with them and increase support for immunisation. The NITAG can also detect potential misunderstandings and/ or opposition to immunisation. A policy or programme will more likely succeed if a stakeholder analysis, along with other key tools, is used to guide its implementation.

1.2. THE MAPPING & ANALYSIS TOOLS

These tools have been developed to make sure the analysis is done in a systematic way. They include 4 steps.

Steps 1 and 2 are the mapping tool:

- The first step is to identify stakeholders; this is done through a brainstorming exercise.
- The second step is to prioritise among the stakeholders to establish which are the most important and influential.

Steps 3 and 4 are the analysis tool:

- The third step is to understand the stakeholders. What is driving the specific stakeholder, how can they be influenced, etc.? This is done through data collection and interviews with the identified stakeholders; they are then grouped based on power and interest in the areas of immunisation.
- The final step is to work out a strategy to interact with and influence the key stakeholders.

1.2.1. Identification of stakeholders

The first step is to identify the stakeholders. Who are stakeholders? A stakeholder is any entity with a declared or conceivable interest or stake in a defined policy area, in this case policy decisions related to immunisation. The range of stakeholders who need to be considered in the analysis will vary according to the complexity of the policy decision/recommendation and the type of reform proposed and, where the stakeholders are not organised, the incentive to include them. Stakeholders can be of any form, size and capacity. They can be individuals, organisations, or unorganised groups. In most cases, stakeholders will fall into one or more of the following categories: international actors (e.g. donors), national or political actors (e.g. legislators, governors), public sector agencies, (e.g. Ministries, Departments, or Agencies) interest groups (e.g. unions, medical associations), commercial/private for-profit, non-profit organisations (NGOs, foundations), civil society members, and users/consumers.

The identification of relevant stakeholders starts with a brainstorming exercise. While performing this exercise the "research team" needs to think of all the organisations and people involved in immunisation, or those having an interest in immunisation and who can potentially be interested in and have an impact on immunisation and immunisation-related policies.

Use a simple table to group the stakeholders:

Government	Donors	Civil Society	Private Sector	Others
MoH	Bilaterals	NGOs	Pharmacies	Community leaders
MoF	UN			
	Others			

Remember to keep a column for "others"; these are actors, which are as yet unknown but might turn out to be critical for decision-making.

1.2.2. Prioritisation

The second step is to prioritise the identified stakeholders. Based on the list of stakeholders, some will have more power than others, some might block decision-making, others might support and facilitate decision-making, and others still might not be as influential as first believed.

Four major attributes are important to determine power and interest:

- The stakeholders' position on the policy issue;
- The level of influence (power) they hold;
- The level of interest they have in the specific area;
- The group/coalition to which they belong or can reasonably be associated with.

These attributes can be identified through various data collection methods, including interviews with country experts knowledgeable about stakeholders or with the actual stakeholders directly. The level of influence depends on the quantity and type of resources and power the stakeholder can bring to promote its position in the specific area of immunisation. The level of interest is the priority and importance the stakeholder attaches to immunisation. Broadly, these attributes signal the capability the stakeholder has to block or promote reform, join with others to form a coalition of support or opposition, and lead the direction/discussion on immunisation and immunisation-related policy issues. Stakeholder analysis therefore provides a detailed understanding of the political, economic, and social impact of reform on interested groups, the hierarchy of authority and power among different groups and the actual perceptions of immunisation among different groups, all of which are important for the NITAG to consider.

1.2.3. Data collection

Several methods can be employed to collect data on stakeholders in a comprehensive and efficient manner. Start with a review of background literature and country studies including National Strategic Plans, immunisation plans such as comprehensive Multi Year Plans (cMYP), Annual Reports, minutes from meetings by the Country Coordination Meetings (CCM) and other key meetings. These can provide a useful understanding of the country's political economy in the area of immunisation.

The next step is to conduct interviews directly with the stakeholders involved in immunisation and local experts in the field of immunisation, as well as other groups and individuals involved, as indicated during the identification process.

Some NITAG members often hold extensive local knowledge and can provide a critical first hand understanding of which stakeholders are relevant. However, unless resources and time do not permit, interviewing of local and international experts or country and/or the stakeholders themselves is imperative.

Broad, all-inclusive interviews will lead to an effective stakeholder analysis process since it will uncover many facets of the country's political economy. The interview content and questions should focus on gaining background information regarding the policy-making process as this information will identify key stakeholders from a variety of groups in the reform process, and on clarifying assumptions about stakeholders' power and interest in the decision-making process. The number of interviews will be determined by the "research team", taking into consideration field conditions and logistical constraints (e.g. sensitivity, access, time, budget, etc.).

1.2.4. Analysis

The next step is to analyse the data and start to understand the different stakeholders better. Data from the interviews, including relative rankings, should be catalogued and presented in charts and/or matrices, highlighting the following attributes:

- Group
- Their interest
- Influence/power
- Position on the policy/reform

A clear assessment of each stakeholder's power and likely impact on the policy-making process is conducted through several steps. The first step is to draw a continuum. Stakeholders are mapped on a continuum indicating support for the reform or proposed policy change on a scale of 0 to 100 from low (far left) to high (far right). The varying degrees of support are marked on the line with a value indicating their reform preference. This mapping exercise also provides a quick visual of the 'lay of the land', highlighting clusters of groups that support, oppose or are indifferent to reform.

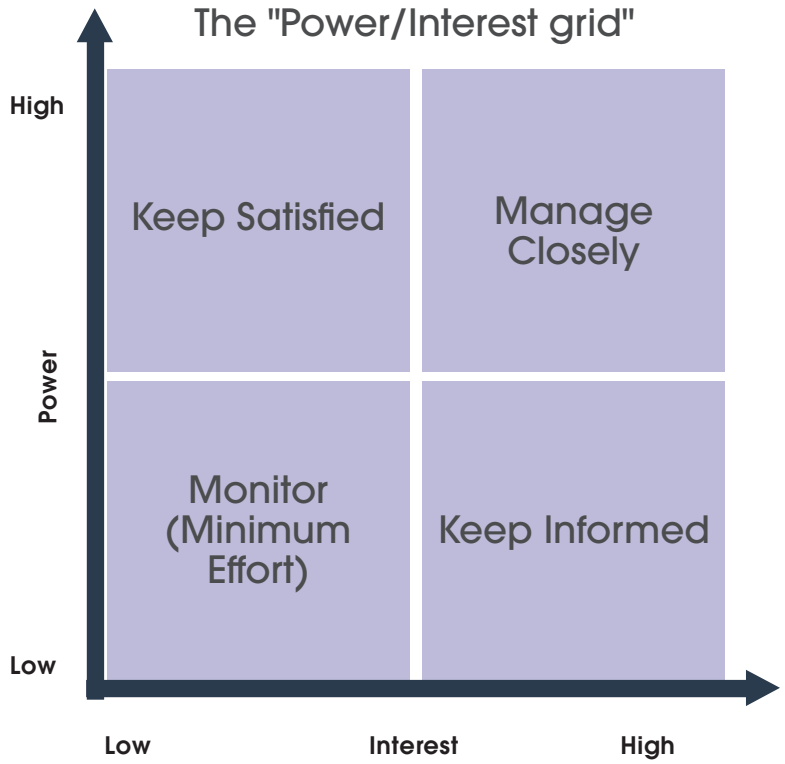
The data collected on the stakeholders are organised relative to power/influence and interest of each stakeholder to understand their potential support or opposition for the proposed reform. A useful tool is the "**Power/Interest grid**". This grid or matrix provides a shorthand categorisation and analysis of which stakeholders will gain or lose from a proposed reform and whether they can significantly impact on the process. To guide strategic responses, stakeholders are categorised by their power and interest using a grid according to the following attributes:

- **Promoters:** Stakeholders who attach a high priority to the policy or reform and whose actions can have an impact on the implementation of the policy;

- **Defenders:** Stakeholders who attach a high priority to the policy or reform but whose actions cannot have an impact on the implementation of the policy;

- **Latents:** Stakeholders whose actions can affect the implementation of the policy or reform but who attach low priority to the issue;

- **Apathetics:** Stakeholders whose actions cannot affect the implementation of the policy or reform and who attach a low priority to the issue.



Think about the following:

- Try to break down actors/stakeholders into critical units. For example, the MoH includes several critical units which might differ in power and influence;
- Define criteria for power and interest. Power in relation to what and who? Power can also be linked to resources, financial, political credibility, etc.;
- Be as specific as possible, identifying individuals within organisations (where possible).

1.2.5. Engagement Strategies

One of the main goals of stakeholder analysis is to reveal, and therefore potentially assist in reducing, the power imbalance among interest groups which is often revealed during policy-reform process. Depending on the attributes of the stakeholder (e.g. their level of influence vs their interest in the issue), strategies can be tailored to address their concerns.

Four different engagement strategies should be developed. These are:

1. High power/low interest stakeholders: "Keep satisfied"
2. High power/high interest stakeholders: "Manage closely"
3. Low power/low interest stakeholders: "Monitor"
4. Low power/high interest stakeholders: "Keep informed"

Even though strategies should be developed for all four groups, the NITAG should advise to focus efforts on group two (High power/high interest stakeholders) and the "Manage closely" strategy. **These are the actors with the highest power and highest interest; they need to be managed in order to influence decision-making.**

2.STAKEHOLDER ANALYSIS IN THE CONTEXT OF IMMUNISATION

2.1. IMPLEMENTATION OF ENGAGEMENT STRATEGIES

Based on the outcome of the stakeholder analysis and the engagement strategies, it is now up to the NITAG to take this information forward and recommend strategies with the aim of:

1. Maintaining or increasing power of reform supporters through building coalitions, and providing information and resources;
2. Converting opposition into support through negotiations, information and/or coalition building, including offering trade-offs;
3. Offsetting or countering powerful and not so powerful opponents;
4. Assessing capacity needs (gaps) to successfully advocate for immunisation and influence decision-making.

The capacity analysis should take into consideration the need to successfully engage with the identified key stakeholders, and match this with the capacity to successfully implement the engagement strategies.

Because stakeholders and their positions may change over the course of negotiations and analyses, the NITAG should conduct stakeholder analyses on a fairly regular basis, thereby allowing for policy design to be adjusted as more becomes known about the political reality.

Ultimately, stakeholder analysis is a critical tool in clarifying the micro-political economy of a policy area and can help identify interested parties that should be incorporated in the decision-making process, in addition to understanding the basis for their inclusion.

2.2. RESOURCES NEEDED TO CONDUCT A STAKEHOLDER ANALYSIS

The resources needed for conducting a stakeholder analysis are: personnel time, travel expenses, access to a phone, copy machine and computer, and interview materials (paper and pens). The planning for a stakeholder analysis should take into account the time and resources it takes to:

- Conduct a brainstorming meeting
- Collect data, including interviews with stakeholders
- Assess data and perform the Grouping exercise
- Complete the Power/interest grid
- Develop engagement strategies

As a reference point, a national-level stakeholder analysis that interviews 35-40 stakeholders requires a four-person team working full-time for about two months, depending upon how quickly the interview appointments are made. The working group should consist of at least two persons who are skilled interviewers, knowledgeable about the health sector, able to analyse qualitative information, and who are computer-literate. For analyses involving a smaller number of stakeholders, fewer resources are required.

REFERENCES

1. Additional resources:
Mindtools: http://www.mindtools.com/pages/article/newPPM_07.htm

2. Schmeer K, Stakeholder analysis Guidelines
http://www.eestum.eu/voorbeelden/Stakeholders_analysis_guidelines.pdf

3. Stakeholder analysis, World Bank
http://www1.worldbank.org/publicsector/anticorrupt/PoliticalEconomy/stakeholderanalysis.htm

4. Documents can be accessed through the NITAG ResourceCenter: www.nitag-resource.org

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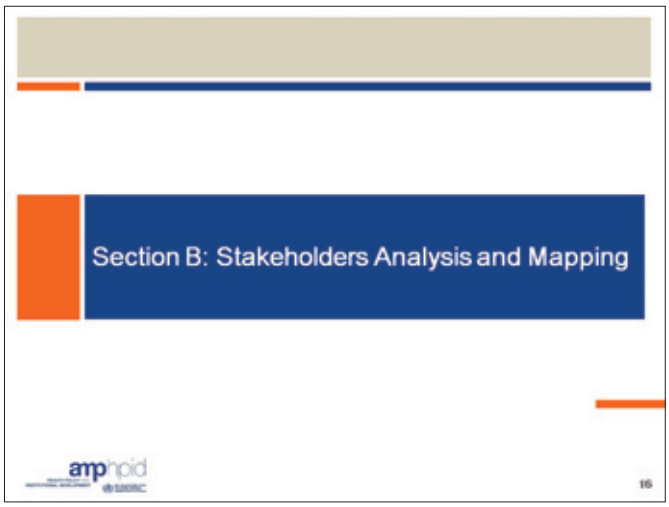
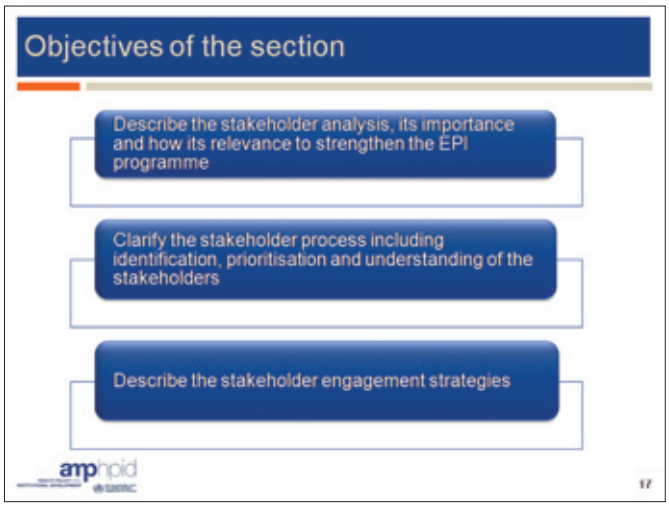
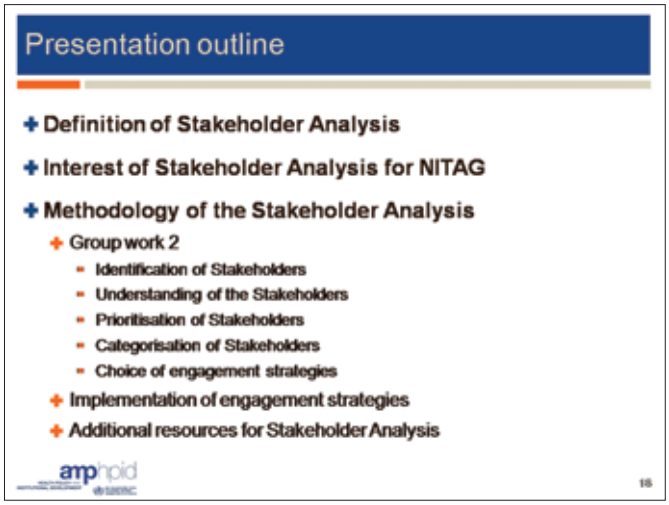
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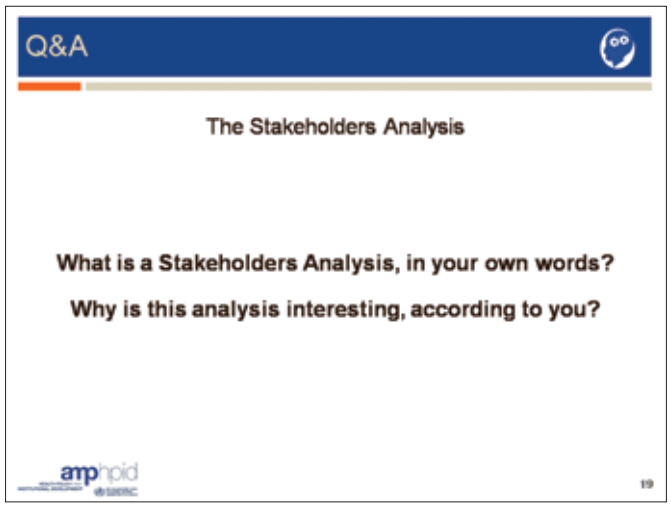
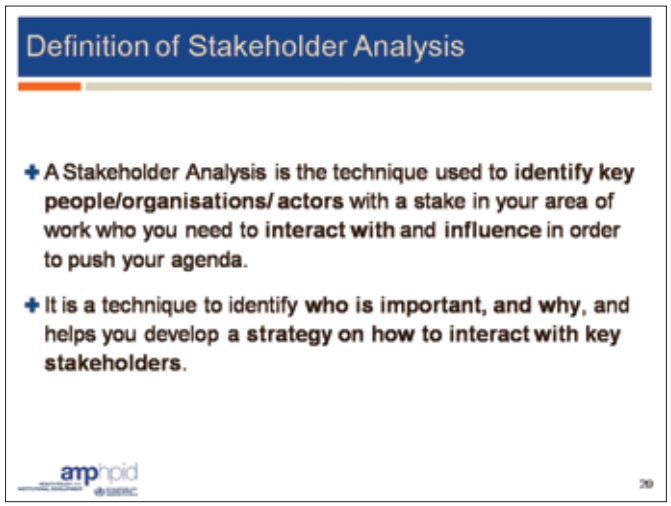
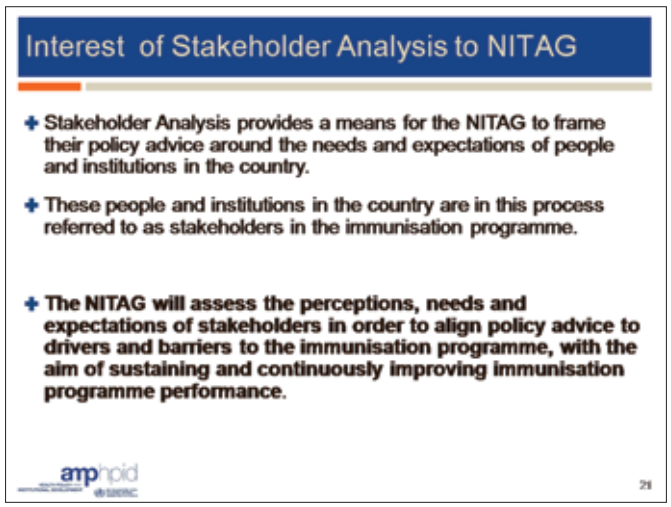
This section explains the principles and methods for performing a stakeholder analysis. It is important that the participants are familiar with the concept and understand the methods as explained in this section.

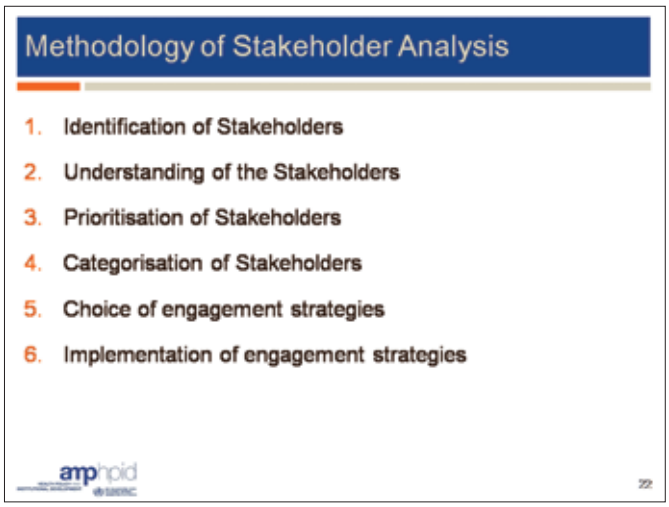
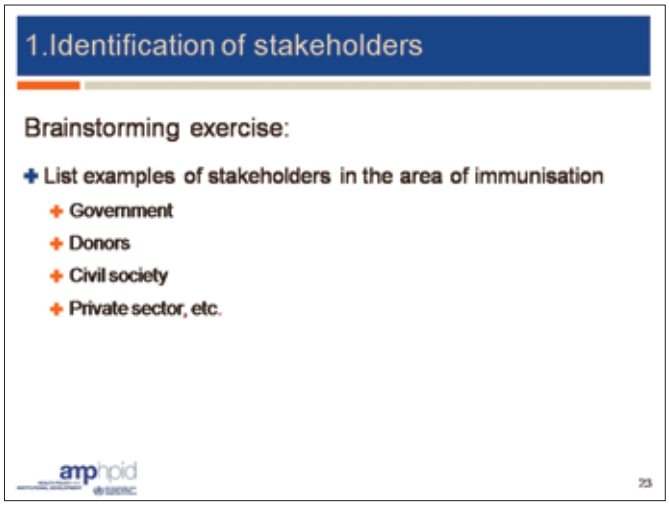
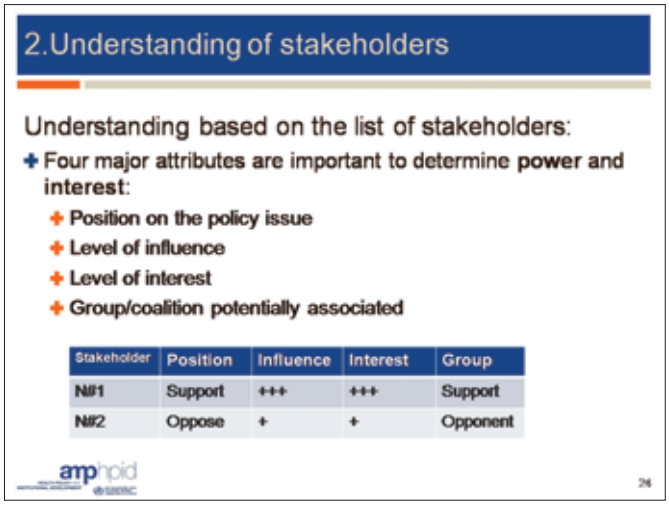
It is important that participants are actively engaged during the presentation. The facilitator should ask questions and provide opportunities for the participants to comment and share their own experiences.

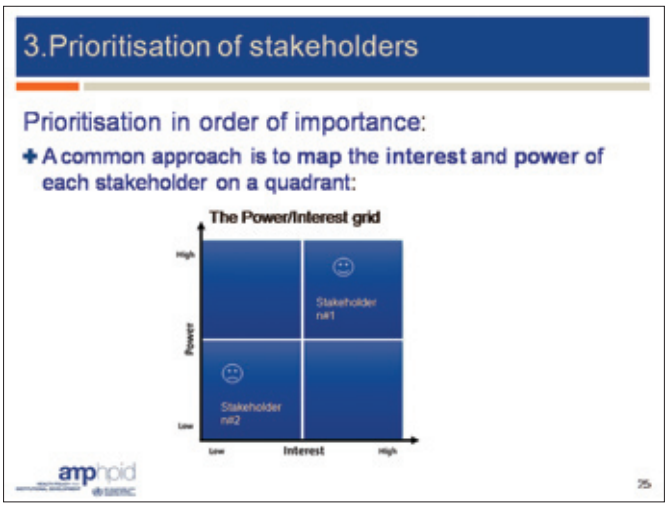
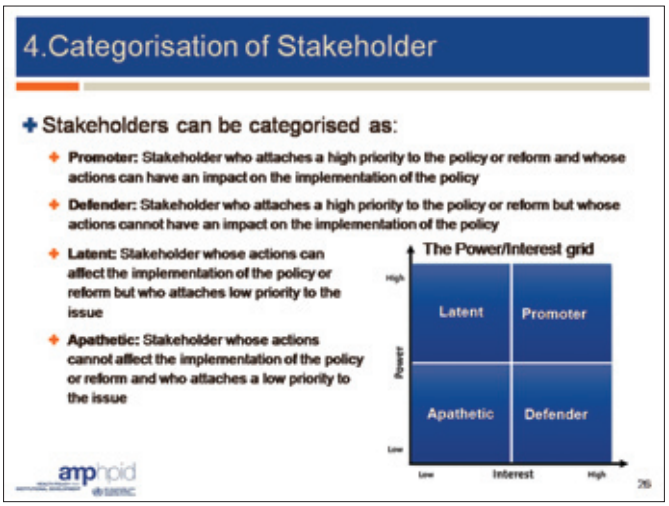
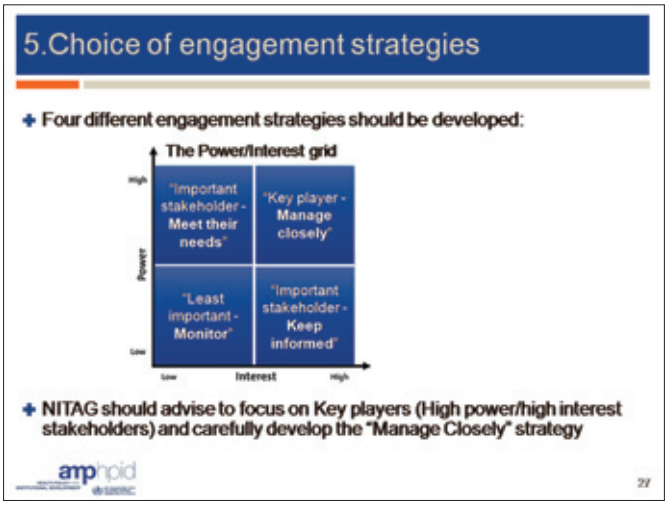
Questions and examples are provided in the handout.

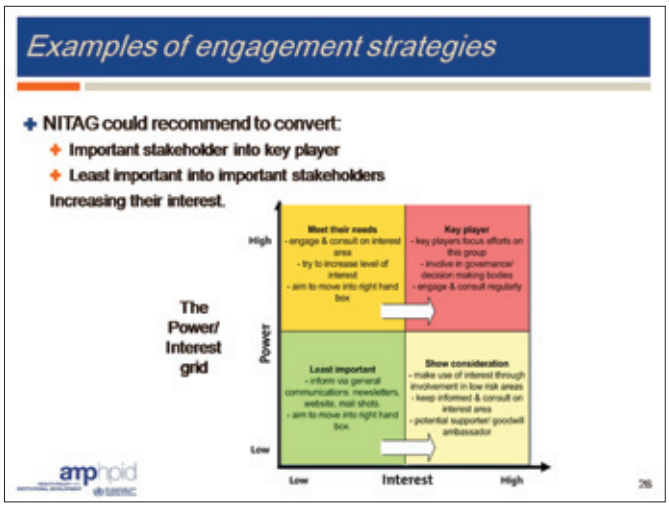
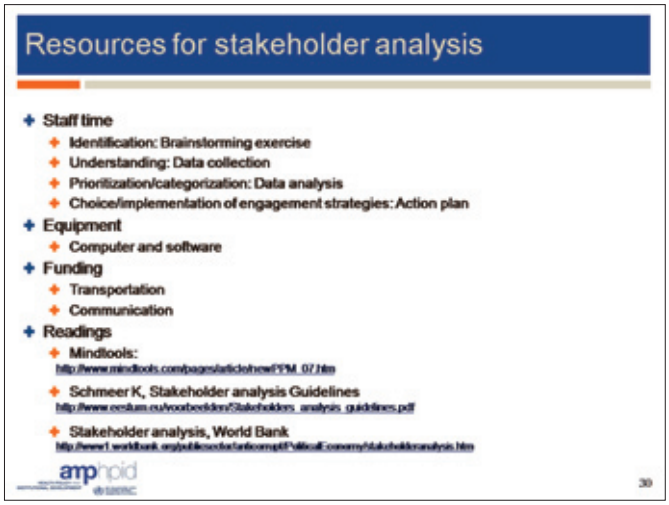
The presentation will end with a group exercise.

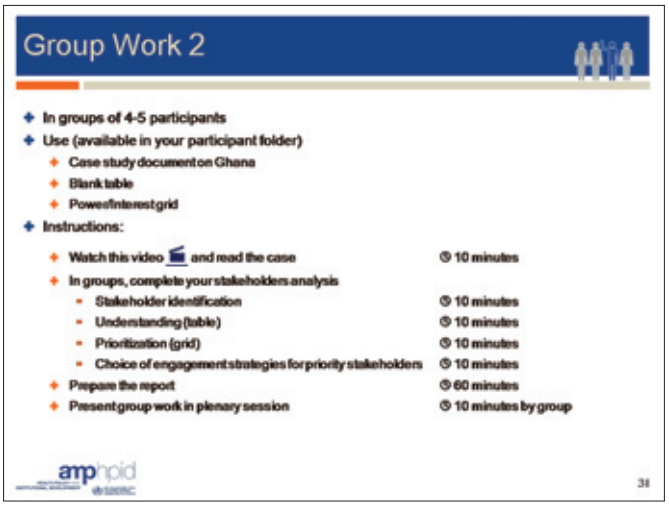
Slides	Facilitation methods
	**Presentation:** Introduce the topic.
	**Presentation:** Present the objectives of the section.
	**Presentation:** The outline of the presentation. Mention that there is a group exercise at the end of the presentation.

Slides	Facilitation methods
	**Q&A:** Ask participants if they have experience of conducting a stakeholder analysis. There are many frameworks but they all have the same objective.
	Presentation:
	Presentation:

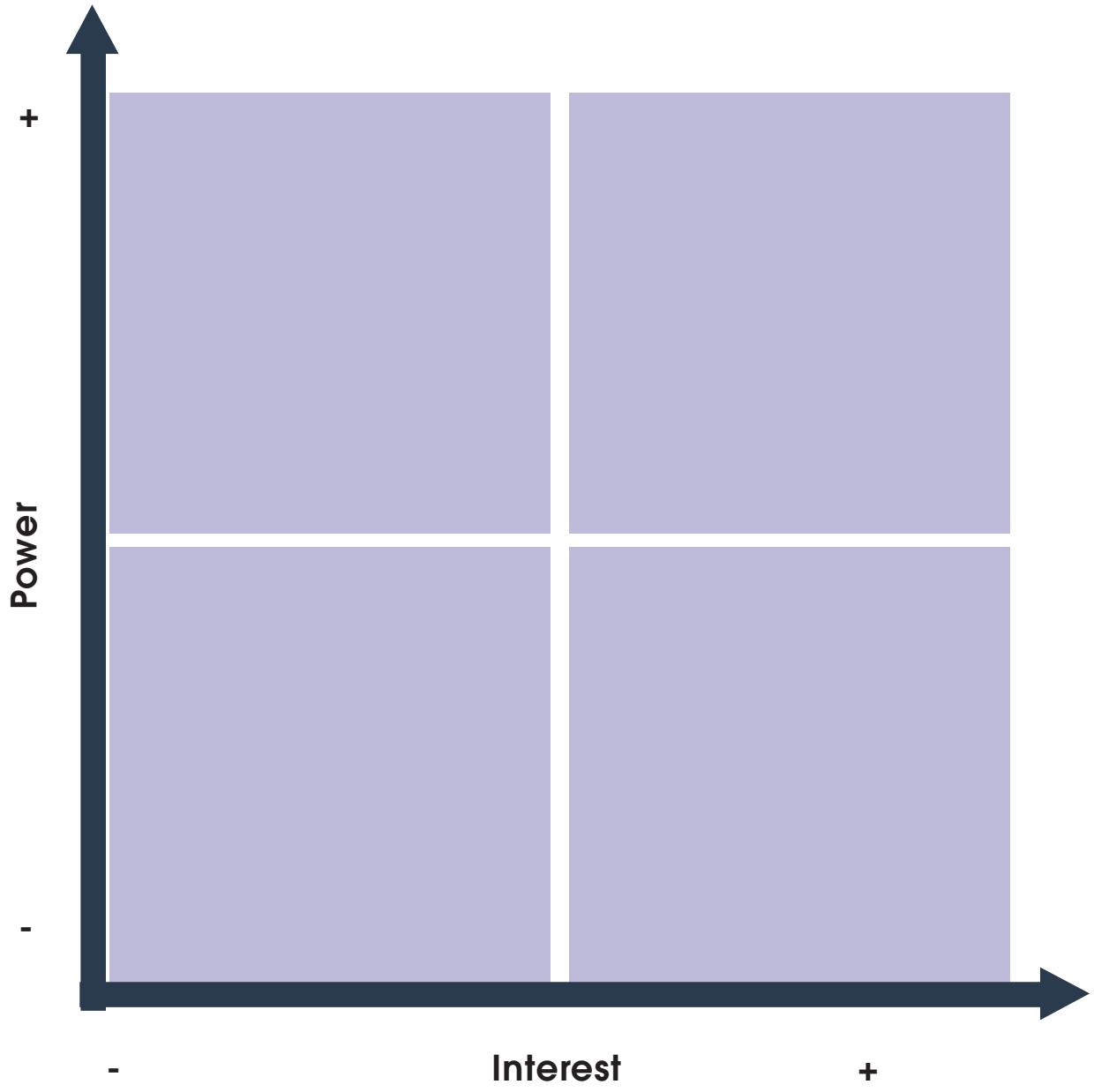
Slides	Facilitation methods
	Presentation:
	Presentation: Give examples of stakeholders in different groups.
	Presentation: Give examples of stakeholders with their position, influence, interest, and group.

Slides	Facilitation methods
	**Presentation:** Keep the same examples of stakeholders and explain their place on this map. Explain that once they have mapped the interests of the stakeholders, they need to prioritise them in order of importance. Different methodologies suggest different ways of analysing stakeholders, some complex and some very simple. A common approach is to map the interest and power or influence of each stakeholder group on a quadrant.
	**Presentation:**
	**Presentation:**

Slides	Facilitation methods
	Presentation:
	Presentation:
	Presentation: Let participants know of the resources listed in their manual.

Slides	Facilitation methods
	**Group work** **Objective:** The assignment is to conduct a stakeholder analysis going through all the steps presented above and present the result in plenary. Give the following instructions to participants: - First, we will watch the video on the Ghana experience. - Second, you will read the 'Case study from Ghana' on the introduction of two new vaccines, available in the annex in your summary. - Using the Ghana movie, which is a snapshot of the events from the launch of the two new vaccines, and the case study, go through the 4 steps of the stakeholder analysis. - You have 1 hour to do this exercise. I suggest you spend 5 minutes on the documents, 10 minutes on each step and 10 minutes to prepare the presentation in plenary. - The rapporteur of each group will present the process focusing on challenges encountered during the analysis.
	**Video support** Click on the link to the video if you have a well-functioning internet connection. Click on the play button if there is no Internet connection.

ANNEX 1: POWER/INTEREST GRID



ANNEX 2: TABLE OF STAKEHOLDERS

STAKEHODERS IDENTIFICATION				
STAKEHOLDERS	**POSITION**	**INFLUENCE**	**INTEREST**	**GROUP**



Supporting Independent
Immunization and Vaccine
Advisory Committees



T R A I N I N G 2

ANALYSIS OF IMMUNISATION IN THE CONTEXT OF HEALTH SYSTEMS AND THE POLICY DECISION-MAKING PROCESS

SUMMARY



FOR
PARTICIPANT

TABLE OF CONTENTS

SECTION A
THE INFLUENCE OF THE HEALTH SYSTEM ON NITAG RECOMMENDATIONS

SUMMARY FOR PARTICIPANT 6

INTRODUCTION

TARGET AUDIENCE

1. UNDERSTANDING THE HEALTH SYSTEM 7

2. HEALTH SYSTEM STRENGTHENING OR VERTICAL APPROACH TO IMPLEMENTATION: THE ROLE OF THE NITAG 8

3. THE CONCEPT OF UNIVERSAL HEALTH COVERAGE 9

4. THE ROLE OF THE NITAG 9

RESOURCES 10

APPENDIX 1: TEMPLATE FOR POLICY RESPONSE 11

SECTION B
STAKEHOLDER ANALYSIS AND MAPPING

SUMMARY FOR PARTICIPANT 14
1. STAKEHOLDER ANALYSIS 14
2. ENGAGEMENT STRATEGIES 15
RESOURCES 15
APPENDIX 1: TEMPLATE FOR STAKEHOLDER IDENTIFICATION 16
APPENDIX 2: POWER/INTEREST GRID 20

SECTION A

THE INFLUENCE OF THE HEALTH SYSTEM ON NITAG RECOMMENDATIONS



FOR
PARTICIPANT

INTRODUCTION

This training is presented in two sections, A and B, that are further described in the text below.

TARGET AUDIENCE

- NITAG members

LEARNING OBJECTIVES

Knowledge and understanding of:

- The immunisation programme in the broader context of the health system;
- The structural environment within which decisions related to immunisation are being made and implemented;

And

- Improved capacity within NITAG to formulate relevant and influential recommendations, based on health system analysis;

1. UNDERSTANDING THE HEALTH SYSTEM

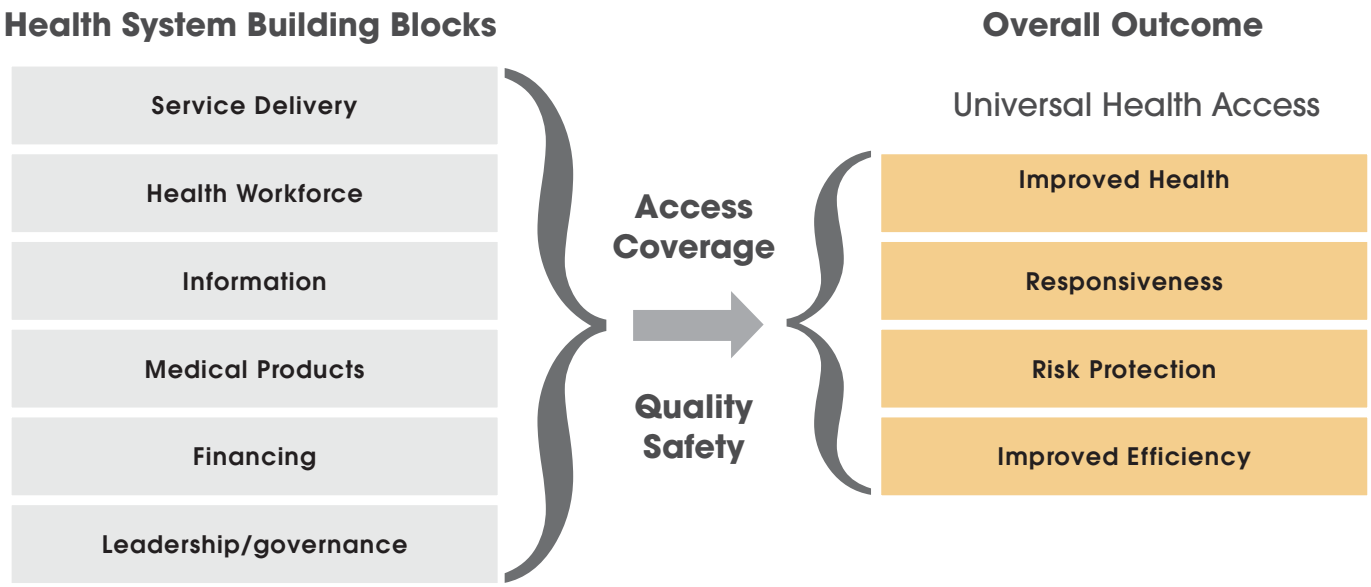
The health system is divided into six building blocks:

- Service delivery
- Health workforce
- Information
- Medical products
- Financing
- Governance and leadership

Together these building blocks constitute the Health System in a country.

A health system is not an end in and of itself, it is instead a means to achieve health outcomes in a population. Health systems should be a vehicle for accelerating progress on health-related goals, but as a vehicle, it is subject to constraints impeding progress. The challenge faced by policy-makers and NITAGs is therefore to figure out how to improve health system performance to achieve better results in the population.
The health system framework includes an input side (the building blocks) and an output/outcome side (the expected impact of the health system on a population).

THE WHO HEALTH SYSTEM FRAMEWORK



The inputs have to be combined so that access, coverage, quality, and safety are maximised, in order to reach the overall outcome and goals:

- Improved health of individuals, families, and communities
- Responsiveness to health threats
- Protection against financial consequences of ill-health
- Improved efficiency ensuring best use of resources available

The immunisation system is imbedded in the health system. It is important to understand how the immunisation system is linked to the boarder health system and how decisions on broader issues also affect the immunisation system, for example decisions related to HR and cadres can have a huge impact on immunisation. Training of health staff is another issue. Interventions related to integration of services (basic package, integrated child health services etc.) can improve immunisation.

2. HEALTH SYSTEM STRENGTHENING OR VERTICAL APPROACH TO IMPLEMENTATION: THE ROLE OF THE NITAG

HEALTH SYSTEM BUILDING BLOCKS	VERTICAL APPROACH	GLOBAL APPROACH
Service Delivery	Through separate project facilities and/or specific facilities	Through general facilities under government supervision
Health Workforce	Temporary employee hired by the project	Government employee on the payroll
Information	Separate reporting through the project	Reporting through national Health Management Information System (HMIS)
Medical Products	Separate disease-specific channels	Through government channels
Financing	Project budget	Government budget
Governance	Separate project not part of National Health Strategic Plan (NHSP)	Part of National Health Strategic Plan (NHSP)

3. THE CONCEPT OF UNIVERSAL HEALTH COVERAGE

The aim of health system strengthening is to address inequitable health outcomes in society by moving towards universal access to fair and responsive health services with social health protection. Universal Health Coverage (UHC) in respect to services and their financing means that all people receive the health services they need without suffering financial hardship when paying for them. The full spectrum of essential, quality health services should be covered including health promotion, prevention and treatment, rehabilitation and palliative care.

Health Financing for UHC is conceptualised in three dimensions. These are:

- Population covered.
- Cost of services covered.
- Services included.

4. THE ROLE OF THE NITAG

The NITAG must have a clear understanding of the country's health system, the strengths and weaknesses of its building blocks and the interaction between the building blocks. The NITAG also should understand how the health system contributes to expected health outcomes in the country and ultimately UHC.

The NITAG needs to be able to assess health system challenges and the need for reform in order to improve effectiveness and efficiency of the health system, especially with regard to immunisation. Key challenges need to be identified and policy options developed.

Building on an analysis of the health system in a country and having a full understanding of the contextual factors driving and obstructing reforms, the NITAG can develop strong and credible policy options for the government to consider.

Policy advice should include:

- Advice on global or vertical approach to intervention;
- Identify cross-cutting issues;
- Support and engage in strategic planning processes;
- Support and strengthen planning infrastructure, Country Coordinating Mechanisms (CCM), Interagency Coordinating Committee (ICC), and others;
- Facilitate engagement with Civil Society Organisations.

RESOURCES

1. WHO (2010); ***Key components of a well-functioning health system***
   http://www.who.int/healthsystems/EN_HSSkeycomponents.pdf
2. WHO (2007); ***Everybody's business: Strengthening health systems to improve health outcomes: WHO framework for action***. WHO ISBN 978 92 4 159607 7
3. Burchett E D H et al. (2014); ***The impact of introducing new vaccines on the health system: Case studies from six low-income countries. Vaccine.*** 32(2014): 6505-6512
4. Favin M et al (2012); ***Why children are not vaccinated: a review of the grey literature.*** Int Health 2012
5. WHO ***Questions and Answers on Universal Health Coverage***

APPENDIX 1: TEMPLATE FOR POLICY RESPONSE

POLICY RESPONSES TO BARRIERS IN IMMUNISATION

CONSTRAINT	PROPOSED POLICY RESPONSE	LINKS TO RELEVANT HEALTH SYSTEM BUILDING BLOCKS
Unavailability of staff, transport and funds for immunisation activities at district level;	Develop and implement retention strategies for health workers; improve district planning; enforce supportive supervision by; training health workers; provision of vehicles (cars, motorbikes, bicycles)	Service Delivery; Health Workforce; Medical products; Governance
Failure to track available data on district immunisation coverage and vaccine stock levels;	Revise policy on data collection methods; integration of EPI data into HMIS; training in data quality; SARA and DQS exercises; training of staff.	Health Workforce; Information; Governance
Community resistance to immunisation	Policies for community awareness	Governance; Health Workforce, Service Delivery
Poor infrastructure, including storage and cold chain equipment	Increase budget allocation for investment in infrastructure; coordination with other PSM activities; training of staff	Governance; Health Workforce; Medical products; Service Delivery
Low allocation from government budget towards immunisation	Increased budget allocation for immunisation (need to advocate for increased allocation from MoF); revised budget and allocation process; prioritisation/ earmarking of immunisation budget	Governance; Financing
Weak leadership and management at district and health facility levels to implement EPI programme	Training of staff in management and leadership, community awareness; strengthening of supportive supervision; performance incentives	Governance; Financing

CONSTRAINT	PROPOSED POLICY RESPONSE	LINKS TO RELEVANT HEALTH SYSTEM BUILDING BLOCKS
Unavailability of staff, transport and funds for immunisation activities at district level		
Failure to track available data on district immunisation coverage and vaccine stock levels		
Community resistance to immunisation		
Poor infrastructure, including storage and cold chain equipment		
Low allocation from government budget towards immunisation		
Weak leadership and management at district and health facility levels to implement EPI programme		

SECTION B

STAKEHOLDER ANALYSIS AND MAPPING



FOR
PARTICIPANT

SUMMARY FOR PARTICIPANT

Policy advice by the NITAG should be framed around the needs and expectations of people and institutions in the country to help them understand the needs and approaches for sustained and continuously improving immunisation programme performance. The people and institutions in the country are in this context referred to as stakeholders in the immunisation programme. The NITAG then needs to be able to identify and assess the perceptions, needs, and expectations of stakeholders in order to align policy advice to drivers and barriers to the immunisation programme with the aim of sustaining and continuously improving immunisation programme performance.
The content of this section is designed to assist NITAG members in conducting a stakeholder analysis.

1. STAKEHOLDER ANALYSIS

• THE PURPOSE OF A STAKEHOLDER ANALYSIS

Stakeholder analysis is a process of systematically gathering and analysing qualitative information to determine whose interests should be taken into account in the decision-making process in immunisation. The purpose is to improve the decision-making process by increasing support or building consensus on policy advice/reforms in the area of immunisation.

• IDENTIFICATION OF STAKEHOLDERS

The stakeholder analysis starts with a brainstorming exercise where actors in the area of immunisation are listed and grouped, using a stakeholder table (see Appendix 2).

• PRIORITISATION OF STAKEHOLDERS AND UNDERSTANDING THE STAKEHOLDERS

Prioritisation of stakeholders is based on the outcome of the data collection:

- capability/interest to block or promote reform;
- capability/interest to join with others to form a coalition of support or opposition;
- capability/interest to lead the direction/discussion on immunisation.

Stakeholders already identified should be assessed based on the following criteria:
Promoters: Stakeholders who attach a high priority to the policy or reform and whose actions can have an impact on the implementation of the policy;
Defenders: Stakeholders who attach a high priority to the policy or reform but whose actions cannot have an impact on the implementation of the policy;
Latents: Stakeholders whose actions can affect the implementation of the policy or reform but who attach low priority to the issue;
Apathetics: Stakeholders whose actions cannot affect the implementation of the policy or reform and who attach a low priority to the issue.

Complete the power/interest grid (see Appendix 2).

2. ENGAGEMENT STRATEGIES

Based on the grouping of stakeholders in the power/interest grid, develop engagement strategies primarily for the key stakeholders (high power/high interest).

RESOURCES

1. A stakeholder process needs to be carefully planned and resources made available.
2. Staff must be assigned.
3. Administrative resources set aside.
4. Financial resources for data collection reserved.

Additional resources

Mindtools: http://www.mindtools.com/pages/article/newPPM_07.htm

Schmeer K, ***Stakeholder analysis Guidelines***

http://www.eestum.eu/voorbeelden/Stakeholders_analysis_guidelines.pdf

Stakeholder analysis, World Bank

http://www1.worldbank.org/publicsector/anticorrupt/PoliticalEconomy/stakeholderanalysis.htm

APPENDIX 1: TEMPLATE FOR STAKEHOLDER IDENTIFICATION

Example: Pulse Polio Immunisation India - Stakeholder Analysis

Mary Hanley, Sayaka Koseki, Erin Morehouse, Glory Song

Stakeholders	Involvement in issue	Interest in issue	Influence/ power	Resources	Position	Impact of assessment on stakeholder
National Level						
Ministry of Health & Family Welfare	Sets national health agenda (including whether to prioritise polio eradication or not), financial provider, and technical assistance provider.	**Medium** - Other health programmes now take priority as polio cases decrease; funding has decreased as this programme is in its 16th year. However, there was a renewed interest in 2011 in polio eradication (i.e. Gates Foundation focus) which may increase the government's interest.	**High** - India mostly finances its own polio eradication programme, so they have decision power on which health issues to allocate funds to. Power to determine which states receive sub-national immunisation days and provide HR and technical expertise to PPI.	**High** - Main source of monetary resource; technical expertise on polio and best practices on running immunisation days.	**Latent** - High influence because of allocation of money and resources, but medium/ low interest because of fatigue (programme was started in 1995) and competing health programmes.	**Medium** - Funding relies somewhat on the outcome of the evaluation: if the PPI is found to be ineffective the MOHFW may reduce the funding to the programme, or increase the funding to improve the programe.

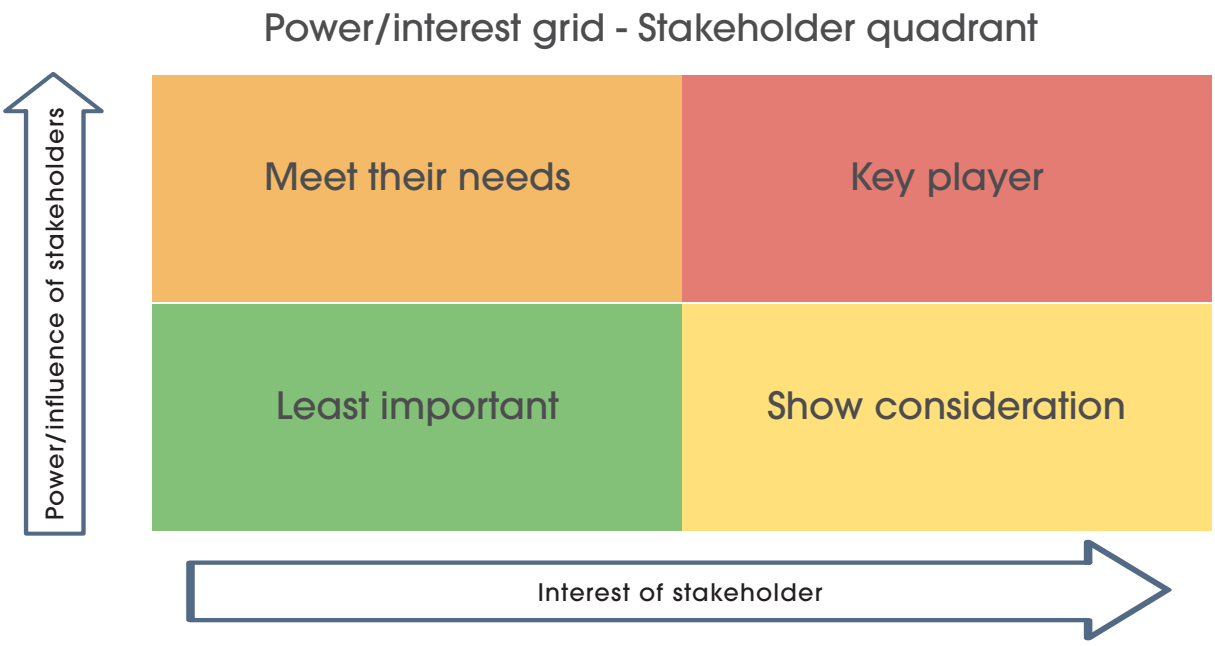
Stakeholders	Involvement in issue	Interest in issue	Influence/ power	Resources	Position	Impact of assessment on stakeholder
State Level						
State Governments/ Union Territories	Upper management for immunisation programmes; In charge of campaigns; Provides vaccines and logistical support.	**High/medium** - States with embedded polio cases may care, although lowered budget seems to show their reduced interest. Low among other states where polio is no longer present.	**High** - Responsible for the programme working in each state, which includes securing and distributing the vaccine, maintaining cold chain supply, training the booth staff, planning and organising the booths.	**High** - Providing technical expertise and logistics, as well as situational assessment determining where booths will be set up according to needs, and placing staff at the booths.	**Latent** - Primary implementers for the state and receive resources for the project; however they have a relatively low priority set for the project.	**Medium** - This project is one of many that they oversee, however, because of the significant resources currently placed in the project, the change in the initiative, due to the evaluation outcome, can have a decent impact.

Stakeholders	Involvement in issue	Interest in issue	Influence/ power	Resources	Position	Impact of assessment on stakeholder
Local Level						
1: 20 Community Workers	Go into 20 assigned households two weeks and again two days before NID to inform residents about upcoming booth days and to encourage them to participate. This often requires that they address fears and concerns about vaccination. On vaccine days, they bring children to the booth, and provide booth workers with lists of families and children to help improve record-keeping.	**High** - 1:20 Community workers will be selected by the community from within the community itself. As a result, they will likely have a vested interest and also social obligations to their neighbours.	**Medium** – 1:20 Community workers serve as the first line of communi-cation to the local population - providing information on NIDs. As a result, their behaviour and speech could be a huge determinant in booth participation. At the same time, 1:20 community workers do not have much say in the implementation of the programme, but they can improve their self-efficacy in group meetings with other workers and come together to problem solve.	**Medium/ Low** – 1:20 Community workers will receive basic training in how to encourage the community to participate in the booth days. However, they are not medically trained, so they will have only the resources given to them at training.	**Promoter** – Workers' level of involvement will directly impact booth participation and programme success. Overall, they should have a high interest in the programme and also have strong influence on programme outcomes. They are at the core of the programme intervention, and thus are in a powerful position to promote change and guarantee success.	**High** – The assessment will decide whether they are productive and influential contributors to the programme. The assessment will also improve their shortcomings if areas of improvement can be highlighted. As they are at the core of the intervention, they will likely be the most scrutinised and the assessment will focus on what they do or do not do productively.

Stakeholders	Involvement in issue	Interest in issue	Influence/ power	Resources	Position	Impact of assessment on stakeholder
Local Level						
Anganwadi Workers	Responsible for overseeing their assigned 1:20 workers. They will be trained alongside the 1:20 workers, but will be further responsible for addressing their problems and concerns. They are still community health workers with responsibilities other than polio vaccination.	**Medium/High -** Participate, but may have fatigue from previous polio eradication efforts where they have been understaffed and overworked. The addition of 1:20 workers may provide relief from feeling of overwork. However, some may feel that 1:20 workers are not as well trained and not valuable to the programme, or a threat to their job security or status in the community. They will be responsible for overseeing the work of the 1:20 workers- which will hopefully decrease their workload, but could potentially increase it with added responsibilities.	**Medium/High -** Responsibilities have a direct impact on programme outcomes, but not much say on the operation or strategy behind the programme. They will have more power than the 1:20 workers because they are medically trained, and will have some power in how the 1:20 workers communicate with their households.	**Medium -** Anganwadi workers have four months of medical training, so they have at least basic level of medical knowledge. However, they are oftentimes lacking in financial support. It is hoped this intervention will increase their resources by having workers available to target individual households, leaving them more time for their other responsibilities.	**Promoter -** Workers' level of involvement will directly impact booth participation and programme success. Overall, they should have a high interest in the programme and also have strong influence on programme outcomes.	**High -** Programme assessment of such factors as booth participation or community awareness may directly reflect the quality/ success of their work. If they do a poor job, they may risk losing their position as an Anganwadi worker and the respect of the community. A strong programme may change the working objectives of Anganwadi workers as they take a leadership role regarding polio vaccinations instead of a personal, active role.

Stakeholders	Involvement in issue	Interest in issue	Influence/ power	Resources	Position	Impact of assessment on stakeholder
Local Level						
Parents and Children Receiving OPVs	Primary Beneficiaries, they will receive more personalised attention to address their fears, concerns, and questions. Parents are more able to have a voice in the programme with individualised attention. Children are more likely to attend the booth consistently, and thus receive more OPV.	**Varies -** Those who have seen the negative effects of polio or the benefits of vaccination may show high interest; others who show mistrust or disdain for the government or the vaccination may actually show aversion towards it. Aversion can also be a result of religious affiliation. Finally, the programme has been going on for years without full eradication of polio so parents may feel programme fatigue or that the programme workers are ineffective. However, with the introduction of 1:20 workers they may have more of an interest in talking to the workers about their individual issues and be more likely to participate in booth days.	**High -** Influence on the success and outcome of the programme because they have the personal decision to take children to the booth after talking to 1:20 workers. Low influence in determining the policy and protocol of the programme.	**Low** - For programme implementation. However, they serve as the direct source for any information on the beneficiary population for evaluation.	**Latent** - Their action can affect the implementation and success of the programme, but given their many other priorities and demands of daily life, they may not be proactive proponents of the programme.	**High -** Since they are the beneficiaries of the programme, the assessment will evaluate whether the programme met their needs, if not, then ideally, adjustments will be made to better address their needs.

APPENDIX 2: POWER/INTEREST GRID



Meet their needs

- engage & consult on interest area
- try to increase level of interest
- aim to move into right hand box

Key player

- key players, focus efforts on this group
- involve in governance/decision-making bodies
- engage & consult regularly

Least important

- minimum effort
- inform via general communications – newsletters, website, mail shots
- aim to move into right hand box

Show consideration

- make use of interest through involvement in low risk areas
- keep informed & consult on interest area
- potential supporter/goodwill ambassador

SIVAC

Supporting Independent
Immunization and Vaccine
Advisory Committees

amphpid

HEALTH POLICY AND
INSTITUTIONAL DEVELOPMENT

WHO COLLABORATING CENTRE
FOR EVIDENCE-INFORMED
IMMUNIZATION POLICYMAKING

T R A I N I N G 3

TECHNICAL AND SCIENTIFIC CAPACITIES OF NITAGS

SECTION A

EVIDENCE ASSESSMENT METHODOLOGIES

SECTION B

DEVELOPMENT OF AN EVIDENCE-BASED RECOMMENDATION NOTE



FOR
FACILITATOR

TABLE OF CONTENTS

SECTION A
EVIDENCE ASSESSMENT METHODOLOGIES

PRESENTATION OF THE SECTION 6
TARGET AUDIENCE
PREREQUISITE SKILLS/KNOWLEDGE
LEARNING OBJECTIVES
CONTENT
1. INTRODUCTION: WHAT IS AN EVIDENCE-BASED RECOMMENDATION? 7
2. DEFINING THE EVIDENCE THAT WILL SUPPORT THE RECOMMENDATION 7
2.1. DEFINING THE RECOMMENDATION FRAMEWORK
2.1.1. FRAMING THE QUESTION
2.1.2. IDENTIFYING OTHER FACTORS
2.2. PROPOSED GENERIC RECOMMENDATION FRAMEWORK
2.3. EXAMPLE OF RECOMMENDATION FRAMEWORKS
2.4. RANKING BY IMPORTANCE THE FACTORS AND SPECIFIC DATA
3. FINDING THE EVIDENCE 16
3.1. SELECTING THE SOURCES OF EVIDENCE
3.2. COLLECTING THE EVIDENCE
3.3. KEEPING A RECORD OF THE SEARCH METHOD AND ITS RESULTS
4. ASSESSING THE QUALITY OF EVIDENCE 18
4.1. EVIDENCE FOR EACH INTERVENTION OUTCOME
4.2. PUBLISHED SYSTEMATIC REVIEWS AND NON-CLINICAL/NON-OBSERVATIONAL STUDIES
REFERENCES 20
FACILITATOR INSTRUCTIONS 21
ANNEX 1: EXAMPLE OF GROUP WORK 40
ANNEX 2: CASP CHECKLIST FOR SYSTEMATIC REVIEWS 41
ANNEX 3: AMSTAR CHECKLIST 43
ANNEX 4: SIGN CHECKLISTS 45

SECTION B
DEVELOPMENT OF AN EVIDENCE-BASED RECOMMENDATION NOTE

PRESENTATION OF THE SECTION 52
LEARNING OBJECTIVES
1. OVERVIEW OF THE PROCESS FOR DEVELOPING AN EVIDENCE-BASED RECOMMENDATION 53
2. DEVELOPING AN EVIDENCE-BASED RECOMMENDATION 54
2.1. ANALYSIS (JUDGEMENT) OF THE BODY OF EVIDENCE
2.1.1. INTERVENTION AND ITS OUTCOME(S)
2.1.2. OTHER FACTORS LISTED IN THE RECOMMENDATION FRAMEWORK
2.2. WRITE-UP OF THE DRAFT RECOMMENDATION NOTE
2.2.1. OUTLINE OF THE DRAFT RECOMMENDATION AND KEY POINTS TO ADDRESS
3. DELIBERATION AND DECISIONS FOR THE PROPOSED RECOMMENDATION 57
REFERENCES 57
FACILITATOR INSTRUCTIONS 58

SECTION A

EVIDENCE ASSESSMENT METHODOLOGIES



FOR
FACILITATOR

PRESENTATION OF THE SECTION

This section presents the initial phases in the process of developing a recommendation, i.e. defining a framework for making a recommendation and evaluating the evidence.

The World Health Organisation has issued a "Guidance for the development of evidence-based vaccine-related recommendations"[1,3] which is directed to its Strategic Advisory Group of Experts on immunisation (SAGE). The content of this section refers largely to the guidelines followed by SAGE. The section also makes reference to immunisation decision-making frameworks used by existing NITAGs[1,2,3,4], publications on knowledge-translation in vaccination policies and relevant guidelines and articles issued by the Grading of Recommendations Assessment Development and Evaluation (GRADE) Working Group, the Evidence-Informed Policy Network (EVIPNet), the US Centers for Disease Control (CDC) and other technical agencies[5]. Examples of recommendation frameworks used by some institutions and a generic framework are presented.

The section presents the principles of the GRADE approach which is primarily used for assessing the quality of epidemiological studies reporting on the outcomes of an intervention (safety and effectiveness). The GRADE approach is increasingly being adopted by organisations worldwide[6], and GRADE has been officially used by SAGE since 2008[7] and by several NITAGs (US ACIP[8], Canadian NACI[9], etc.) for several years. SAGE and NITAGs have been collaborating with the GRADE Working Group in order to adapt the method to vaccine-relevant evidence[10].

The section also presents other tools and checklists for assessing the quality of non-clinical studies.

This session will guide experts in defining the framework of a recommendation (evidence that will guide the recommendation) and evaluating the evidence relevance and quality.

After presentation of the methods and concepts, group exercises will be organised for practical application of the principles presented.

TARGET AUDIENCE

NITAG's Executive Secretariat, Chairman, and Members

PREREQUISITE SKILLS/KNOWLEDGE

Skills in performing literature reviews, knowledge of NITAG mode of operations (Sections A & B of Training 1) and analysis of the health system and immunisation context (Sections A & B of Training 2).

LEARNING OBJECTIVES

- Learn how to frame a question to guide the search of evidence
- Learn how to define the framework for a decision considering clinical data (from clinical trials or observational studies), and health system, socio-cultural, and equity issues
- Learn which are the most relevant databases for most NITAG topics and how to use them to find evidence at the international, national, regional, or local levels
- Learn which tools are available to evaluate the quality of data and how to use them

CONTENT

- Training resources: section content, slide deck, facilitator's notes
- Resources for the participant: short summary of the course and templates

1. INTRODUCTION: WHAT IS AN EVIDENCE-BASED RECOMMENDATION?

Low- and middle-income countries face a detrimental gap between research, policy, and practice, which often delays policy formulation regarding new interventions, including vaccines. One of the reasons for this delay is the challenge in finding and using relevant evidence for decision-making. To improve evidence-based decision-making processes on immunisation and vaccines, WHO recommends the establishment of sustainable National Immunisation Technical Advisory Groups (NITAGs). This recommendation is supported by global immunisation partners (UNICEF, SAGE, and stakeholders of the Decade of vaccines - Global Vaccine Action Plan). NITAGs make recommendations on issues such as the introduction of new vaccines, appropriate vaccine schedules, financing, and research priorities and strategies.

A recommendation from the NITAG should be based on evidence collected, reviewed, and synthesised through a systematic, credible, and transparent process. The recommendations should be communicated in an understandable way[11].

The process described here includes some of the steps in the GRADE approach for issuing an evidence-based recommendation.

2. DEFINING THE EVIDENCE THAT WILL SUPPORT THE RECOMMENDATION

Two actions need to be undertaken:

1. Define the recommendation framework
2. Rank by level of importance the intervention outcome and other factors to consider in making the recommendation

2.1 DEFINING THE RECOMMENDATION FRAMEWORK

To issue a recommendation on a vaccine (or another intervention), the NITAG will have to define the framework of the recommendation, i.e. ***the different elements to take into account in issuing the recommendation, which will then govern the search of evidence.*** The recommendation framework will consider the effects of the intervention as well as other elements which will influence the decision. Regarding the effects of the intervention, it is important to define the outcome(s) that will be taken into account in the recommendation. The outcome should be specified vis-a-vis the population under study and in comparison with another intervention.

Defining the recommendation framework ensures transparency about the grounds for decisions

2.1.1 Framing the question about the effects (outcomes) of the intervention (PICO method)

A question on the effect of an intervention is traditionally framed using the PICO method. The method is primarily used when conducting systematic reviews of clinical studies but is also recognised by experts as a useful approach in guideline development. It can be used in any research context. The PICO method is an approach for formulating focused research questions about an intervention. This step is important for the evidence search that follows as it helps focus on the area of enquiry when conducting the literature review.

PICO: **P = Population, Patient, or Problem**
I = Intervention
C = Comparator
O = Outcome

P = Population, Patient, or Problem

The first step in defining the evidence to look for is to define the problem, the disease, or the population concerned by the recommendation.

The population specifically targeted needs to be defined. The following factors need to be considered:

- Age (e.g. 2-6 months, over 2 year)
- Disease (e.g. HIV infected, healthy)
- Settings (e.g. whole country, poor/ rich area, specific geographical region)
- Sex
- Others

It should be kept in mind that subgroups of interest might emerge later in the process: recommendations may differ between different **subgroups** of patients, or evidence quality may differ among subgroups and this may result in different recommendations.

I = Intervention

The type of intervention considered for the population, the problem, or the patient needs to be defined:

- Introduction of a new vaccine
- Two different vaccines
- Addition of a booster dose

C = Comparator

The comparator is the situation of reference that needs to be compared with the intervention the NITAG is considering, e.g. recommending the intervention versus not vaccinating at all in the case of a new vaccine.

The two questions that need to be answered in order to define a comparator are:

- Which recommendations are used in the country and outside the country?
- Which interventions are used in the country and outside the country?

The comparator may be obvious or not. However, NITAG will, by consensus, select **only one comparator of interest.** The recommendation on the intervention for the specific population will be made in regard to this comparator. If several comparators are of interest, several specific questions should be framed.

O = Outcome

The outcome is the effect of the intervention that will be measured or explored. An outcome can refer to **desirable** (benefits, less burden, and savings) or **undesirable** effects (including harms, greater burdens, and costs) of an intervention. It is very **important** to identify all known and plausible outcomes that are important to those affected by an intervention.

Effects of both the intervention and the comparator defined in the question need to be assessed by using a range of outcomes that need to be specified. Evidence on each outcome will be rated and analysed.

The PICO approach is not restricted to questions in vaccination. Examples of PICO questions are presented below:

Ex 1: "Is the use of sodium hydroxide a viable alternative to phenol for nail matrix ablation?"

- Population: people with ingrown toenail
- Intervention: use of sodium hydroxide for nail ablation
- Comparator: Use of phenol for nail ablation
- Outcomes: healing rate, satisfaction, post-op pain

Ex 2: "In HIV-infected infants, should the measles immunisation schedule be modified in comparison with the generally recommended schedule?"

- P = HIV-infected infants
- I = the measles immunisation schedule
- C = the generally recommended schedule
- O = decreased morbidity of HIV-infected infants, minor or serious adverse events, including fever and diarrhoea

The NITAG or the designated Working Group must therefore make a list of the intervention effects which are relevant to the decision-making process. The effects studied usually focus on the safety, efficacy, and effectiveness of the intervention. For each of these effects, specific type of data should be defined. The outcomes selected should be those **important to the patients.** To identify those outcomes, the Working Group will refer to the literature, members' experiences, or even patient associations. Once outcomes of the intervention have been selected, they must be categorised as critical, important, or non-critical (e.g. "nice to have"). Because there are usually constraints in resources that can be devoted to the search of evidence, SAGE has recommended that the five most critical outcomes be studied first[12].

If, after reviewing the literature, there is evidence lacking for an important outcome, this should be acknowledged in the report, rather than ignoring the outcome.

Examples of intervention outcomes considered in a recommendation framework (adapted from Kimman (2006), *Vaccine evaluation model for decision-making*) can be found in Section 2.2.

2.1.2 Identifying other factors to take into account in the recommendation framework

Decision about an intervention is not only guided by its effects. There are other elements which should also be considered before making a recommendation, whether it is in regards to the introduction of a new vaccine or other immunisation issues.

When the recommendation concerns a new vaccine introduction or any other immunisation strategy issue, NITAG will draw up a recommendation framework based on their opinion, experience or literature review.

The table below provides an example of a list of other elements, besides the effects of the intervention, which can be considered in the recommendation framework. And specific data on each element forming the recommendation framework is defined. Although NITAGs are not involved in the implementation of a recommendation, they need to take into account the context in which the recommendation will be implemented and bear in mind the possible impact of the recommendation on the systems in place, for example, whether the monitoring system is strong enough to monitor possible vaccine-induced serotype conversions, can be a key factor in the recommendation framework.

New vaccine introduction guidance is provided in the **WHO "Principles and considerations for adding a vaccine to a national immunisation programme: from decision to implementation and monitoring"** available at http://www.who.int/immunization/documents.

WHO recommends that policy-makers consider the following factors when deciding about inclusion of a vaccine in a national immunisation programme:

- The vaccine characteristics
- The disease targeted by the vaccine
- Economic considerations
- Health system and programmatic issues

In some situations, equity and acceptability can be important factors to consider in the decision-making process.

The final recommendation framework will therefore include factors related to the effects or outcomes of the intervention studied and other factors important for the decision.

2.2 PROPOSED GENERIC RECOMMENDATION FRAMEWORK

1. VACCINE AND IMMUNISATION CHARACTERISTICS	
Element	**Specific data**
Safety	Type, consequences, and frequency of short, and long-term adverse events following vaccination
	Risk groups or risk factors for adverse events
	Contraindications
Efficacy and Effectiveness	Type-specific protection afforded
	Critical determinants of the immune response associated with protection
	Duration of protection and waning of immunity if any
	Interference regarding protection or immunity with other vaccines
Vaccine indirect effects	Impact on resistance to antibiotics and antivirals
	Herd immunity
	Potential negative population impact through change in age of infection for unprotected individuals, e.g. rubella or varicella vaccine, or emergence of non-vaccine serotypes
Vaccine characteristics	Vaccine presentation and formulation
	Dosage and route of administration
	Administration schedule and possibility of co-administration with other vaccines
	Flexibility of vaccination schedules
	Cold chain and logistic requirements

2. DISEASE	
Element	**Specific data**
Burden of disease	Incidence of morbidity and mortality, age-specific morbidity and mortality, risk groups, serotype/serogroup distribution, epidemic potential, disease occurrence over time, changes in epidemiology over time
Clinical characteristics of disease	Signs and symptoms of disease, severe forms of disease, long-term complications of disease, medical management of disease
Use and costs of healthcare	Primary/secondary/tertiary care implications, short- and long-term use of healthcare (e.g. treatments, hospitalisation)
Alternative preventive and control measures	Alternative preventive and control measures (e.g. health education, hygiene, vector control) and their effectiveness, costs, and practicality
	Other existing vaccines against the same disease and their effectiveness, costs, and practicality
Regional and international considerations	Existence of regional and global recommendations
	Disease potential for international spread and pandemic potential

3. ECONOMIC AND OPERATIONAL CONSIDERATIONS	
Element	**Specific data**
Vaccine-related costs and resource use	Direct and indirect costs of administering the vaccine as they compare to those of other existing vaccines or other prevention or control measures
Vaccine availability	Availability of vaccine and long-term supply
	Available suppliers and competition dynamic in the market
Vaccine affordability	Availability of fiscal space to effectively implement and sustain the recommendation in the programme
	Prevailing prices for the vaccine in the market and price estimations for the specific country
Socio-economic and social impacts of disease	School and work absenteeism
	Indirect cost to patients and families
	Productivity losses
	Stigma around a disease
Economic impact of intervention on immunisation programme as well as health sector	Reduction in healthcare costs
	Health gains (years of life saved, QALY gained, etc.)
	Cost-effectiveness ratio of vaccination programme

4. HEALTH POLICY AND PROGRAMMATIC ISSUES	
Element	**Specific data**
Interaction with other existing intervention and control strategies	Impacts of programme (catch-up) on safety and efficacy of other vaccines and other healthcare sectors
Feasibility	Accessibility of target population
	Availability of the vaccine and long-term supply in public and private sector, including collaborations with insurance sector
Vaccine registration and regulations	National regulatory authority requirements for licensing the vaccine and/or its use in a different schedule as originally recommended
Impact on resources	Availability of human, technical, and financial resources for distribution (including cold chain sustainability); consider additional training needs of health workers
Ability to evaluate	Availability of information systems to manage the vaccine supply chain and measure related performance metrics, i.e. coverage and vaccine utilisation
	Existence and reliability of surveillance system
Acceptability	Perception of the public and medical community about the disease and the vaccine
Equity	Universality, accessibility, and gratuity of services for all the inhabitants in the country, including vulnerable, hard-to-reach and immigrant populations
Social considerations	Non-health-related effects of vaccination, ethical considerations, legal implications, etc.

NB: Vaccine safety data should always be selected as a component of a recommendation framework.

2.3 EXAMPLE OF A RECOMMENDATION FRAMEWORK

Factors which underpin the development of SAGE recommendations

MAIN FACTORS	SPECIFIC ELEMENTS
Epidemiologic features of the disease	- Disease burden, including age-specific mortality and morbidity - Specific risk groups - Epidemic potential - Disease occurrence over time (i.e. secular trends) - Serogroup or serotype distribution (for serogroup- or serotype-specific vaccines) - Changes in epidemiological features over time.
Clinical characteristics of the targeted disease	- Clinical management - Disease severity and fatality
Use and costs of healthcare	- Primary/secondary/tertiary care implications - Long-term complications and medical care requirements
Vaccine characteristics	- Cold chain and logistical concerns - Vaccine schedule(s)
Vaccine indirect effects	- Indirect effects (potential impact on strain selection, herd immunity, potential safety concerns of live attenuated vaccines in contacts of vaccinees, serotype replacement)
Vaccine efficacy and effectiveness	- Efficacy - Effectiveness and population impact of the vaccine
Feasibility	- Social and programmatic acceptability of the schedule(s) - Ability to reach the target populations
Ability to evaluate	- Ability to monitor programme impact
Vaccine availability	- Vaccine availability
Vaccine safety	- Safety
Economic considerations	- Cost of illness - Vaccine and vaccine delivery costs - Potential for vaccine price reductions - Cost-effectiveness of immunisation programmes - Affordability of immunisation

MAIN FACTORS	SPECIFIC ELEMENTS
Health system considerations	- Possible interactions with other interventions and control strategies - Possible impact of vaccine introduction on the wider health system
Social impacts Legal considerations Ethical considerations	

Evidence-based recommendations include scientific evidence regarding vaccine safety and effectiveness as well as other factors important to the decision: social values, feasibility, sustainability, etc., which are equally critical to the final recommendation.

2.4 RANKING BY IMPORTANCE THE FACTORS AND SPECIFIC DATA TO CONSIDER IN MAKING THE RECOMMENDATION (NON-CRITICAL, IMPORTANT, CRITICAL)

Among the elements selected for the recommendation framework and the related specific data, some are of utmost importance for the decision and some are less important. For example, in the type of data considered in the safety factor, risk of anaphylactic shock and mild flatulence as a rare adverse effect are not of the same importance. The data should therefore be ranked according to their level of importance, from critical (high priority), important (medium priority) to non-critical (low priority).

Values and preferences should guide the ranking of the intervention outcomes whenever possible. In the same way, in considering vaccine presentation in the recommendation framework, fewer numbers of doses may be more important than the flexibility of the administration schedule. Literature searches will focus on critical and important data.

3. FINDING THE EVIDENCE

Once the factors to examine for issuing the recommendation have been identified, the NITAG Secretariat and the responsible Working Group are to find the evidence related to each of them and rate the evidence quality using the following steps:

1. Selecting the sources of evidence
2. Collecting the evidence for each specific datapoint
3. Keeping the record of the search method and its results

3.1 SELECTING THE SOURCES OF EVIDENCE

Working Group members will need to look at various sources of evidence. It is important to collect published literature as well as grey literature relevant to the topic considered.
Published literature includes: scientific articles, WHO clinical guidelines, vaccine recommendations by SAGE, literature reviews, etc.
Grey literature covers any document that has not been peer-reviewed or published commercially, including national annual immunisation reports, country reports on AEFIs and epidemiology, social acceptability reports, etc.
The main sources of published literature (clinical guidelines, vaccine recommendations, scientific articles, literature reviews, economic evaluations reports, etc.) with international data are:

Generic databases:

- WHO databases: http://www.who.int/library/databases/en/
- The Cochrane library:http://www.thecochranelibrary.com
- MEDLINE/PubMed: http://www.ncbi.nlm.nih.gov/pubmed
- Centre for reviews and dissemination: http://www.crd.york.ac.uk/crdweb/SearchPage.asp
- Mac Master health forum, Health System Evidence: http://www.mcmasterhealthforum.org/healthsystemsevidence-en

Vaccine-specific:

- WHO IVB database: http://www.who.int/immunization/documents/positionpapers/en/index.html
- The NITAG resource center (NRC):http://www.nitag-resource.org/en/digitalHibrary/search.php
- OLIVES (On-line International Vaccine Economics and Statistics): http://www.provac-olives.com/node/[1]

Reviewers are also expected to collect national and regional population-based data[11,13]. The following databases provide specific national and regional data (country reports, epidemiological data, etc.)

- Demographic and Health Survey studies: http://www.measuredhs.com/
- PubMed national studies using the MeSH term[ii] of the country of interest
- Specific WHO regional databases: http://www.who.int/library/databases/en/

In order to identify all sources of scientific data nationally and regionally, it is advised to contact NITAG liaison and ex-officio members, local researchers, and other experts. In addition, it is advised to contact NITAG members from countries with similar characteristics and to look for information they might have generated on the same topic if national evidence is not available[11]. National, regional, and local reports, and other types of grey literature can be found through simple searches on Google[14].

NB: While many of the prioritised databases above provide free online access, such access often does not include full-text systematic reviews. In such cases, three options are available:

1. The Health InterNetwork Access to Research Initiative (HINARI) which provides institutions in low-income countries with free access to many published reviews and studies[iii]
2. The Cochrane Library which provides free access to Cochrane reviews in low-income countries and in countries with a national subscription
3. Journals that make their content available free of charge either as soon as they are published or after a defined period of time (e.g. one year)

3.2 COLLECTING THE EVIDENCE

Once the elements of the recommendation framework have been defined, the NITAG Working Group will then search the evidence on each of them. Evidence on the intervention outcomes should be searched for both the intervention and the comparator. Evidence on intervention outcome (safety and effectiveness) should be searched across several studies, e.g. systematic reviews. Search on the outcome(s) of interest for the recommendation framework should be guided by the PICO question. The NITAG Working Group will either perform a systematic review or will search published systematic reviews. Most recent reviews (less than 3 years) should be given priority, as they often offer sufficient findings[12]. Thorough literature reviews are important for identifying knowledge gaps.

3.3 KEEPING A RECORD OF THE SEARCH METHOD AND ITS RESULTS

It is of utmost importance that the search and collection of data be done as systematically as possible and that the processes used be made transparent so as to ensure their reproducibility[14,15]. The literature search should be carefully documented. The research process and results are to be summarised in a search form.
A template form is available in the summary.

[ii] The National Library of Medicine's Medical Subject Headings (MeSH) is the controlled vocabulary used for indexing articles for the MEDLINE®subset of PubMed. http://www.ncbi.nlm.nih.gov/mesh/68005842
[iii] http://www.who.int/hinari/en/

4. ASSESSING THE QUALITY OF EVIDENCE

Once the information has been collected for each specific datapoint, it needs to be assessed through a systematic and standardised process:

1. Assess the quality of each clinical/epidemiological study retrieved and report on each study for each outcome if conducting a systematic review of studies on the intervention outcome
2. Assess the quality of existing systematic reviews and non-clinical/epidemiological studies identified in the search phase

To perform a systematic review of intervention outcome (safety and effectiveness) reported in clinical and observational studies, the NITAG Working Group can primarily use the GRADE quality grading process, which has been the one used by SAGE and adequately fits the purpose of issuing evidence-based policies[16]. The steps involved with GRADE involves assessing each individual study and then assessing the quality of the evidence across studies; it applies to a body of evidence, not to individual studies. The overall rating of the quality of studies reviewed is categorised as high, moderate, low, or very low.

For assessing existing systematic reviews and non-clinical studies (such as socio-anthropological studies, economic evaluations) there are other methods proposed to rate the quality of studies.

It is to be kept in mind that **a particular quality of evidence does not necessarily imply a particular strength of recommendation.**

4.1 ASSESSING THE QUALITY OF EVIDENCE FOR EACH INTERVENTION OUTCOME REPORTED IN CLINICAL/ OBSERVATIONAL STUDIES, ACROSS STUDIES IF PERFORMING SYSTEMATIC REVIEWS ON INTERVENTION OUTCOMES

Steps in assessing data quality when performing a systematic review are listed below. The quality of studies found needs to be assessed before they can be included in the final list of studies that will be used to make the recommendation[14].

There are various methods for grading evidence in healthcare. The most widely used is GRADE, which is mainly used for systematic reviews of clinical and observational studies. A list of articles on the GRADE methodology and a link to a video are provided in the resources folder of this training. A specific topic on GRADE is also proposed in Training 4 of the training manual.

To perform a systematic review of articles using GRADE:

- Select the outcomes of interest
- Rate their importance
- Search studies and evaluate studies on each outcome
- Summarise findings for each outcome
- Rate the quality of evidence for each outcome
- Grade overall quality of evidence across outcomes

4.2 ASSESSING QUALITY OF EVIDENCE OF PUBLISHED SYSTEMATIC REVIEWS AND NON-CLINICAL/NON-OBSERVATIONAL STUDIES

GRADE is particularly adequate for assessing evidence on safety and effectiveness when conducting systematic reviews. It is possible that NITAGs may not need to carry out systematic reviews but will use the results of published systematic reviews. In that case, NITAGs will need to assess the quality of these reviews. In addition, NITAGs have to consider other factors, including programmatic, financing, and socio-cultural characteristics related to the local context. Therefore the NITAG Secretariat needs to use other evidence rating methods for covering non-clinical/non-observational data.

- **A Measurement Tool to Assess Systematic Reviews (AMSTAR)** is a specific appraisal method for rating the evidence of systematic reviews [IV]. The checklist that was developed by this Canadian group is user-friendly and can be applied to all kinds of systematic reviews.

- **The Critical Appraisal Skills Programme (CASP)** is a UK-based programme that provides appraisal methods for rating the evidence of systematic reviews, RCTs, economic evaluations, qualitative studies, and other types of studies [V].

- **The critical appraisal of qualitative research**[17] method looks at four main components:
  1. credibility, i.e. whether or not the representation of data fits the views of the participants studied [V]
  2. transferability, i.e. whether research findings are transferable to other specific settings
  3. dependability, i.e. whether the research process is logical, traceable, and clearly documented
  4. and confirmability, i.e. the extent to which findings are qualitatively confirmable

This aspect is addressed in the section on socio-anthropological approach to immunisation in Training 4.

- **The Scottish Intercollegiate Guidelines Network (SIGN)**[VI] has developed a specific system for grading recommendations in evidence-based guidelines. Their checklists are available in the summary.

[IV] *http://amstar.ca/About_Amstar.php*
[V] *http://www.casp-uk.net/#!casp-tools-checklists/c18f8*
[VI] *http://www.sign.ac.uk/methodology/checklists.html*

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FACILITATOR INSTRUCTIONS

IMPORTANT NOTES:

It is important to introduce participants to the context of this section (goal of Training 3), where it is placed in Training 3, and what the next sections are.

This section presents the key concepts and approach for issuing an evidence-based recommendation. It is important that participants grasp each step of the process.
The session will comprise literature searches in specific databases, and retrieving and evaluating articles using the tools and checklists presented. The exercises will ideally concern a topic currently on the agenda of the participating NITAGs; nevertheless facilitators will also prepare beforehand articles to be used for the exercises if needed.

Knowledge objectives

At the end of this section, participants will be able to :

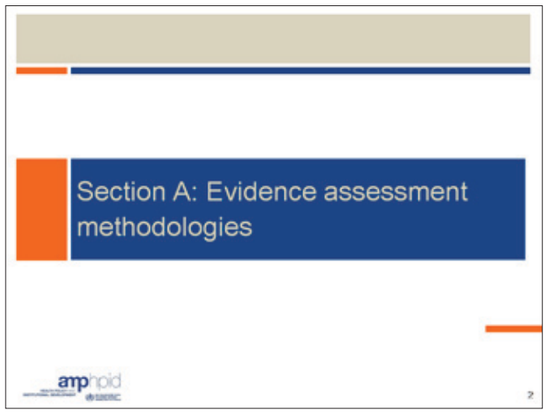
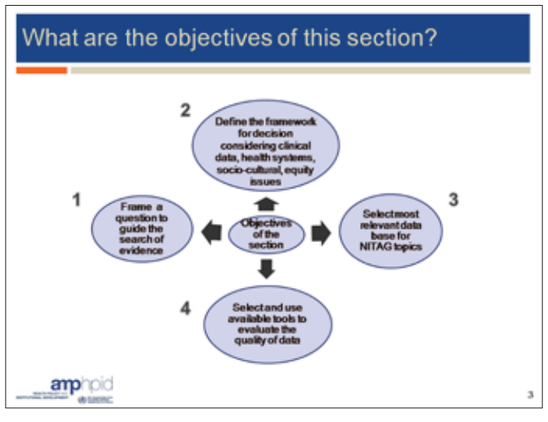
- Frame a question to guide the search of evidence
- Define the framework for decision considering clinical data, health systems, socio-cultural, and equity issues
- Select and use available tools to evaluate the quality of data
- Prepare the most relevant database for most NITAG topics

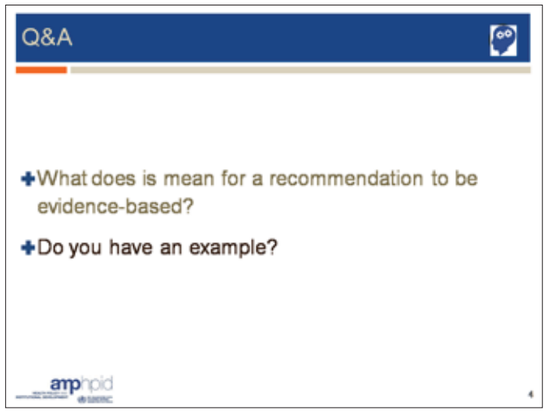
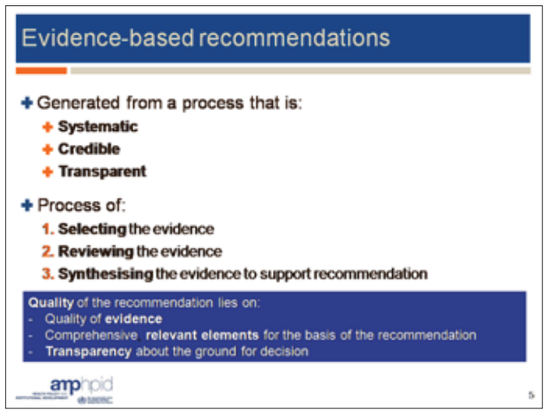
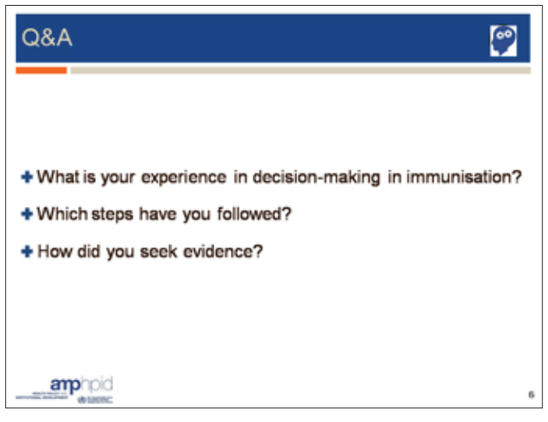
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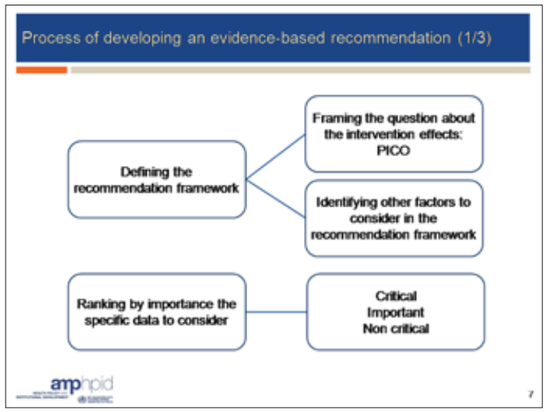
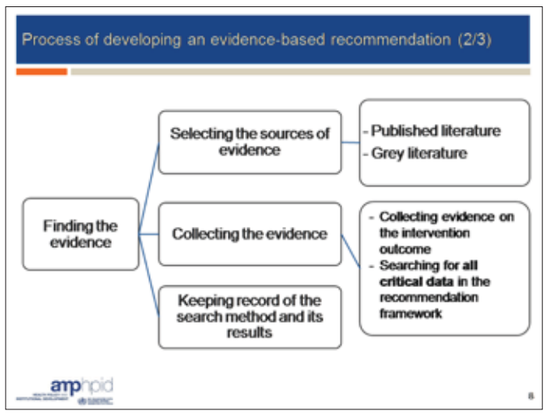
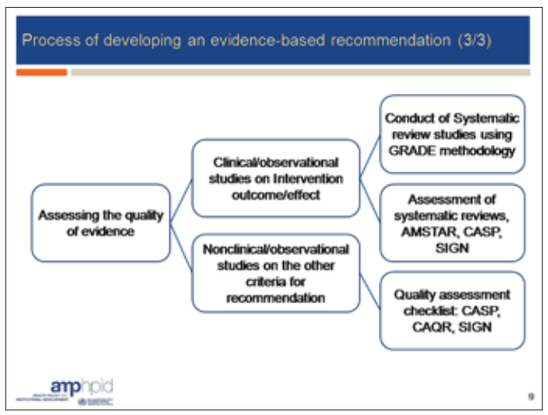
		TIME
STEP 1	Presentation 1-8, Q&A slides 3,4 & 6	30'
STEP 2	Presentation 10-25 "recommendation framework"	40'
	Group work 16	60'
	Group work 25	90'
STEP 3	Presentation 26-35 "finding evidence" &	5'
	Group work 35	90'
STEP 4	Presentation 36-46 "assess the quality of evidence"	35'
	Group work 46	90'
	TOTAL	480' 8HRS

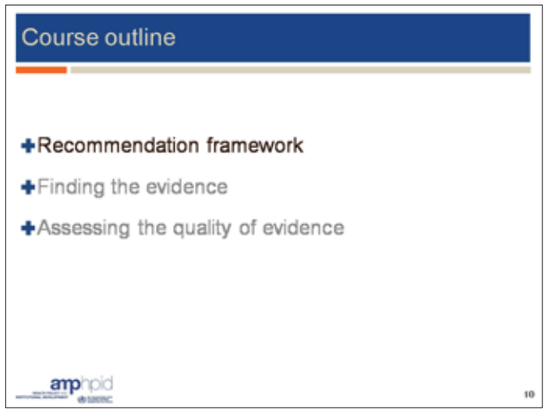
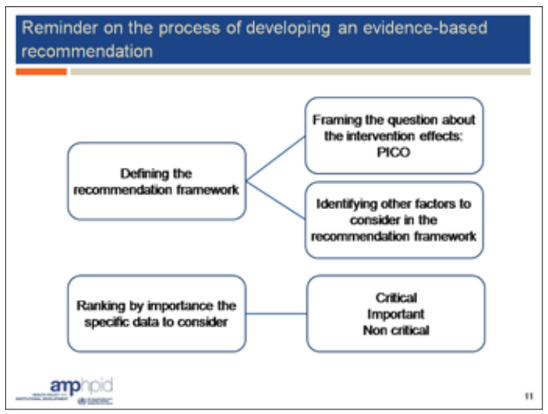
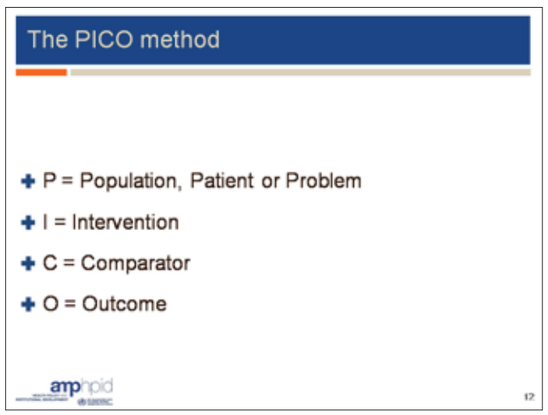
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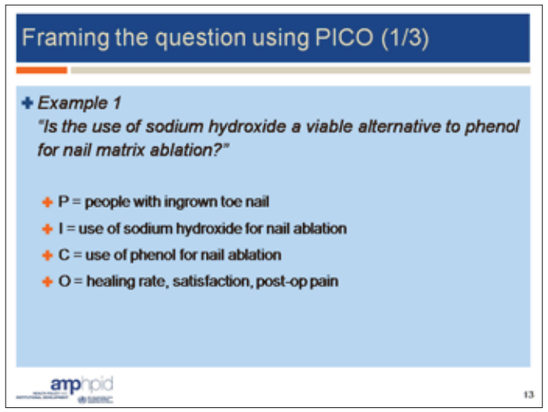
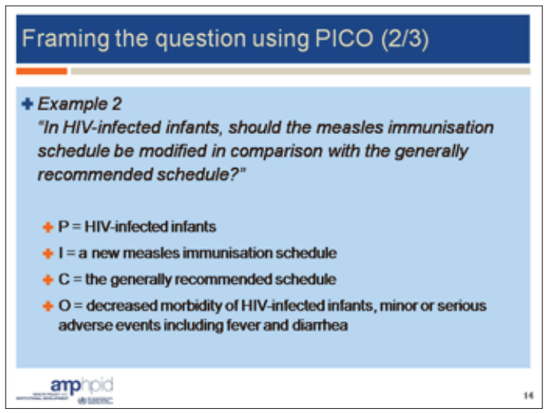
- PowerPoint presentation
- Content document and facilitator instructions
- Internet connexion
- Systematic review on Rotavirus.pdf
- Flipchart, markers

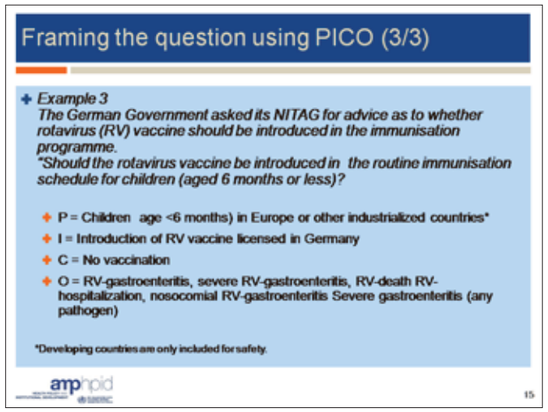
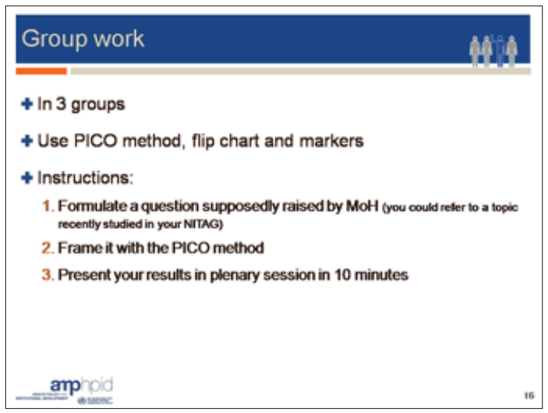
Slides	Facilitation methods
	**Presentation:** introduction of the session This section presents methodologies for identifying data and evaluating the relevance and the quality of data. This section is followed by a second section on the development of an evidence-based recommendation note. 5'
	
	Presentation **Q&A:** Ask participants about their expectations from studying this module. 5'

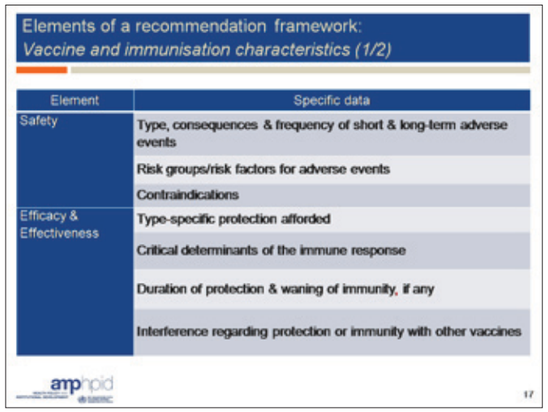
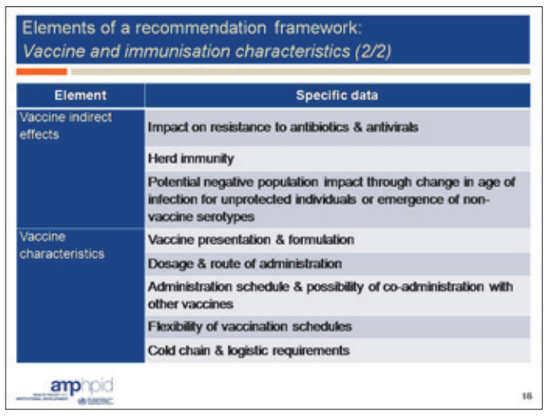
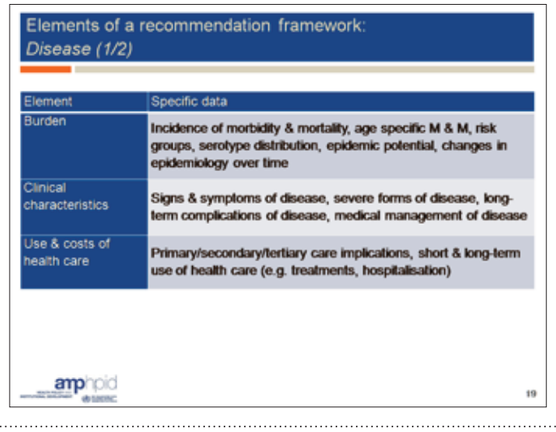
Slides	Facilitation methods
	**Q&A:** Ask participants: - What is the definition of 'evidence-based'? - Do you have an example? 2'
	**Presentation:** show the slide and elaborate on the content, stressing the words in bold 3'
	**Q&A:** Ask participants: - What are your experiences in decision-making in immunisation? - What are the steps you have followed? - How did you seek evidence? 2'

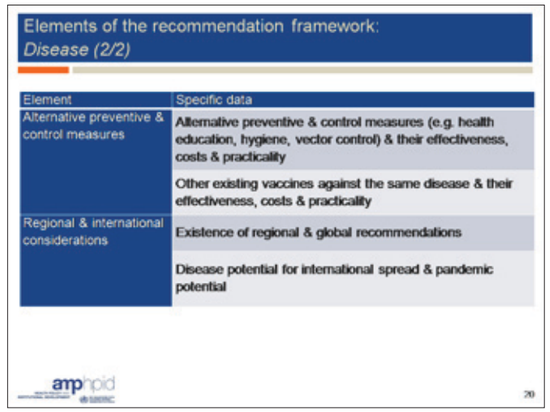
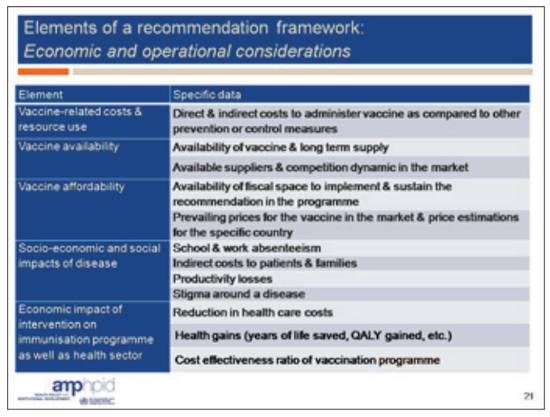
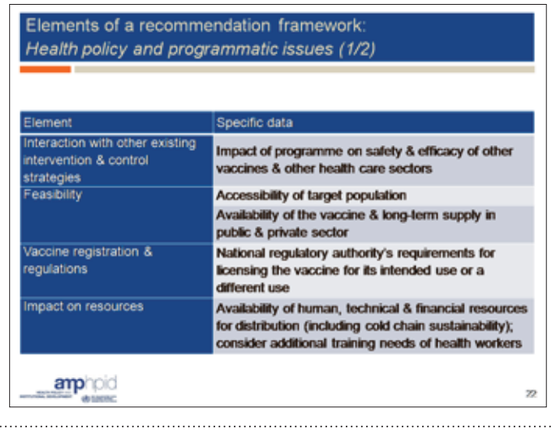
Slides	Facilitation methods
	**Presentation:** 1. Show slides 6-8 and describe the sub-steps of each main step on the left column. 2. Clarify that the steps presented here are adapted from the process described by the GRADE approach for issuing a recommendation. 5'
	**Presentation:** 5'
	**Presentation:** Emphasise that an evidence-based recommendation includes use of transparent and systematic methods. **Q&A:** Encourage questions for clarification. 5'

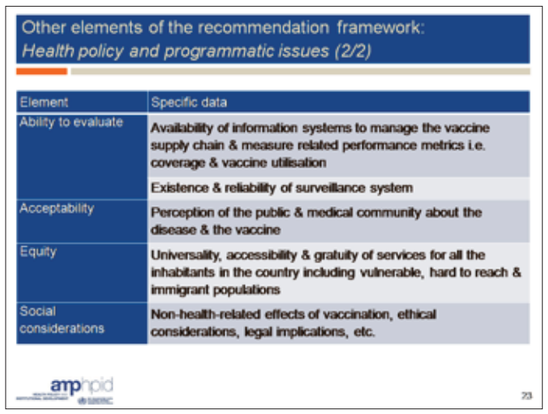
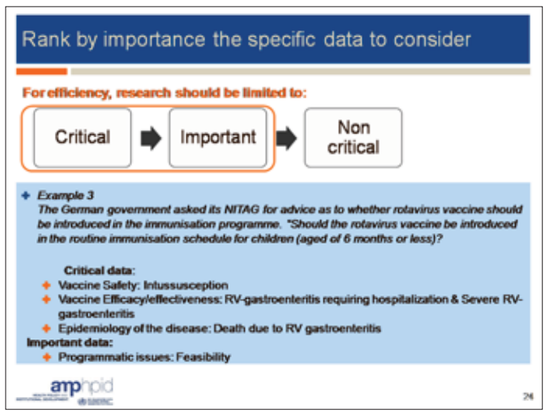
Slides	Facilitation methods
	**Presentation:** Indicate that the first point concerns the recommendation framework. 1'
	**Presentation:** Remind participants of each of the sub-steps. 4'
	**Presentation:** 1'

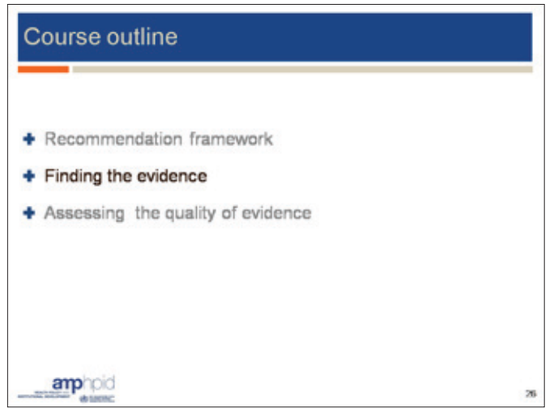
Slides	Facilitation methods
	**Presentation:** 1. Explain example 1. 2. Stress that the PICO approach does not only apply to vaccines but to any intervention considered for a recommendation. It helps ensure a focused evidence search. 4'
	**Presentation and Q&A:** 1. Show example 2. 2. Ask participants to frame the question regarding the intervention using the PICO method, and show the results in a staggered manner: Q. What is our P? A. HIV-infected infants Q. What is our I? A. The measles immunisation schedule Q. What is our C? A. The generally recommended schedule Q. What is our O? A. Decreased morbidity of HIV-infected infants, minor, or serious adverse events, including fever and diarrhoea 5'

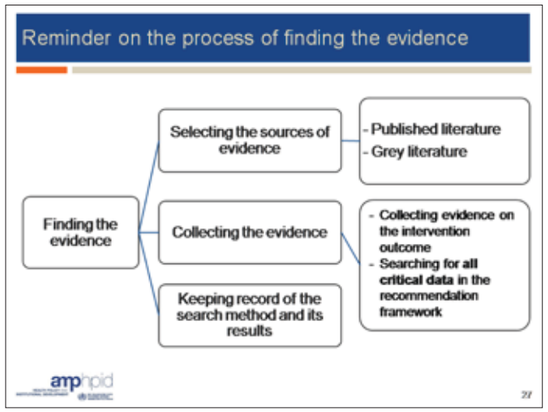
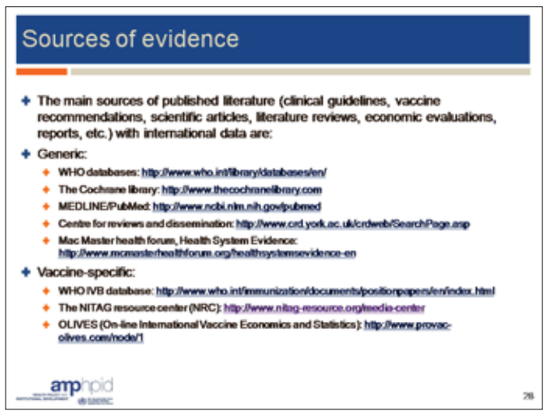
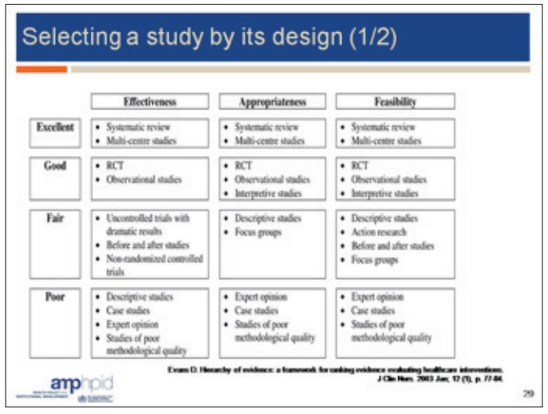
Slides	Facilitation methods
	**Presentation and Q&A:** 1. Show example 3. 2. Ask participants to frame the question regarding the intervention using the PICO method, and show the result : Q. What is our P? A. Children aged <6 months in Europe or other industrialised countries Q. What is our I? A. RV vaccine licensed in Germany Q. What is our C? A. No vaccination Q. What is our O? A. RV-gastroenteritis, severe RV-gastroenteritis, RV-death, RV-hospitalisation, nosocomial RV-gastroenteritis, severe gastroenteritis (any pathogen) 5'
	**Group work:** Objective: the aim of this exercise is to use the PICO method to frame a question about the effect of an intervention. 1. Organise participants in 3 groups and give to each: - a flip chart - markers (5') 2. Ask participants to: - Formulate a query supposedly from the MoH regarding the effect of a vaccine (you could refer to a topic recently studied in your NITAG) (5') - Frame it with the PICO method (20') - Present your results in plenary session in 10 minutes (30' in total. 10' per group) 60'

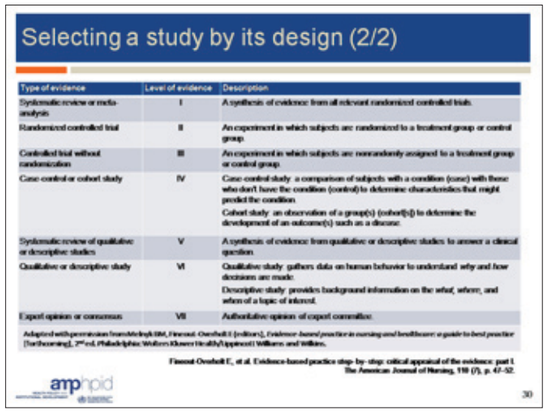
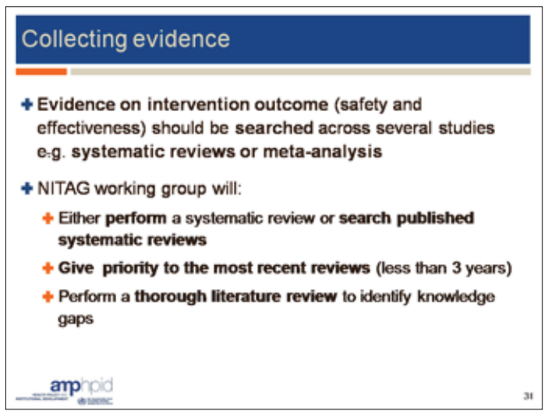
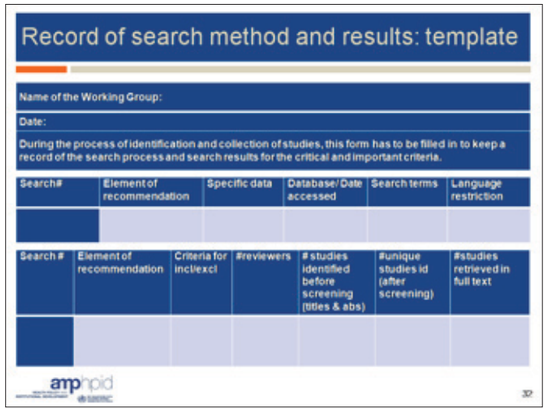
Slides	Facilitation methods
	Presentation: 1. Emphasise that: - There are outcomes/effects of an intervention a NITAG might want to study when preparing a recommendation - It is not enough to just state the type of outcome (e.g. safety) but experts should be specific and define the specific data point for each outcome being considered 2'
	Presentation: 2'
	Presentation: 2'

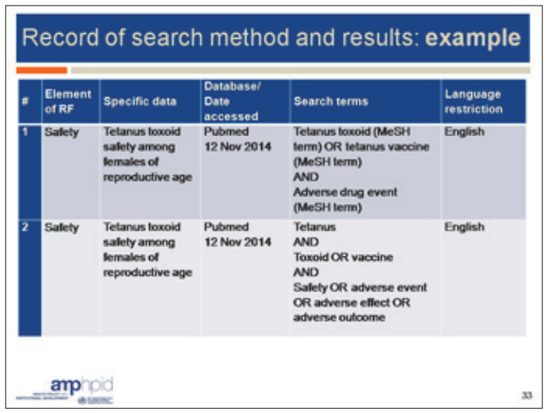
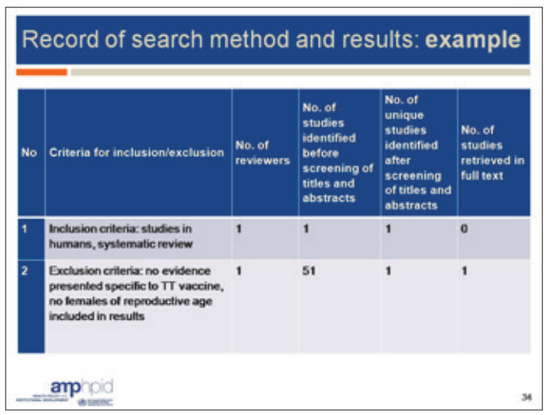
Slides	Facilitation methods
	Presentation: 2'
	Presentation: 2'
	Presentation: 2'

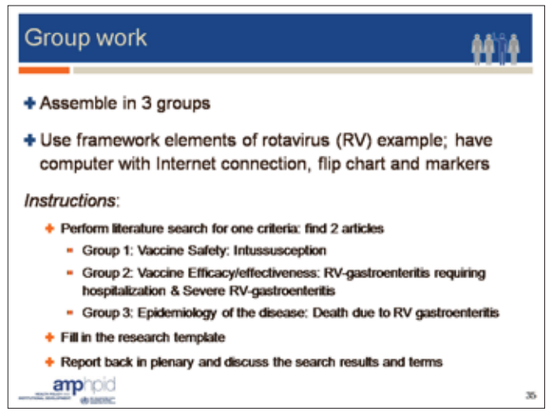
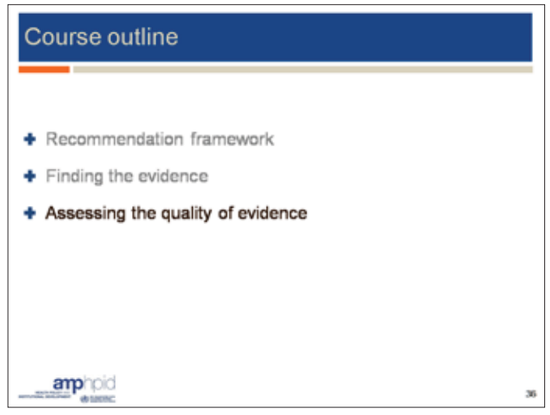
Slides	Facilitation methods
	**Presentation:** Explain the importance of this process as a clearly-defined framework will allow for focused research of evidence. Reiterate the importance of establishing upfront the basis for the decision. **Questions/Answers:** Encourage questions for clarification. 2'
	**Presentation:** 1. Explain that for efficiency, research should be limited to critical and important data of the recommendation framework. 2. Clarify the examples given here for the RV question shown earlier. 5'

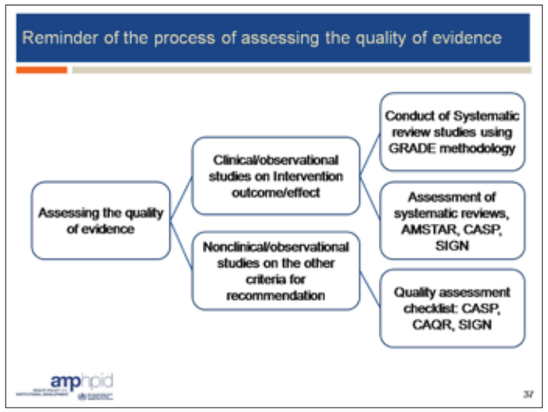
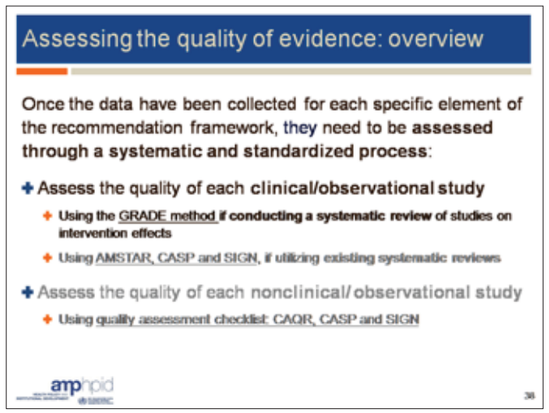
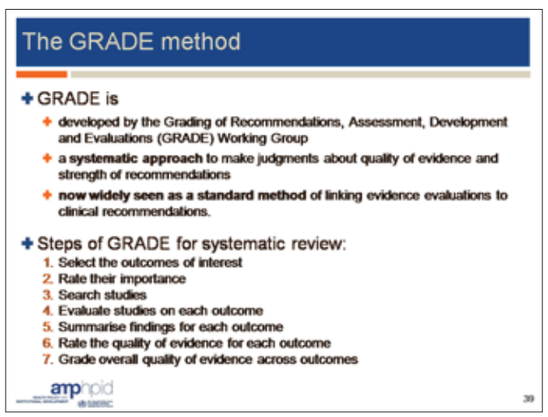
Slides	Facilitation methods
	**Group work:** Objective: the aim of this exercise is to consider all the elements of a recommendations framework & to rank them by importance. 1. Organise participants in 3 groups and give to each: - a topic from example 2 (see in Annex 1) - a flip chart - markers (5') 2. Ask participants to: - Consider all elements of a recommendations framework related to: - Vaccine and immunisation characteristics - The disease - Economic and operational considerations - Health policy and programmatic issues (25') - For each specific datapoint, decide if it is critical/ important/non-critical data (15') - Prepare 2 flip chart sheets to present a) all the elements of the recommendation by category & b) a summary table with the critical data and the important data for restitution in plenary (15') 3. Ask one participant from each group to report back in plenary (30' in total, 10' per group) 90'
	**Presentation:** State that the session continues with the step about finding the evidence. 1'

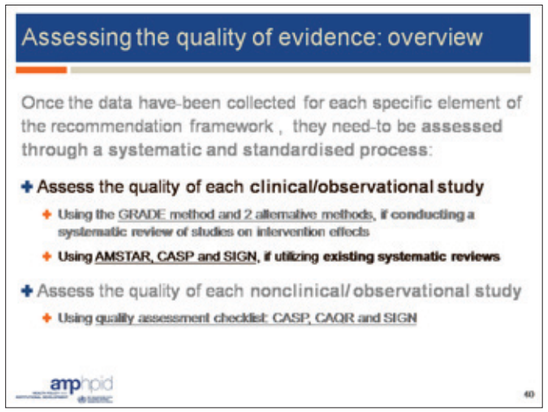
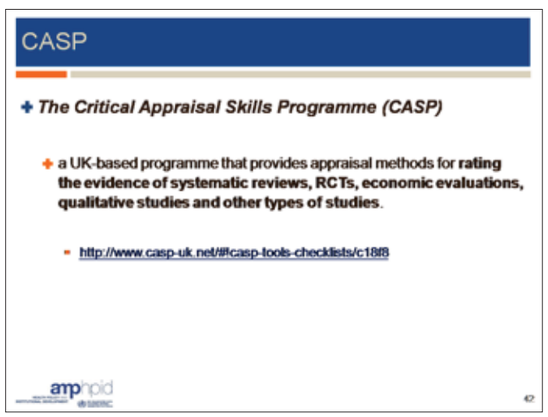
Slides	Facilitation methods
	Presentation: Introduce the topic stating that: Once the factors which will inform the recommendation have been identified (recommendation framework) and ranked by level of importance, 3 sub-steps in finding evidence are important: 1) Select the sources of evidence in published and grey literature 2) Collect the evidence for each datapoint (on the intervention outcome and other elements) 3) Keep a record of the search method and its results 4'
	Demonstration: 1. Click on the link to the WHO database and show: - the access to WHOLIS: World Health Organisation's library online catalogue - the access to read the WHOLIS tutorial 2. Click on the link to the NITAG resource center (NRC) and show the research engine by type of document, vaccine, or region. 3. Tell participants that there will be an opportunity to practice on these tools 5'
	Presentation: Point to the different types of studies and the ranking attributed to them for responding to different types of evidence 2'

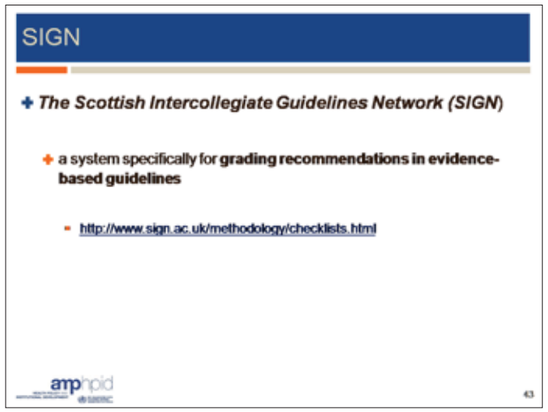
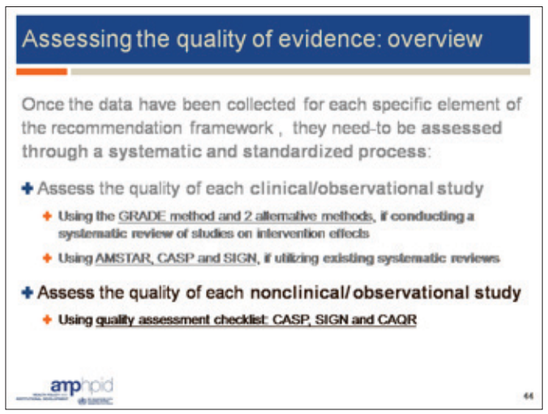
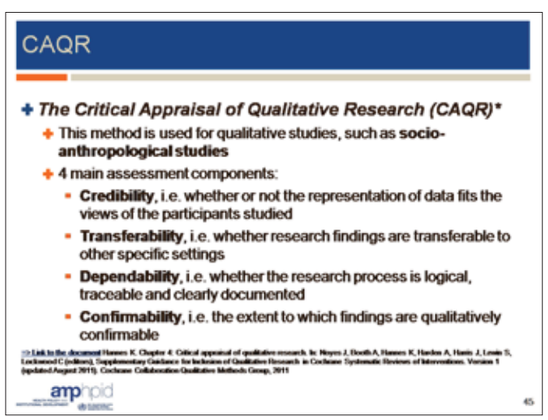
Slides	Facilitation methods
	Presentation: Point to the different types of studies and the ranking of the level of evidence they provide (I = the highest) 2'
	Presentation: 2'
	Presentation: List all elements to be entered in this template 4'

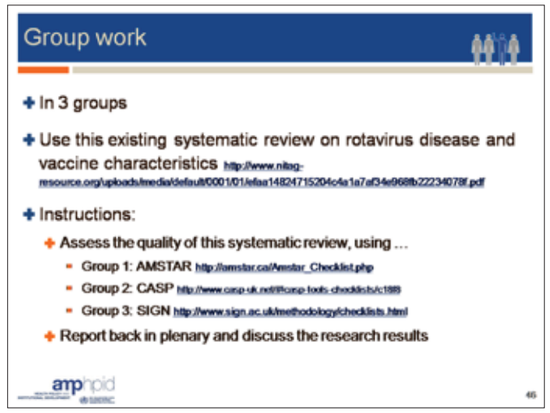
Slides	Facilitation methods
	**Presentation:** Show the 2 examples on how the search was conducted and recorded, especially what terms were used in searching the evidence. 2'
	**Presentation:** 2'

Slides	Facilitation methods
	**Group work:** Objective: the aim of this exercise is to find evidence. 1. Ask the participants to go back to their previous groups to continue the exercise for the rotavirus example and give to each : - a flip chart - markers (5') Ensure each group has a computer with Internet connection 2. Ask the participants to: - Perform a literature search for their criteria and find 2 articles (including one systematic review) Group 1: Vaccine Safety: Intussusception Group 2: Vaccine Efficacy/effectiveness: RV-gastroenteritis requiring hospitalisation & Severe RV-gastroenteritis Group 3: Epidemiology of the disease: Death due to RV gastroenteritis (25') - Fill in the research template as guided (30') 3. Ask one participant from each group to report back in plenary (30'in total and 10' per group) 90'
	**Presentation:** Indicate that the next step addresses the assessment of quality. 1'

Slides	Facilitation methods
	Presentation: Reminder of each sub-step 4'
	Presentation: 2'
	Presentation: Explain that: - GRADE method is used by SAGE and more experienced NITAGs. NITAGs may not need to perform their own systematic reviews, however the most important aspect in developing the recommendation is to be transparent about the process used. 2'

Slides	Facilitation methods
	Presentation: Explain that: - Whereas GRADE is used to assess the quality of evidence arising from several studies, there are other methods available to grade the quality of individual studies. 2'
	Presentation & demonstration: - Read the text - Click on the link to show the checklists 5'
	Presentation & demonstration: - Read the text - Click on the link to show the checklists 5'

Slides	Facilitation methods
	Presentation & demonstration: - Read the text - Click on the link to show the checklists 5'
	Presentation: 2'
	Presentation & demonstration: - Read the text - Click on the link to show participants the description of the methodology 5'

Slides	Facilitation methods
	Group work: *Objective: the aim of this exercise is to assess the quality of a systematic review* 1. Ask the participants to go back to their previous groups to continue the exercise on the rotavirus example and give to each : - a flip chart - markers - a checklist (see in Annexes 2, 3 & 4): Ensure each group has a computer with Internet connection Group 1: AMSTAR Group 2: CASP Group 3: SIGN (5') 2. Ask participants to: - Assess the quality of the systematic review, using: Group 1: AMSTAR Group 2: CASP Group 3: SIGN - Fill in the checklist templates (in Annexes) (30') - Prepare a summary to explain the results in plenary session (25') 3. Ask one participant from each group to report back in plenary (30' in total and 10' per group) 90'

ANNEX 1: EXAMPLE OF GROUP WORK

Example 2

"In HIV-infected infants, should the measles immunisation schedule be modified in comparison with the generally recommended schedule?"

- **P = HIV-infected infants**
- **I = the measles immunisation schedule**
- **C = the generally recommended schedule**
- **O = decreased morbidity of HIV-infected infants, minor or serious adverse events, including fever and diarrhoea**

ANNEX 2: CASP CHECKLIST FOR SYSTEMATIC REVIEWS

10 QUESTIONS TO HELP YOU MAKE SENSE OF A REVIEW

HOW TO USE THIS APPRAISAL TOOL

Three broad issues need to be considered when appraising the report of a systematic review:

- **Are the results of the review valid?** **(Section A)**
- **What are the results?** **(Section B)**
- **Will the results help locally?** **(Section C)**

The 10 questions on the following pages are designed to help you think about these issues systematically.
The first two questions are screening questions and can be answered quickly. If the answer to both is "yes", it is worth proceeding with the remaining questions.

There is some degree of overlap between the questions, you are asked to record a "yes", "no", or "can't tell" to most of the questions. A number of prompts are given after each question. These are designed to remind you why the question is important. Record your reasons for your answers in the spaces provided.

A. Are the results of the review valid?	
Screening Questions	
1. Did the review address a clearly-focused question? **HINT:** an issue can be 'focused' in terms of: • The population studied • The intervention given • The outcome considered	Yes ☐ Can't tell ☐ No ☐
2. Did the authors look for the right type of papers? **HINT:** 'The best sort of studies' would: • Address the review's question • Have an appropriate study design (usually RCTs for papers evaluating interventions)	Yes ☐ Can't tell ☐ No ☐
> Is it worth continuing?	Yes ☐ No ☐

A. Are the results of the review valid?	
Detailed Questions	
3. Do you think the important, relevant studies were included? **HINT:** Look for: • Which bibliographic databases were used • Follow up from reference lists • Personal contact with experts • Search for unpublished as well as published studies • Search for non-English language studies	Yes ☐ Can't tell ☐ No ☐
4. Did the review's authors do enough to assess the quality of the included studies? **HINT:** The authors need to consider the rigour of the studies they have identified. Lack of rigour may affect the studies' results. ("All that glisters is not gold" Merchant of Venice)	Yes ☐ Can't tell ☐ No ☐
5. If the results of the review have been combined, was it reasonable to do so? **HINT:** Consider whether • The results were similar from study to study • The results of all the included studies are clearly displayed • The results of the different studies are similar • The reasons for any variations in results are discussed	Yes ☐ Can't tell ☐ No ☐
B. What are the results?	
6. What are the overall results of the review? **HINT:** Consider • If you are clear about the review's 'bottom line' results • What these are (numerically if appropriate) • How were the results expressed (NNT, odds ratio, etc.)	
7. How precise are the results? **HINT:** Look at the confidence intervals, if given	
C. Will the results help locally?	
8. Can the results be applied to the local population? **HINT:** Consider whether • The patients covered by the review could be sufficiently different to your population to cause concern • Your local setting is likely to differ much from that of the review	Yes ☐ Can't tell ☐ No ☐
9. Were all important outcomes considered? **HINT:** Consider whether • Is there other information you would like to have seen	Yes ☐ Can't tell ☐ No ☐
10. Are the benefits worth the harms and costs? **HINT:** Consider • Even if this is not addressed by the review, what do you think?	Yes ☐ Can't tell ☐ No ☐

ANNEX 3: AMSTAR - A MEASUREMENT TOOL TO ASSESS THE METHODOLOGICAL QUALITY OF SYSTEMATIC REVIEWS

1. Was an 'a priori' design provided? The research question and inclusion criteria should be established before the conduct of the review. *Note: Need to refer to a protocol, ethics approval, or pre-determined/a priori published research objectives to score a "yes."*	Yes ☐ No ☐ Can't answer ☐ Not applicable ☐
2. Was there duplicate study selection and data extraction? There should be at least two independent data extractors and a consensus procedure for disagreements should be in place. *Note: 2 people do study selection, 2 people do data extraction, consensus process or one person checks the other's work.*	Yes ☐ No ☐ Can't answer ☐ Not applicable ☐
3. Was a comprehensive literature search performed? At least two electronic sources should be searched. The report must include years and databases used (e.g. Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialised registers, or experts in the particular field of study, and by reviewing the references in the studies found. *Note: If at least 2 sources + one supplementary strategy used, select "yes" (Cochrane register/Central counts as 2 sources; a grey literature search counts as supplementary).*	Yes ☐ No ☐ Can't answer ☐ Not applicable ☐
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion? The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review) based on their publication status, language, etc. *Note: If review indicates that there was a search for "grey literature" or "unpublished literature," indicate "yes." SINGLE database, dissertations, conference proceedings, and trial registries are all considered grey for this purpose. If searching a source that contains both grey and non-grey, must specify that they were searching for grey/ unpublished lit.*	Yes ☐ No ☐ Can't answer ☐ Not applicable ☐
5. Was a list of studies (included and excluded) provided? A list of included and excluded studies should be provided. *Note: Acceptable if the excluded studies are referenced. If there is an electronic link to the list but the link is dead, select "no."*	Yes ☐ No ☐ Can't answer ☐ Not applicable ☐
6. Were the characteristics of the included studies provided? In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions, and outcomes. The ranges of characteristics in all the studies analysed, e.g. age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. *Note: Acceptable if not in table format as long as they are described as above.*	Yes ☐ No ☐ Can't answer ☐ Not applicable ☐

7. Was the scientific quality of the included studies assessed and documented? 'A priori' methods of assessment should be provided (e.g. for effectiveness studies if the author(s) chose to include only randomised, double-blind, placebo-controlled studies, or allocation concealment as inclusion criteria); for other types of studies alternative items will be relevant. *Note: Can include use of a quality scoring tool or checklist, e.g. Jadad scale, risk of bias, sensitivity analysis, etc., or a description of quality items, with some kind of result for EACH study ("low" or "high" is fine, as long as it is clear which studies scored "low" and which scored "high"; a summary score/range for all studies is not acceptable).*	Yes ☐ No ☐ Can't answer ☐ Not applicable ☐
8. Was the scientific quality of the included studies used appropriately in formulating conclusions? The results of the methodological rigour and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. *Note: Might say something such as "the results should be interpreted with caution due to poor quality of included studies." Cannot score "yes" for this question if scored "no" for question 7.*	Yes ☐ No ☐ Can't answer ☐ Not applicable ☐
9. Were the methods used to combine the findings of studies appropriate? For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e. Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e. is it sensible to combine?). *Note: Indicate "yes" if they mention or describe heterogeneity, i.e. if they explain that they cannot pool because of heterogeneity/variability between interventions.*	Yes ☐ No ☐ Can't answer ☐ Not applicable ☐
10. Was the likelihood of publication bias assessed? An assessment of publication bias should include a combination of graphical aids (e.g. funnel plot, other available tests) and/or statistical tests (e.g. Egger regression test, Hedges-Olken). *Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.*	Yes ☐ No ☐ Can't answer ☐ Not applicable ☐
11. Was the Conflict of interest included? Potential sources of support should be clearly acknowledged in both the systematic review and the included studies. *Note: To get a "yes," must indicate source of funding or support for the systematic review AND for each of the included studies.*	Yes ☐ No ☐ Can't answer ☐ Not applicable ☐

Source: Shea et al. *BMC Medical Research Methodology* 2007 7:10 doi:10.1186/1471-2288-7-10

ANNEX 4: SIGN CHECKLISTS

Methodology Checklist 1: Systematic reviews and Meta-analyses

SIGN

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C,. et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10.* Available from http://www.biomedcentral.com/1471-2288/7/10 (cited 10 Sep 2012)

Study identification (Include author, title, year of publication, journal title, pages)

Guideline topic: | Key Question No:

Before completing this checklist, consider:

- Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO, reject. IF YES, complete the checklist.

Checklist completed by:

SECTION 1: INTERNAL VALIDITY

	In a well-conducted systematic review	**Does this study do it?**
1.1	The research question is clearly defined and the inclusion/exclusion criteria must be listed in the paper.	Yes ☐ No ☐ **If no, reject**
1.2	A comprehensive literature search is carried out.	Yes ☐ No ☐ Not applicable ☐ **If no, reject**
1.3	At least two people should have selected studies.	Yes ☐ No ☐ Can't say ☐
1.4	At least two people should have extracted data.	Yes ☐ No ☐ Can't say ☐
1.5	The status of publication was not used as an inclusion criterion.	Yes ☐ No ☐
1.6	The excluded studies are listed.	Yes ☐ No ☐
1.7	The relevant characteristics of the included studies are provided.	Yes ☐ No ☐
1.8	The scientific quality of the included studies was assessed and reported.	Yes ☐ No ☐
1.9	Was the scientific quality of the included studies used appropriately?	Yes ☐ No ☐
1.10	Appropriate methods are used to combine the individual study findings.	Yes ☐ No ☐ Not applicable ☐

SECTION 1: INTERNAL VALIDITY		
In a well-conducted systematic review		**Does this study do it?**
1.11	The likelihood of publication bias was assessed appropriately.	Yes ☐ No ☐ Not applicable ☐
1.12	Conflicts of interest are declared.	Yes ☐ No ☐
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review?	High quality (++) ☐ Acceptable (+) ☐ Low quality (-) ☐ Unacceptable – reject (0) ☐
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes ☐ No ☐
2.3	**Note**	

SIGN

Methodology Checklist 1: Systematic reviews and Meta-analyses

Notes for completion of checklist

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C,. et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10.* Available from http://www.biomedcentral.com/1471-2288/7/10 (cited 10 Sep 2012)

'Must' refers to a statement that has to be fulfilled for the question to receive a yes answer. 'Should' statements are a mark of quality but not a necessity for a yes answer. These should be used to assess the overall quality of the paper.

SECTION 1: INTERNAL VALIDITY		
In a well-conducted systematic review:		**Notes**
1.1	The research question is clearly defined and the inclusion/exclusion criteria must be listed in the paper.	The PICO must be clear in the paper even if not directly referred to. The research question and inclusion criteria should be established before the review is conducted.
1.2	A comprehensive literature search is carried out.	At least two relevant electronic sources must be searched. The report must list the databases used (e.g. Central, EMBASE, and MEDLINE). (Cochrane register/Central counts as two sources; a grey literature search counts as supplementary.) (PubMed and MEDLINE count as one database.) Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. Dates for the search should be provided. The paragraph above is the minimum requirement. All searches should be supplemented by consulting current contents, reviews, textbooks, specialised registers, or/and experts in the particular field of study, and by reviewing the references in the studies found. The paragraph above is a quality criterion which affects the overall rating of the review. This criterion will not apply in the case of a prospective meta-analysis - this is where meta-analysis is based on pre-selected studies identified for inclusion before the results of those studies are known. Such reports must state that they are prospective.
1.3	At least two people should have selected studies.	At least two people should select papers. There should be a consensus process to resolve any differences.
1.4	At least two people should have extracted data.	At least two people should extract data and should report that a consensus was agreed. One person checking the other's data extraction is accurate is acceptable.

SECTION 1: INTERNAL VALIDITY		
In a well-conducted systematic review:		Notes
1.5	The status of publication was not used as an inclusion criterion.	The authors should state that they searched for reports regardless of their publication status. The authors should state whether or not they excluded any reports (from the systematic review) based on their publication status. If review indicates that there was a search for "grey literature" or "unpublished literature," indicate "yes." SIGLE database, dissertations, conference proceedings, and trial registries are all considered grey for this purpose. If searching a source that contains both grey and non-grey, must specify that they were searching for grey/unpublished lit.
1.6	The excluded studies are listed.	Limiting the excluded studies to references is acceptable.
1.7	The relevant characteristics of the included studies are provided.	In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions, and outcomes. The ranges of characteristics in all the included studies, e.g. age, race, sex, relevant socio-economic data, disease status, duration, severity, or other diseases should be reported. (Note that a format other than a table is acceptable, as long as the information noted here is provided). Absence of this will make it impossible to form guideline recommendations. Mark as (-); original papers would need to be examined.
1.8	The scientific quality of the included studies was assessed and documented.	It can include use of a quality scoring tool or checklist, e.g. risk of bias assessment, or a description of quality items, with some kind of result for EACH study ("low" or "high" is fine, as long as it is clear which studies scored "low" and which scored "high"; a summary score/range for all studies is not acceptable. Absence of this will make it impossible to form guideline recommendations. Mark as (-)
1.9	Was the scientific quality of the included studies used appropriately?	Examples include sensitivity analysis based on study quality, exclusion of poor quality studies, and statements such as 'the results should be interpreted with caution due to poor quality of included studies. The results of the methodological rigour and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. Cannot score "yes" for this question if scored "no" for question 1.8.

SECTION 1: INTERNAL VALIDITY		
In a well-conducted systematic review:		Notes
1.10	Appropriate methods are used to combine the individual study findings.	Studies that are very clinically heterogeneous should not be combined in a meta-analysis. Look at the forest plot–do the results look similar across the studies? For the pooled result, a test should be done to assess statistical heterogeneity, i.e. Chi-squared (χ^2) test for homogeneity and/or I^2 test for inconsistency. If significant heterogeneity is apparent, the authors should have explored possible explanations using methods such as sensitivity analysis or meta-regression. A random effects analysis may be used to take account of between-study variation but is not a 'fix' for heterogeneity. Planned subgroup analyses should be pre-specified and limited in number because conducting many subgroup analyses increases the probability of obtaining a statistically significant result by chance. Conclusions based on post-hoc subgroup analyses must be interpreted with caution. Cannot score "yes" for this question if scored "no" for question 1.8.
1.11	The likelihood of publication bias was assessed appropriately.	The possibility of publication bias should be assessed where possible, commonly done by visual inspection of a funnel plot together with a statistical test for asymmetry (e.g. Egger regression test) although other statistical and modelling approaches may be reported. Absence of a funnel plot doesn't mean the likelihood of publication bias was not assessed appropriately (there are other methods); 10 studies is just a ballpark minimum number for a funnel plot and a plot is of little use when there are few studies.
1.12	Conflicts of interest are declared.	Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review?	Rate the overall methodological quality of the study, using the following as a guide: **High quality (++):** Majority of criteria met. Little or no risk of bias. **Acceptable (+):** Most criteria met. Some flaws in the study with an associated risk of bias. **Low quality (-):** Either most criteria not met, or significant flaws relating to key aspects of study design. **Reject (0):** Poor-quality study with significant flaws. Wrong study type. Not relevant to guideline.

SECTION B

DEVELOPMENT OF
AN EVIDENCE-BASED
RECOMMENDATION NOTE



FOR
FACILITATOR

PRESENTATION OF THE SECTION

This section presents the principles for utilising the evidence collected towards the formulation of a recommendation; it also presents the structure of a recommendation note.
Presentation of concepts will be followed by practical exercises. Exercises will aim at developing mock recommendations where participants will apply the methodology used on topics relevant to their situation.

LEARNING OBJECTIVES

- Learn the steps for writing a recommendation note
- Understand the principles for forming a judgement from the evidence collected
- Understand the processes of deliberation and decision concerning the proposed recommendation

1. OVERVIEW OF THE PROCESS FOR DEVELOPING AN EVIDENCE-BASED RECOMMENDATION

NITAGs make evidence-based recommendations on issues related to vaccines and immunisation such as the introduction of new vaccines, appropriate vaccine schedules, financing, and research priorities and strategies. Such recommendations should be evidence-based as sound, quality recommendations are more likely to be considered by policy-makers.
NITAGs' recommendations should be generated from a systematic, credible, and transparent process of **selecting, reviewing, and synthesising the evidence** for supporting the recommendation.
The recommendations should be communicated in an understandable and stimulating way to policy-makers.
The quality of the recommendation is a balance between comprehensiveness of the framework of the recommendation, including examining benefits and harms of the intervention as well as patients' values and preferences, context-specific issues, and the quality of evidence informing the recommendation.

Who is in charge of the whole process?

- The Executive Secretariat of the NITAG, or
- A Working Group (WG), if decided by the NITAG Executive Secretariat and Chair (See Training 1 Section B)

The overall process of developing a recommendation includes:

a. Defining the recommendation framework
b. Selecting critical and important data
c. Finding the evidence on critical and important data
d. Evaluating the quality of the evidence
e. Making judgement on the use of the evidence collected for formulating a recommendation
f. Drafting a proposed recommendation for discussion
g. Deliberating and taking a decision on the recommendation

The steps a) to d) have been addressed in Section A of this training. Section B focuses on steps e), f) and g).

2. DEVELOPING AN EVIDENCE-BASED RECOMMENDATION

After the type of evidence needed to issue the recommendation has been identified and the quality of evidence assessed and summarised in a document, the information is now analysed and discussed to provide a recommendation for or against a particular vaccination issue. **The strength of the quality of evidence alone cannot justify a strong recommendation. Other considerations play a role in issuing a recommendation.**

2.1 ANALYSIS (JUDGEMENT) OF THE BODY OF EVIDENCE

2.1.1 Judgement on the intervention and its outcome(s)

A systematic review of the literature on the intervention's outcomes is the driver of an evidence-based recommendation. Considerable resources (time, finance, varied expertise in the team, including bio-statistics) are utilised in performing a systematic review. NITAGs may instead consider using already available systematic reviews of good quality (WHO, Cochrane).

In making a judgement on the intervention's effects, NITAGs may consider its desirable outcomes vs undesirable outcomes as they compare to those of the alternative intervention (comparator). Examples of such outcomes are listed in the table below.

Table: Example of desirable and undesirable outcomes of an intervention vs comparator [2]

Desirable outcomes	Undesirable outcomes
Reduction in morbid events	Short-term minor side effects
Improved quality of life	Long-term rare serious adverse events
Decreased resource use	Increased resource use
	Inconvenience

2.1.2 Judgement of evidence on the other factors listed in the recommendation framework

Other elements to consider in the framework will depend on the specific topic being considered for the recommendation. Nevertheless, factors that are likely to be included in the decision-making process are related to the local context: the disease, health systems, and the environment in which the recommendation will be implemented. Judgement on issues around health system and context will consider the evidence on:

- Organisation and leadership
- Infrastructure
- Human and financial resources
- Quality of care
- Quality of data
- Enabling implementation factors: physical, socio-cultural environment, and political

There are other elements to take into account for the recommendation and they will depend on the specific topic being studied by the NITAG. Training 2 addresses the extent to which health systems and environmental issues can influence a recommendation: ***"Analysis of immunisation in the context of health systems and the decision-making process"***

2.2 WRITE-UP OF THE DRAFT RECOMMENDATION NOTE

2.2.1 Outline of the draft recommendation and key points to address

1. Executive summary

It is drafted after the finalisation of the recommendation note.

2. Introduction

2.1 Context of the question

Who included the topic in the NITAG agenda?

- Was it the annual work plan, or suggested by the Ministry of Health or a NITAG member? Further clarification should be enquired if needed.
- If the topic was added to the NITAG agenda per official request from the Ministry, this should be mentioned and the letter should be joined to the report.
- Why was the topic added to the agenda? Opportunity of introduction of a new vaccine, ongoing epidemic, new data on vaccine efficacy or disease burden?
- Does the Minister of Health exert leadership on the question?

2.2 General information on the subject

- Brief description of the problem identified.

3. Methodology

In developing an evidence-based recommendation, NITAG members should always describe the research process which needs to be transparent and accessible to policy-makers and a wide range of stakeholders who are mostly unfamiliar with the language of research. The methodology section should clarify the following points:

- Does the recommendation note employ systematic and transparent methods to identify, select, and assess research evidence?
  - Describe the recommendation framework (i.e. the PICO questions on the intervention as well as other identified elements taken into account)
  - Describe how research evidence was identified, selected, and assessed in ways that are easily understood. This objective can be achieved by using techniques such as explanatory 'boxes' within the note to clarify or highlight particular concepts, or through the inclusion of additional appendices. The methods should be systematic in nature and reported in a transparent yet understandable way.
- How was the recommendation developed?
  - Was a Working Group established?
- How was the discussion organised and the recommendation adopted?
  - Was the recommendation note reviewed for both scientific quality and system relevance?

4. Analysis of the evidence

This section will include and discuss:

- The judgement of the intervention outcomes from systematic reviews (if NITAG performed a systematic review, the summary of the evidence quality assessment should be included in summary tables)
- The judgement on health systems and context issues which were taken into account in the recommendation framework
- Given that recommendation notes are typically context-specific, a recommendation note would also ideally discuss the evidence on local applicability and equity considerations of the findings

5. Conclusion and recommendation formulation

This section refers back to the evidence of each element of the decision-making framework and the judgement presented in the previous section to draw conclusions on:

- Potential benefits, harms of the intervention compared to the alternative
- Possible options
- Cost and cost-effectiveness of each option
- Implementation of each option: efficiency, local applicability, acceptability (by different stakeholders), equity, feasibility (expertise and human resources available? budget available? timeline for implementation suitable?), potential barriers, sustainability

Recommendation options are clearly formulated and the link to the available evidence is well demonstrated.
Note: the formulation of the recommendation is done after NITAG deliberation on the report presented by the WG/Secretariat.

The suggested formulations of a recommendation are: *"We recommend that"; "Policy-makers should/should not"*. The recommendation should avoid wording such as: *"We suggest"* or *"Policy-makers might"*.

NB: Whatever format is chosen, the minimum that a recommendation note should contain is a list of key messages, a report, and a reference list for those who wish to read more. Furthermore, in general, when there are options, it is preferable to present recommendations in favour of a particular management approach rather than against an approach.

3. DELIBERATION AND DECISIONS FOR THE PROPOSED RECOMMENDATION

The NITAG WG/Secretariat presents to the NITAG members the report with the proposed recommendation options for discussion and deliberation.
NITAG members have to discuss the options, evidence, and judgements presented. All the NITAG members should have sufficient time to express their views without feeling intimidated. The NITAG members should discuss the following:

- What are the options being proposed?
- Are they confident in the evidence supporting these options?
- What are their opinions on the balance between the benefits and harms of each option?
- Does each option fit the organisational (infrastructure, human resource, and structure of the health system) and socio-environmental context (demographic and geographic patterns)?
- What are the potential barriers (political, financial, logistical, socio-cultural, etc.) to the implementation of each option? What are the potential solutions to these barriers?
- Who are the potential supporters and opponents of each option? Refer to Section B of Training 2 *("Stakeholder analysis and mapping")* for more details on how to deal with potential opponents (patient associations, anti-vaccine lobbies, finance ministries, etc.)

The NITAG members should decide which option will be recommended to the government. The decision can be made by vote or consensus according to NITAG mode of operation[1].
Not infrequently, members may find themselves reluctant to make a recommendation for or against a particular strategy, and also conclude that an "only-in-research" recommendation is inappropriate. The reasons for this decision may be[3]:

- Confidence in the intervention's effect is so low that the NITAG feels that the issue of a recommendation is too speculative.
- The trade-offs between benefit and harm are closely balanced, and the values, preferences, and resource implications not known or too variable.

If no recommendation is issued, the NITAG has to specify the rationale for this decision.

REFERENCES

1. Duclos, P., ***National Immunisation Technical Advisory Groups (NITAGs): guidance for their establishment and strengthening.*** Vaccine, 2010. 28 Suppl 1: p. A18-25.
2. Fretheim A, S.H., Oxman AD., ***Improving the use of research evidence in guideline development: 5. Group processes.*** Health Res Policy Syst., 2006.4(17).
3. Andrews, J.C., et al., GRADE guidelines: 15. ***Going from evidence to recommendation-determinants of a recommendation's direction and strength.*** J Clin Epidemiol, 2013. 66(7): p. 726-35.

FACILITATOR INSTRUCTIONS

IMPORTANT NOTES:

This section presents the key concepts and approach for drafting an evidence-based recommendation. It is important that participants grasp each step of the process.

The exercises will ideally concern a topic currently on the agenda of the participating NITAGs; nevertheless, facilitators will also prepare articles to be used for the exercises beforehand, if needed. For the exercises, links to experienced NITAGs are provided in the slide deck from where examples of recommendations can be retrieved.

Knowledge objectives

At the end of this section, participants will be able to:

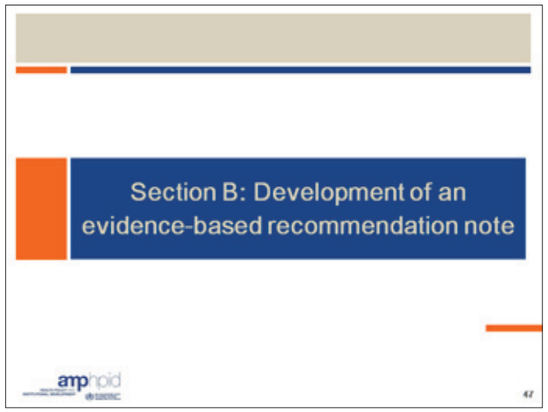
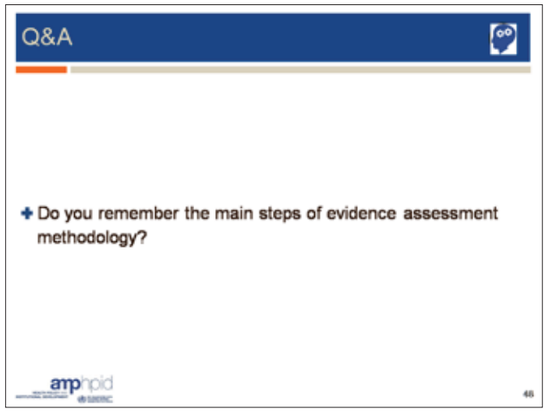
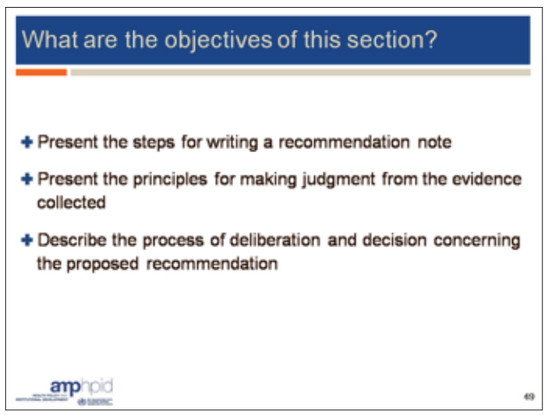
- Present the principles of the analysis of the body of evidence collected
- Describe the different steps for writing a recommendation note
- Describe the process of NITAG deliberation and decision

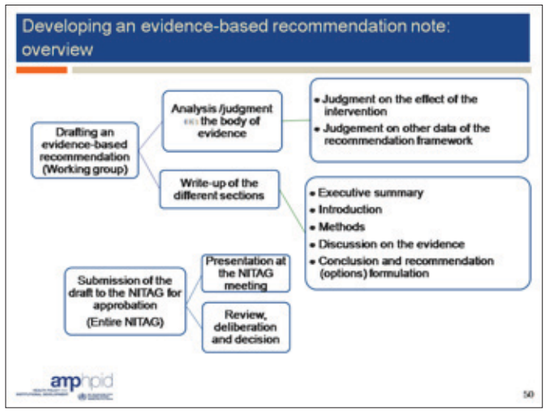
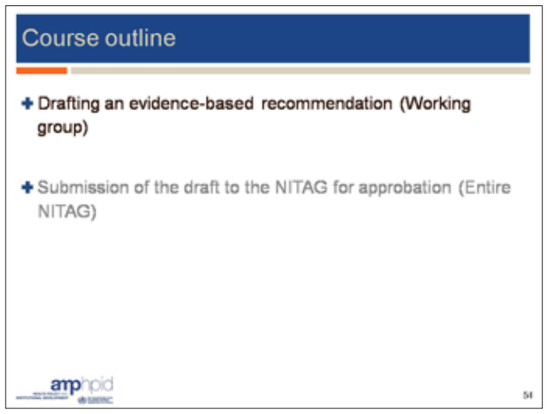
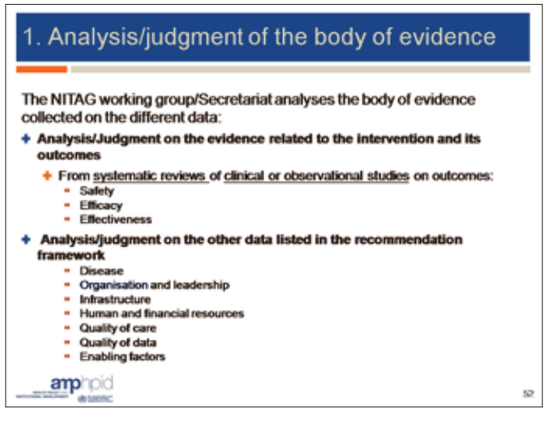
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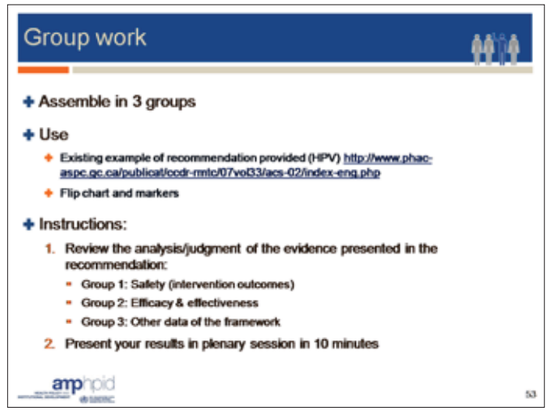
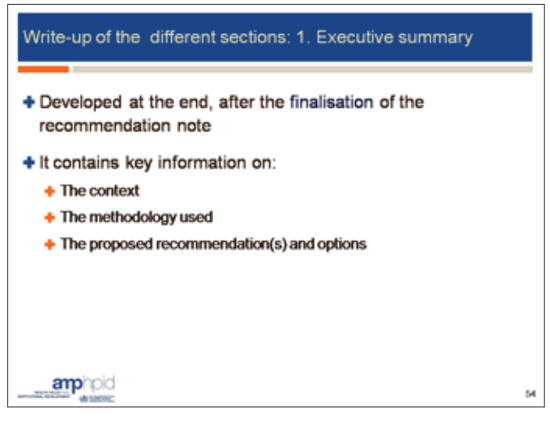
		TIME
STEP 1	Presentation 1-5 Slide 2 – Q&A	5' 5'
STEP 2	Presentation 5-13 "Drafting an evidence-based recommendation (Working Group)" Group work slide 7	40' 60'
STEP 3	Presentation 14-18 "Submission of the draft to NITAG"	16''
	TOTAL	126'

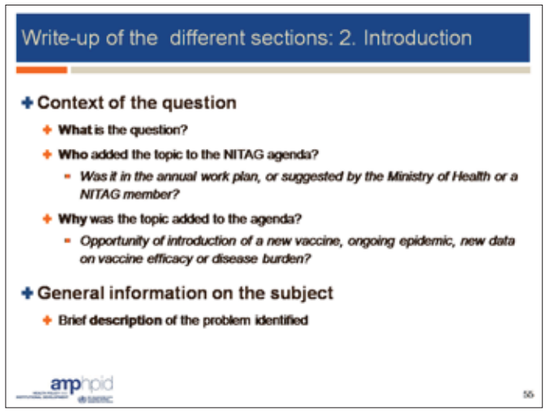
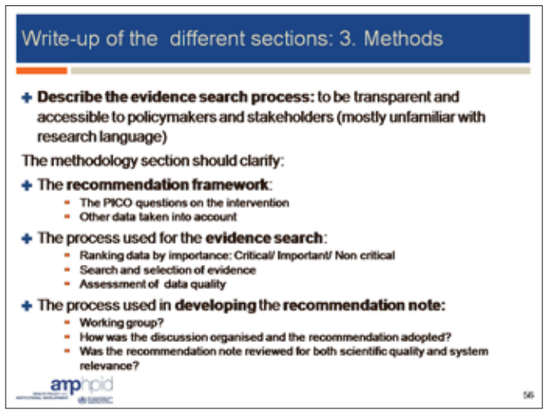
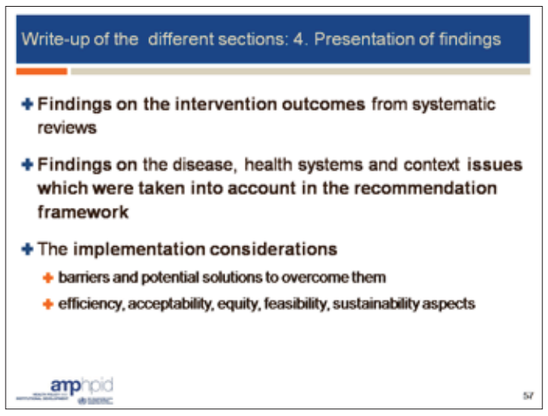
Training material

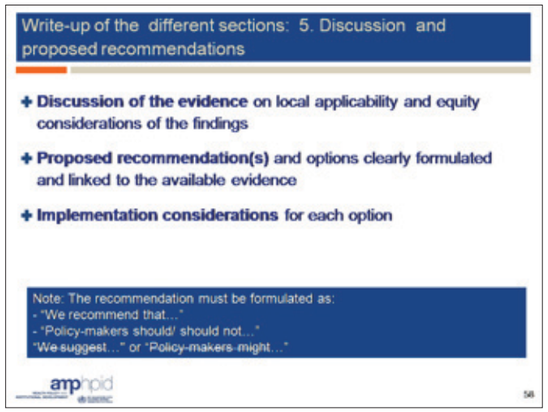
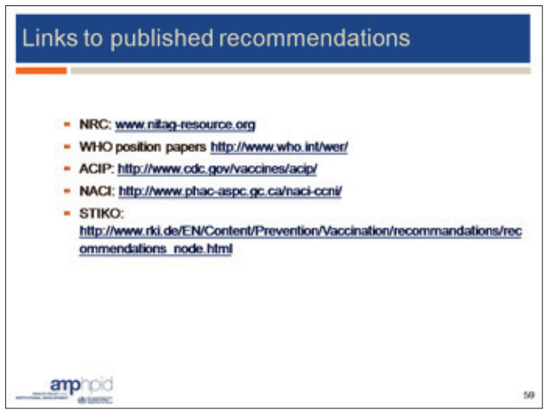
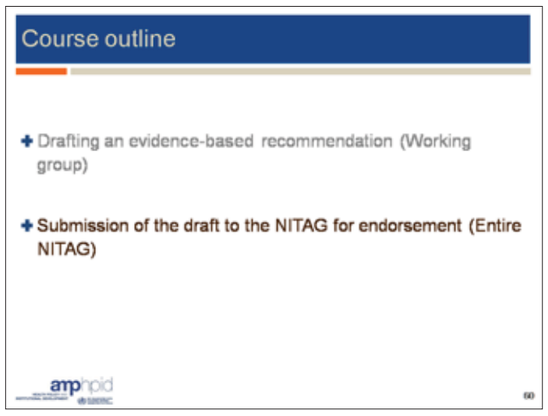
- PowerPoint presentation
- Content document and facilitator instructions
- Internet connection
- Example of published recommendations
- Flip chart and markers

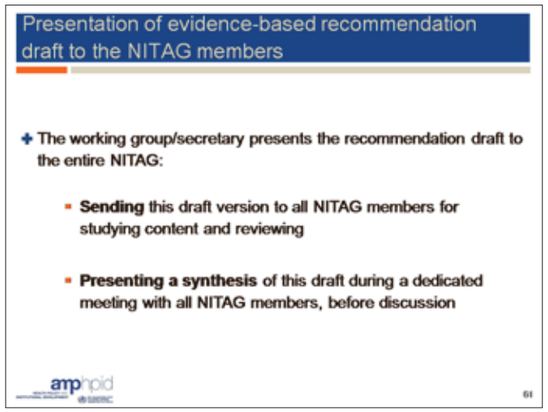
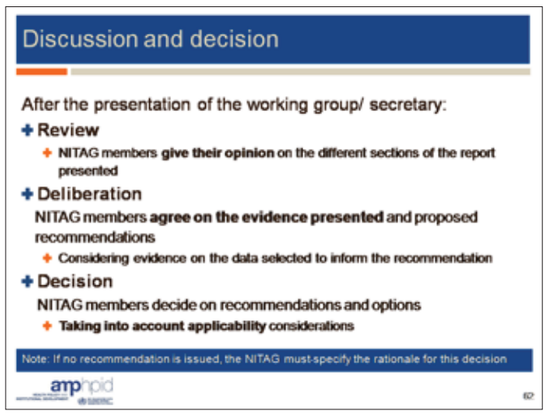
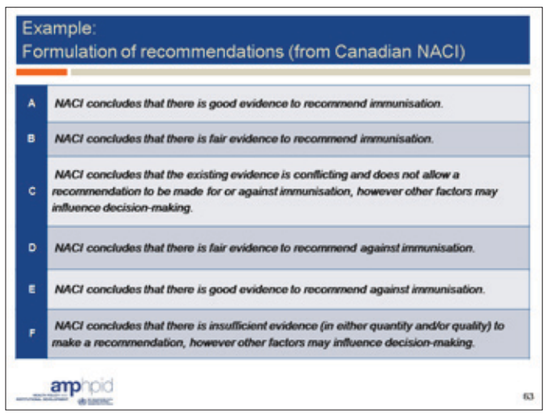
Slides	Facilitation methods
	**Presentation:** Introduction of the session This section presents methodologies to prepare an evidence-based recommendation note. This section is the continuation of the 1st section on evidence assessment. 5'
	**Q&A:** Ask participants what they remember about evidence assessment methodology. 5'
	**Presentation:** Present the 3 learning objectives. 5'

Slides	Facilitation methods
	**Presentation:** Describe steps and sub-steps. **Q&A:** Encourage questions for clarification. 5'
	**Presentation:** Clarify that the course starts with the presentation on the analysis of the evidence collected. 1'
	**Presentation:** 5'

Slides	Facilitation methods
	**Group work:** Objective: the aim of this exercise is to review an existing recommendation note to improve it. 1. Organise participants into 3 groups and give to each: - an example of a recommendation note http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/07vol33/acs-02/index-eng.php - a flip chart - markers (5') 2. Ask participants to: - Review the recommendation, assessing to what extent the principles presented earlier are reflected in the document (25') - Present their results in plenary session in 10 minutes (30' in total, 10' per group) 60'
	**Presentation:** Indicate that this part will address the different sections of a recommendation note. 5'

Slides	Facilitation methods
	Presentation: 5'
	Presentation: 5'
	Presentation: Q&A: Encourage questions for clarification. 5'

Slides	Facilitation methods
	Presentation: 5'
	Presentation: Click on each link and comment on the document. 1'
	Presentation: Mention that once the WG has prepared the draft recommendation note, this will be taken before the NITAG meeting for discussion and decision; thereafter, the note can be finalised and the recommendation issued. 1'

Slides	Facilitation methods
	Presentation: 5'
	Presentation: Q&A: Encourage questions for clarification. 5'
	Presentation: 5'

SIVAC
Supporting Independent Immunization and Vaccine Advisory Committees
amphid
HEALTH POLICY AND INSTITUTIONAL DEVELOPMENT
WHO COLLABORATING CENTRE FOR EVIDENCE-INFORMED IMMUNIZATION POLICYMAKING

T R A I N I N G 3

TECHNICAL AND SCIENTIFIC CAPACITIES OF NITAGS

SUMMARY



FOR
PARTICIPANT

TABLE OF CONTENTS

SECTION A
EVIDENCE ASSESSMENT METHODOLOGIES

LEARNING OBJECTIVES 6

1. WHAT IS AN EVIDENCE-BASED RECOMMENDATION? 6

2. WHAT IS THE PROCESS FOR ISSUING AN EVIDENCE-BASED RECOMMENDATION? 6

- 2.1. DEFINE THE EVIDENCE THAT WILL SUPPORT THE RECOMMENDATION
- 2.2. FIND THE EVIDENCE AND COLLECT IT
- 2.3. ASSESS THE QUALITY OF EVIDENCE

3. RESOURCES: GENERIC RECOMMENDATION FRAMEWORK 8

4. FACTORS WHICH UNDERPIN THE DEVELOPMENT OF SAGE RECOMMENDATIONS 11

5. LIST OF ARTICLES ON THE GRADE METHODOLOGY 12

6. OTHER DATA QUALITY ASSESSMENT TOOLS 15

APPENDIX 1: AMSTAR CHECKLIST. A MEASUREMENT TOOL TO ASSESS THE METHODOLOGICAL QUALITY OF SYSTEMATIC REVIEWS 16

APPENDIX 2: CASP CHECKLISTS 18

APPENDIX 3: SIGN CHECKLISTS 22

TEMPLATES FOR THE PARTICIPANTS 65

SECTION B
DEVELOPMENT OF AN EVIDENCE-BASED RECOMMENDATION NOTE

LEARNING OBJECTIVES 68

1. STEPS IN THE DEVELOPMENT OF A RECOMMENDATION NOTE 68

1.1. ANALYSIS (JUDGEMENT) OF THE BODY OF EVIDENCE

1.1.1. JUDGEMENT ON THE INTERVENTION AND ITS OUTCOME(S)

1.2.2. JUDGEMENT ON EVIDENCE ON THE OTHER ELEMENTS IDENTIFIED IN THE RECOMMENDATION FRAMEWORK

1.2. OUTLINE OF A DRAFT RECOMMENDATION NOTE

2. DELIBERATION AND DECISION CONCERNING THE PROPOSED RECOMMENDATION 72

SECTION A

EVIDENCE ASSESSMENT METHODOLOGIES



FOR
PARTICIPANT

SUMMARY FOR PARTICIPANT

LEARNING OBJECTIVES

- Learn how to frame a question to guide the search for evidence
- Learn how to define the framework for deliberation considering clinical data (from clinical trials or observational studies , health system, socio-cultural, and equity issues among others)
- Learn which are the most relevant databases for most NITAG topics and how to use them to find evidence at the international, national, regional, or local levels
- Learn which tools are available to evaluate the quality of data and how to use them (e.g. GRADE for systematic reviews)

1. WHAT IS AN EVIDENCE-BASED RECOMMENDATION?

It is a recommendation generated from a systematic, credible, and transparent process of selecting, reviewing, and synthesising the evidence.

2. WHAT IS THE PROCESS FOR ISSUING AN EVIDENCE-BASED RECOMMENDATION?

2.1 DEFINE THE EVIDENCE THAT WILL SUPPORT THE RECOMMENDATION

1. Define the recommendation framework:

- Frame the question about the effects (outcomes) of the intervention (PICO method)
- Identify the other criteria that need to be considered in the recommendation

2. Rank by level of importance the intervention outcome and the other criteria to be considered in making the recommendation:

- Critical
- Important
- Non-critical

An example of a generic recommendation framework is included in this summary.
Defining the recommendation framework ensures transparency about the grounds for the decision.

2.2 FIND THE EVIDENCE AND COLLECT IT

1. Select the sources of evidence

- Published literature with international data:
  - > Generic: WHO databases, Cochrane library, Medline/PubMed, Center for reviews and dissemination, MacMaster Health Forum
  - > Vaccine-specific: WHO IVB database, NITAG resource center, OLIVES

- Published literature with national, regional, local data:
  - > Demographic and Health Survey studies: http://www.measuredhs.com/
  - > PubMed national studies using the MeSH term of the country of interest.
  - > Specific WHO regional databases: http://www.who.int/library/databases/en/

2. Search for the evidence

- Search evidence on each of the factors listed in the recommendation framework
- Evidence on the intervention outcomes should be searched for both the intervention and the comparator as stated in the question
- Evidence on intervention outcome (safety and effectiveness) should be searched across studies, e.g. systematic reviews. Priority should be given to systematic reviews and more recent publications (less than 3 years)

3. Keep a record of the search method and its results

- Record details of the search methods and results by using a search form

2.3 ASSESS THE QUALITY OF EVIDENCE

Once the data have been collected for each specific intervention outcome/criterion and other elements of the recommendation framework, they need to be assessed through a systematic and standardised process.

1. For conducting a systematic review of studies on the intervention outcome: assess the quality of each clinical/observational study retrieved and report on each study for each outcome/criterion

For intervention outcomes reported in clinical/observational studies, the NITAG Working Group can primarily use the GRADE quality grading process, which has been used by SAGE and adequately fits the purpose of issuing evidence-based policies. GRADE first applies to individual studies and then to the body of evidence across the selected studies.

2. For assessing the quality of systematic reviews: AMSTAR, CASP, and SIGN are tools which can be used

3. For assessing the quality of non-clinical/observational studies (sociology, anthropology, economic evaluations, etc.) identified in the search phase the following tools can be used:

- SIGN for assessing the quality of any type of clinical and quantitative study
- Critical appraisal method for qualitative evidence
- Critical Appraisal Skills Programme (CASP) for any type of study (systematic reviews, RCTs, economic evaluations, qualitative studies, etc.)

A particular quality of evidence does not necessarily imply a particular strength of recommendation.

(1) *The National Library of Medicine's Medical Subject Headings (MeSH) is the controlled vocabulary used for indexing articles for the MEDLINE@subset of PubMed.* ***http://www.ncbi.nlm.nih.gov/mesh/68005842***

(2) *Lewin S, Bosch-Capblanch X, Oliver S, Akl EA, Vist GE, et al.Guidance for Evidence-Informed Policies about Health Systems: Assessing How Much Confidence to Place in the Research Evidence. PLoS Med., 2012.9(3): e1001187.*

3. RESOURCES: GENERIC RECOMMENDATION FRAMEWORK

ISSUE	ELEMENT	SPECIFIC DATA
1. Vaccine and immunisation characteristics	**Safety**	Type, consequences, and frequency of short- and long-term adverse events following vaccination
		Risk groups or risk factors for adverse events
		Contraindications
	Efficacy and Effectiveness	Type-specific protection afforded
		Critical determinants of the immune response associated with protection
		Duration of protection and waning of immunity if any
		Interference regarding protection or immunity with other vaccines
	Vaccine indirect effects	Impact on resistance to antibiotics and antivirals
		Herd immunity
		Potential negative population impact through change in age of infection for unprotected individuals, e.g. rubella or varicella vaccine, or emergence of non-vaccine serotypes
	Vaccine characteristics	Vaccine presentation and formulation
		Dosage and route of administration
		Administration schedule and possibility of co-administration with other vaccines
		Flexibility of vaccination schedules
		Cold chain and logistic requirements
2. Disease	**Burden of disease**	Incidence of morbidity and mortality, age-specific morbidity and mortality, risk groups, serotype/serogroup distribution, epidemic potential, disease occurrence over time, changes in epidemiology over time
	Clinical characteristics disease	Signs and symptoms of disease, severe forms of disease, long-term complications of disease, medical management of disease
	Use and costs of healthcare	Primary/secondary/tertiary care implications, short- and long-term use of healthcare (e.g. treatments, hospitalisation)
	Alternative preventive and control measures	Alternative preventive and control measures (e.g. health education, hygiene, vector control) and their effectiveness, costs, and practicality
		Other existing vaccines against the same disease and their effectiveness, costs, and practicality

ISSUE	ELEMENT	SPECIFIC DATA
2. Disease	**Regional and international considerations**	Existence of regional and global recommendations
		Disease potential for international spread and pandemic risk
3. Economic and operational considerations	**Vaccine-related costs and resource use**	Direct and indirect costs of administering the vaccine as they compare to those of other existing vaccines or other prevention or control measures
	Vaccine availability	Availability of vaccine and long-term supply
		Available suppliers and competition dynamic in the market
	Vaccine affordability	Availability of fiscal space to effectively implement and sustain the recommendation in the programme
		Prevailing prices for the vaccine in the market and price estimations for the specific country
	Socio-economic and social impacts of disease	School and work absenteeism
		Indirect cost to patients and families
		Productivity losses
		Stigma around a disease
	Economic impact of intervention on immunisation programme as well as health sector	Reduction in healthcare costs
		Health gain (years of life saved, QALY gained, etc.)
		Cost-effectiveness ratio of vaccination programme
4. Health policy and programmatic issues	**Interaction with other existing intervention and control strategies**	Impacts of programme (catch-up) on safety and efficacy of other vaccines and other healthcare sectors
	Feasibility	Accessibility of target population
		Availability of the vaccine and long-term supply in public and private sector, including collaborations with insurance sector
	Vaccine registration and regulations	National regulatory authority requirements for licensing the vaccine and/or its use in a different schedule as originally recommended

ISSUE	ELEMENT	SPECIFIC DATA
4. Health policy and programmatic issues	**Impact on resources**	Availability of human, technical, and financial resources for distribution (including cold chain sustainability)
	Ability to evaluate	Availability of information systems to manage the vaccine supply chain and measure related performance metrics, i.e. coverage and vaccine utilisation
		Existence and reliability of surveillance system
	Acceptability	Perception of the public and medical community about the disease and the vaccine
	Equity	Universality, accessibility, and gratuity of services for all the inhabitants in the country, including vulnerable, hard-to-reach and immigrant populations
	Social considerations	Non-health-related effects of vaccination, ethical considerations, legal implications, etc.

NB: Vaccine safety data should always be selected as a component of a recommendation framework.

4. FACTORS WHICH UNDERPIN THE DEVELOPMENT OF SAGE RECOMMENDATIONS

In making recommendations, the WHO advisory group on immunisation SAGE takes into account certain factors and outlines the specific information to consider in relation with those factors. The table below presents the factors which underpin the development of SAGE recommendations.

MAIN FACTORS	SPECIFIC ELEMENTS
Epidemiologic features of the disease	- Disease burden, including age-specific mortality and morbidity - Specific risk groups - Epidemic potential - Disease occurrence over time (i.e. secular trends) - Serogroup or serotype distribution (for serogroup- or serotype-specific vaccines) - Changes in epidemiological features over time
Clinical characteristics of the targeted disease	- Clinical management - Disease severity and fatality
Use and costs of healthcare	- Primary/secondary/tertiary care implications - Long-term complications and medical care requirements
Vaccine characteristics	- Cold chain and logistical concerns - Vaccine schedule(s)
Vaccine indirect effects	- Indirect effects (potential impact on strain selection, herd immunity, potential safety concerns of live attenuated vaccines in contacts of vaccines, serotype replacement)
Vaccine efficacy and effectiveness	- Efficacy - Effectiveness and population impact of the vaccine
Feasibility	- Social and programmatic acceptability of the schedule(s) - Ability to reach the target populations
Ability to evaluate	- Ability to monitor programme impact
Vaccine availability	- Vaccine availability
Vaccine safety	- Safety
Economic considerations	- Cost of illness - Vaccine and vaccine delivery costs - Potential for vaccine price reductions - Cost-effectiveness of immunisation programmes - Affordability of immunisation
Health system considerations	- Possible interactions with other interventions and control strategies - Possible impact of vaccine introduction on the wider health system
Social impacts Legal considerations Ethical considerations	

5. LIST OF ARTICLES ON THE GRADE METHODOLOGY

Video on GRADE methodology:
www.who.int/immunization/sage/working_mechanisms

List of articles available on the NITAG Resource Center www.nitag-resource.org
Free access (click on links):

1. Guyatt GH, Oxman AD, Schünemann HJ, Tugwell P, Knotterus A.
GRADE guidelines: ***A new series of articles in the Journal of Clinical Epidemiology***.
J Clin Epidemiol. 2010 Dec 27

2. Guyatt G, Oxman AD, Akl E, Kunz R, Vist G, Brozek J, Norris S, Falck-Ytter Y, Glasziou P, Debeer H, Jaeschke R, Rind D, Meerpohl J, Dahm P, Schünemann HJ.
GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables.
J Clin Epidemiol. 2011 Jan 3

3. Guyatt GH, Oxman AD, Kunz R, Atkins D, Brozek J, Vist G, Alderson P, Glasziou P, Falck-Ytter Y, Schunemann HJ.
GRADE guidelines 2. Framing the question and deciding on important outcomes.
J Clin Epidemiol. 2011 Jan 3

4. Balshem H, Helfand M, Schunemann HJ, Oxman AD, Kunz R, Brozek J, Vist GE, Falck-Ytter Y, Meerpohl J, Norris S, Guyatt GH.
GRADE guidelines: 3. Rating the quality of evidence - introduction.
J Clin Epidemiol. 2011 Jan 6

5. Guyatt GH, Oxman AD, Vist G, Kunz R, Brozek J, Alonso-Coello P, Montori V, Akl EA, Djulbegovic B, Falck-Ytter Y, Norris SL, Williams JW Jr, Atkins D, Meerpohl J, Schünemann HJ.
GRADE guidelines: 4. Rating the quality of evidence - risk of bias.
J Clin Epidemiol. 2011 Jan 20

6. Guyatt GH, Oxman AD, Montori V, Vist G, Kunz R, Brozek J, Alonso-Coello P, Djulbegovic B, Atkins D, Falck-Ytter Y, Williams JW Jr, Meerpohl J, Norris SL, Akl EA, Schünemann HJ.
GRADE guidelines: 5. Rating the quality of evidence – publication bias.
J Clin Epidemiol. 2011 Aug 1

7. Guyatt G, Oxman AD, Kunz R, Brozek J, Alonso-Coello P, Rind D, Devereaux P, Montori VM, Freyschuss B, Vist G, Jaeschke R, Williams JW Jr, Murad MH, Sinclair D, Falck-Ytter Y, Meerpohl J, Whittington C, Thorlund K, Andrews J, Schünemann HJ.
GRADE guidelines: 6. Rating the quality of evidence - imprecision.
J Clin Epidemiol. 2011 Aug 12

8. Guyatt GH, Oxman AD, Kunz R, Woodcock J, Brozek J, Helfand M, Alonso-Coello P, Glasziou P, Jaeschke R, Akl EA, Norris S, Vist G, Dahm P, Shukla VK, Higgins J, Falck-Ytter Y, Schünemann HJ; The GRADE Working Group.
GRADE guidelines: 7. Rating the quality of evidence - inconsistency.
J Clin Epidemiol. 2011 Aug 2

9. Guyatt GH, Oxman AD, Kunz R, Woodcock J, Brozek J, Helfand M, Alonso-Coello P, Falck-Ytter Y, Jaeschke R, Vist G, Akl EA, Post PN, Norris S, Meerpohl J, Shukla VK, Nasser M, Schünemann HJ;
GRADE guidelines: 8. Rating the quality of evidence - indirectness.
J Clin Epidemiol. 2011 Aug 1

10. Guyatt GH, Oxman AD, Sultan S, Glasziou P, Akl EA, Alonso-Coello P, Atkins D, Kunz R, Brozek J, Montori V, Jaeschke R, Rind D, Dahm P, Meerpohl J, Vist G, Berliner E, Norris S, Falck-Ytter Y, Murad MH, Schünemann HJ; The GRADE Working Group.
GRADE guidelines: 9. Rating up the quality of evidence.
J Clin Epidemiol. 2011 Aug 1

11. Brunetti M, Shemilt I, et al.; The GRADE Working Group.
GRADE guidelines: 10. Considering resource use and rating the quality of economic evidence.
J Clin Epidemiol. 2013 Feb

12. Guyatt G, Oxman AD, Sultan S, Brozek J, Glasziou P, Alonso-Coello P, Atkins D, Kunz R, Montori V, Jaeschke R, Rind D, Dahm P, Akl EA, Meerpohl J, Vist G, Berliner E, Norris S, Falck-Ytter Y, Schünemann HJ.
GRADE guidelines: 11. Making an overall rating of confidence in effect estimates for a single outcome and for all outcomes.
J Clin Epidemiol. 2012 Apr 30.

13. Guyatt GH, Oxman AD, Santesso N, Helfand M, Vist G, Kunz R, Brozek J, Norris S, Meerpohl J, Djulbecovic B, Alonso-Coello P, Post PN, Busse JW, Glasziou P, Christensen R, Schünemann HJ.
GRADE guidelines: 12. Preparing Summary of Findings tables binary outcomes.
J Clin Epidemiol. 2012 May 18.

14. Thorlund K, Oxman AD, Walter SD, Patrick D, Furukawa TA, Johnston BC, Karanicolas P, Akl EA, Vist G, Kunz R, Brozek J, Kupper LL, Martin SL, Meerpohl JJ, Alonso-Coello P, Christensen R, Schunemann HJ.
GRADE guidelines: 13. Preparing Summary of Findings tables continuous outcomes.
J Clin Epidemiology 2013 Feb;66(2):173-83

15. Andrews J, Guyatt G, Oxman AD, Alderson P, Dahm P, Falck-Ytter Y, Nasser M, Meerpohl J, Post PN, Kunz R, Brozek J, Vist G, Rind D, Akl EA, Schünemann HJ.
GRADE guidelines: 14. Going from evidence to recommendations: the significance and presentation of recommendations.
J Clin Epidemiol. 2013 Jul

16. Andrews J, Guyatt G, Oxman AD, Alderson P, Dahm P, Falck-Ytter Y, Nasser M, Meerpohl J, Post PN, Kunz R, Brozek J, Vist G, Rind D, Akl EA, Schünemann HJ.
GRADE guidelines: 15. Going from evidence to recommendations: determinants of a recommendation's direction and strength.
J Clin Epidemiol. 2013 Jan 9



6. OTHER DATA QUALITY ASSESSMENT TOOLS

All checklists are available on the NITAG Resource Center www.nitag-resource.org

The AMSTAR checklist:

A measurement tool to assess the methodological quality of systematic reviews

The CASP checklists:

1. for assessing systematic reviews
2. for assessing qualitative studies

The SIGN checklists:

1. for assessing systematic reviews and meta-analyses
2. for assessing controlled trials
3. for assessing cohort studies
4. for assessing case-control studies
5. for assessing economic studies
6. for assessing diagnostic studies (this checklist is not included in the folder, concerns comparison of specific diagnostic tests)

APPENDIX 1: AMSTAR checklist

A measurement tool to assess the methodological quality of systematic reviews

1. Was an 'a priori' design provided? The research question and inclusion criteria should be established before the conduct of the review. *Note: Need to refer to a protocol, ethics approval, or pre-determined/a priori published research objectives to score a "yes."*	Yes ☐ No ☐ Can't answer ☐ Not applicable ☐
2. Was there duplicate study selection and data extraction? There should be at least two independent data extractors and a consensus procedure for disagreements should be in place. *Note: 2 people do study selection, 2 people do data extraction, consensus process or one person checks the other's work.*	Yes ☐ No ☐ Can't answer ☐ Not applicable ☐
3. Was a comprehensive literature search performed? At least two electronic sources should be searched. The report must include years and databases used (e.g., Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. *Note: If at least 2 sources + one supplementary strategy used, select "yes" (Cochrane register/Central counts as 2 sources; a grey literature search counts as supplementary).*	Yes ☐ No ☐ Can't answer ☐ Not applicable ☐
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion? The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc. *Note: If review indicates that there was a search for "grey literature" or "unpublished literature," indicate "yes." SINGLE database, dissertations, conference proceedings, and trial registries are all considered grey for this purpose. If searching a source that contains both grey and non-grey, must specify that they were searching for grey/unpublished lit.*	Yes ☐ No ☐ Can't answer ☐ Not applicable ☐
5. Was a list of studies (included and excluded) provided? A list of included and excluded studies should be provided. *Note: Acceptable if the excluded studies are referenced. If there is an electronic link to the list but the link is dead, select "no."*	Yes ☐ No ☐ Can't answer ☐ Not applicable ☐
6. Were the characteristics of the included studies provided? In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analysed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported. *Note: Acceptable if not in table format as long as they are described as above.*	Yes ☐ No ☐ Can't answer ☐ Not applicable ☐

7. Was the scientific quality of the included studies assessed and documented? 'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other types of studies alternative items will be relevant. *Note: Can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, etc., or a description of quality items, with some kind of result for EACH study ("low" or "high" is fine, as long as it is clear which studies scored "low" and which scored "high"; a summary score/range for all studies is not acceptable).*	Yes ☐ No ☐ Can't answer ☐ Not applicable ☐
8. Was the scientific quality of the included studies used appropriately in formulating conclusions? The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. *Note: Might say something such as "the results should be interpreted with caution due to poor quality of included studies." Cannot score "yes" for this question if scored "no" for question 7.*	Yes ☐ No ☐ Can't answer ☐ Not applicable ☐
9. Were the methods used to combine the findings of studies appropriate? For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, I2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). *Note: Indicate "yes" if they mention or describe heterogeneity, i.e., if they explain that they cannot pool because of heterogeneity/variability between interventions.*	Yes ☐ No ☐ Can't answer ☐ Not applicable ☐
10. Was the likelihood of publication bias assessed? An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). *Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.*	Yes ☐ No ☐ Can't answer ☐ Not applicable ☐
11. Was the conflict of interest included? Potential sources of support should be clearly acknowledged in both the systematic review and the included studies. *Note: To get a "yes," must indicate source of funding or support for the systematic review AND for each of the included studies.*	Yes ☐ No ☐ Can't answer ☐ Not applicable ☐
Source: Shea *et al. BMC Medical Research Methodology* 2007 7:10 doi:10.1186/1471-2288-7-10	

APPENDIX 2: CASP CHECKLISTS

Available from: http://www.casp-uk.net/#!casp-tools-checklists/c18f8

CASP Checklist for systematic reviews

10 QUESTIONS TO HELP YOU MAKE SENSE OF A REVIEW

How to use this appraisal tool

Three broad issues need to be considered when appraising the report of a systematic review:

- **Are the results of the review valid? (Section A)**
- **What are the results? (Section B)**
- **Will the results help locally? (Section C)**

The 10 questions on the following pages are designed to help you think about these issues systematically.

The first two questions are screening questions and can be answered quickly. If the answer to both is "yes", it is worth proceeding with the remaining questions.

There is some degree of overlap between the questions, you are asked to record a "yes", "no" or "can't tell" to most of the questions. A number of prompts are given after each question. These are designed to remind you why the question is important. Record your reasons for your answers in the spaces provided.

A. ARE THE RESULTS OF THE REVIEW VALID?

Screening Questions

1. Did the review address a clearly-focused question? HINT: an issue can be 'focused' in terms of: • The population studied • The intervention given • The outcome considered	Yes ☐ Can't tell ☐ No ☐
2. Did the authors look for the right type of papers? HINT: 'The best sort of studies' would: • Address the review's question • Have an appropriate study design (usually RCTs for papers evaluating interventions)	Yes ☐ Can't tell ☐ No ☐
> Is it worth continuing?	Yes ☐ No ☐



Detailed Questions	
3. Do you think the important, relevant studies were included? HINT: Look for: • Which bibliographic databases were used • Follow up from reference lists • Personal contact with experts • Search for unpublished as well as published studies • Search for non-English language studies	Yes ☐ Can't tell ☐ No ☐
4. Did the review's authors do enough to assess the quality of the included studies? HINT: The authors need to consider the rigour of the studies they have identified. Lack of rigour may affect the studies' results. ("All that glisters is not gold" Merchant of Venice – Act II Scene VII)	Yes ☐ Can't tell ☐ No ☐
5. If the results of the review have been combined, was it reasonable to do so? HINT: Consider whether • The results were similar from study to study • The results of all the included studies are clearly displayed • The results of the different studies are similar • The reasons for any variations in results are discussed	Yes ☐ Can't tell ☐ No ☐

B. WHAT ARE THE RESULTS?	
6. What are the overall results of the review? HINT: Consider • If you are clear about the review's 'bottom line' results • What these are (numerically if appropriate) • How were the results expressed (NNT, odds ratio etc)	
7. How precise are the results? HINT: Look at the confidence intervals, if given	

C. WILL THE RESULTS HELP LOCALLY?	
8. Can the results be applied to the local population? HINT: Consider whether • The patients covered by the review could be sufficiently different to your population to cause concern • Your local setting is likely to differ much from that of the review	Yes ☐ Can't tell ☐ No ☐
9. Were all important outcomes considered? HINT: Consider whether • Is there other information you would like to have seen	Yes ☐ Can't tell ☐ No ☐
10. Are the benefits worth the harms and costs? HINT: Consider • Even if this is not addressed by the review, what do you think?	Yes ☐ Can't tell ☐ No ☐

CASP Checklist for qualitative studies

Screening Questions

1. Was there a clear statement of the aims of the research?

HINT: Consider

- What was the goal of the research?
- Why it was thought important?
- Its relevance

Yes ☐ Can't tell ☐ No ☐

2. Is a qualitative methodology appropriate?

HINT: Consider

- If the research seeks to interpret or illuminate the actions and/or subjective experiences of research participants
- Is qualitative research the right methodology for addressing the research goal?

Yes ☐ Can't tell ☐ No ☐

- Is it worth continuing?

Detailed Questions

3. Was the research design appropriate to address the aims of the research?

HINT: Consider

- If the researcher has justified the research design (e.g. have they discussed how they decided which method to use)?

Yes ☐ Can't tell ☐ No ☐

4. Was the recruitment strategy appropriate to the aims of the research?

HINT:Consider

- If the researcher has explained how the participants were selected
- If they explained why the participants they selected were the most appropriate to provide access to the type of knowledge sought by the study
- If there are any discussions around recruitment (e.g. why some people chose not to take part)

Yes ☐ Can't tell ☐ No ☐

5. Was the data collected in a way that addressed the research issue?

HINT: Consider

- If the setting for data collection was justified
- If it is clear how data were collected (e.g. focus group, semi-structured interview etc.)
- If the researcher has justified the methods chosen
- If the researcher has made the methods explicit (e.g. for interview method, is there an indication of how interviews were conducted, or did they use a topic guide)?
- If methods were modified during the study. If so, has the researcher explained how and why?
- If the form of data is clear (e.g. tape recordings, video material, notes etc)
- If the researcher has discussed saturation of data

Yes ☐ Can't tell ☐ No ☐

6. Has the relationship between researcher and participants been adequately considered?

HINT: Consider

- If the researcher critically examined their own role, potential bias and influence during
- (a) Formulation of the research questions
- (b) Data collection, including sample recruitment and choice of location
- How the researcher responded to events during the study and whether they considered the implications of any changes in the research design

Yes ☐ Can't tell ☐ No ☐



7. Have ethical issues been taken into consideration? HINT: Consider • If there are sufficient details of how the research was explained to participants for the reader to assess whether ethical standards were maintained • If the researcher has discussed issues raised by the study (e.g. issues around informed consent or confidentiality or how they have handled the effects of the study on the participants during and after the study) • If approval has been sought from the ethics committee	Yes ☐ Can't tell ☐ No ☐
8. Was the data analysis sufficiently rigorous? HINT: Consider • If there is an in-depth description of the analysis process • If thematic analysis is used. If so, is it clear how the categories/themes were derived from the data? • Whether the researcher explains how the data presented were selected from the original sample to demonstrate the analysis process • If sufficient data are presented to support the findings • To what extent contradictory data are taken into account • Whether the researcher critically examined their own role, potential bias and influence during analysis and selection of data for presentation	Yes ☐ Can't tell ☐ No ☐
9. Is there a clear statement of findings? HINT: Consider • If the findings are explicit • If there is adequate discussion of the evidence both for and against the researcher's arguments • If the researcher has discussed the credibility of their findings (e.g. triangulation, respondent validation, more than one analyst) • If the findings are discussed in relation to the original research question	Yes ☐ Can't tell ☐ No ☐
10. How valuable is the research? HINT: Consider • If the researcher discusses the contribution the study makes to existing knowledge or understanding e.g. do they consider the findings in relation to current practice or policy? or relevant research-based literature? • If they identify new areas where research is necessary • If the researchers have discussed whether or how the findings can be transferred to other populations or considered other ways the research may be used	Yes ☐ Can't tell ☐ No ☐

APPENDIX 3: SIGN CHECKLISTS

Available from http://www.sign.ac.uk/methodology/checklists.html

SIGN

Methodology Checklist 1: Systematic reviews and Meta-analyses

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C,. et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10.* Available from http://www.biomedcentral.com/1471-2288/7/10 (cited 10 Sep 2012)

Study identification (Include author, title, year of publication, journal title, pages)

Guideline topic: | Key Question No:

Before completing this checklist, consider:

- Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO reject. IF YES complete the checklist.

Checklist completed by:

SECTION 1: INTERNAL VALIDITY

	In a well-conducted systematic review	**Does this study do it?**
1.1	The research question is clearly defined and the inclusion/ exclusion criteria must be listed in the paper.	Yes ☐ No ☐ **If no reject**
1.2	A comprehensive literature search is carried out.	Yes ☐ No ☐ Not applicable ☐ **If no reject**
1.3	At least two people should have selected studies.	Yes ☐ No ☐ Can't say ☐
1.4	At least two people should have extracted data.	Yes ☐ No ☐ Can't say ☐
1.5	The status of publication was not used as an inclusion criterion.	Yes ☐ No ☐
1.6	The excluded studies are listed.	Yes ☐ No ☐
1.7	The relevant characteristics of the included studies are provided.	Yes ☐ No ☐
1.8	The scientific quality of the included studies was assessed and reported.	Yes ☐ No ☐
1.9	Was the scientific quality of the included studies used appropriately?	Yes ☐ No ☐
1.10	Appropriate methods are used to combine the individual study findings.	Yes ☐ No ☐ Can't say ☐ Not applicable ☐



SECTION 1: INTERNAL VALIDITY		
In a well-conducted systematic review		**Does this study do it?**
1.11	The likelihood of publication bias was assessed appropriately.	Yes ☐ No ☐ Not applicable ☐
1.12	Conflicts of interest are declared.	Yes ☐ No ☐
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review?	High quality (++) ☐ Acceptable (+) ☐ Low quality (-) ☐ Unacceptable – reject 0 ☐
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes ☐ No ☐
2.3	**Note**	

NOTES ON THE USE OF METHODOLOGY CHECKLIST 1: SYSTEMATIC REVIEWS AND META-ANALYSES

SIGN

Methodology Checklist 1: Systematic reviews and Meta-analyses
Notes for completion of checklist

SIGN gratefully acknowledges the permission received from the authors of the AMSTAR tool to base this checklist on their work: *Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C,. et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Medical Research Methodology 2007, 7:10 doi:10.1186/1471-2288-7-10.* Available from http://www.biomedcentral.com/1471-2288/7/10 (cited 10 Sep 2012)

Must refers to a statement that has to be fulfilled for the question to receive a yes answer. Should statements are a mark of quality but not a necessity for a yes answer. These should be used to assess the overall quality of the paper.

SECTION 1: INTERNAL VALIDITY

	In a well-conducted systematic review:	Notes
1.1	The research question is clearly defined and the inclusion/ exclusion criteria must be listed in the paper.	The PICO must be clear in the paper even if not directly referred to. The research question and inclusion criteria should be established before the review is conducted.
1.2	A comprehensive literature search is carried out.	At least two relevant electronic sources must be searched. The report must list the databases used (e.g., Central, EMBASE, and MEDLINE). (Cochrane register/Central counts as two sources; a grey literature search counts as supplementary). (PubMed and MEDLINE count as one database.) Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. Dates for the search should be provided. The paragraph above is the minimum requirement. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or/and experts in the particular field of study, and by reviewing the references in the studies found. The paragraph above is a quality criteria which affects the overall rating of the review. *Notes* This criterion will not apply in the case of prospective meta-analysis - this is where meta-analysis is based on pre-selected studies identified for inclusion before the results of those studies are known. Such reports must state that they are prospective.
1.3	At least two people should have selected studies.	At least two people should select papers. There should be a consensus process to resolve any differences

SECTION 1: INTERNAL VALIDITY		
In a well-conducted systematic review:		Notes
1.4	At least two people should have extracted data.	At least two people should extract data and should report that a consensus was agreed. One person checking the others data extraction is accurate is acceptable.
1.5	The status of publication was not used as an inclusion criterion.	The authors should state that they searched for reports regardless of their publication status. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status. If review indicates that there was a search for "grey literature" or "unpublished literature," indicate "yes." SIGLE database, dissertations, conference proceedings, and trial registries are all considered grey for this purpose. If searching a source that contains both grey and non-grey, must specify that they were searching for grey/unpublished lit.
1.6	The excluded studies are listed.	Limiting the excluded studies to references is acceptable.
1.7	The relevant characteristics of the included studies are provided.	In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the included studies e.g., age, race, sex, relevant socio-economic data, disease status, duration, severity, or other diseases should be reported. (Note that a format other than a table is acceptable, as long as the information noted here is provided). Absence of this will make it impossible to form guideline recommendations. Mark as (-) original papers would need to be examined.
1.8	The scientific quality of the included studies was assessed and documented	It can include use of a quality scoring tool or checklist, e.g. risk of bias assessment, or a description of quality items, with some kind of result for EACH study ("low" or "high" is fine, as long as it is clear which studies scored "low" and which scored "high"; a summary score/range for all studies is not acceptable. Absence of this will make it impossible to form guideline recommendations. Mark as (-)
1.9	Was the scientific quality of the included studies used appropriately?	Examples include sensitivity analysis based on study quality, exclusion of poor-quality studies, and statements such as 'the results should be interpreted with caution due to poor quality of included studies' The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. Cannot score "yes" for this question if scored "no" for question 1.8.

SECTION 1: INTERNAL VALIDITY		
In a well-conducted systematic review:		Notes
1.10	Appropriate methods are used to combine the individual study findings.	Studies that are very clinically heterogeneous should not be combined in a meta-analysis. Look at the forest plot–do the results look similar across the studies? For the pooled result a test should be done to assess statistical heterogeneity i.e. Chi-squared (χ^2) test for homogeneity and/or I^2 test for inconsistency. If significant heterogeneity is apparent the authors should have explored possible explanations using methods such as sensitivity analysis or meta-regression. A random effects analysis may be used to take account of between-study variation but is not a 'fix' for heterogeneity. Planned subgroup analyses should be pre-specified and limited in number because conducting many subgroup analyses increases the probability of obtaining a statistically significant result by chance. Conclusions based on post-hoc subgroup analyses must be interpreted with caution. Cannot score "yes" for this question if scored "no" for question 1.8.
1.11	The likelihood of publication bias was assessed appropriately	The possibility of publication bias should be assessed where possible, commonly done by visual inspection of a funnel plot together with a statistical test for asymmetry (e.g., Egger regression test) although other statistical and modelling approaches may be reported. Absence of a funnel plot doesn't mean the likelihood of publication bias was not assessed appropriately (there are other methods); 10 studies is just a ballpark minimum number for a funnel plot and a plot is of little use when there are few studies.
1.12	Conflicts of interest are declared.	Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	What is your overall assessment of the methodological quality of this review?	Rate the overall methodological quality of the study, using the following as a guide: **High quality (++):** Majority of criteria met. Little or no risk of bias.. **Acceptable (+):** Most criteria met. Some flaws in the study with an associated risk of bias. **Low quality (-):** Either most criteria not met, or significant flaws relating to key aspects of study design. **Reject (0):** Poor quality study with significant flaws. Wrong study type. Not relevant to guideline.

SIGN

Methodology Checklist 2: Controlled Trials

Study identification *(Include author, title, year of publication, journal title, pages)*

Guideline topic:	Key Question No:	Reviewer:

Before completing this checklist, consider:

1. Is the paper a **randomised controlled trial** or a **controlled clinical trial**? If in doubt, check the study design algorithm available from SIGN and make sure you have the correct checklist. If it is a **controlled clinical trial** questions 1.2, 1.3, and 1.4 are not relevant, and the study cannot be rated higher than 1+
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO REJECT (give reason below). IF YES complete the checklist.

Reason for rejection: ☐ 1. Paper not relevant to key question ☐ 2. Other reason (please specify):

SECTION 1: INTERNAL VALIDITY

	In a well-conducted RCT study...	*Does this study do it?*
1.1	The study addresses an appropriate and clearly-focused question. [I]	Yes ☐ No ☐ Can't say ☐
1.2	The assignment of subjects to treatment groups is randomised. [II]	Yes ☐ No ☐ Can't say ☐
1.3	An adequate concealment method is used. [III]	Yes ☐ No ☐ Can't say ☐
1.4	Subjects and investigators are kept 'blind' about treatment allocation. [IV]	Yes ☐ No ☐ Can't say ☐
1.5	The treatment and control groups are similar at the start of the trial. [V]	Yes ☐ No ☐ Can't say ☐
1.6	The only difference between groups is the treatment under investigation. [VI]	Yes ☐ No ☐ Can't say ☐
1.7	All relevant outcomes are measured in a standard, valid and reliable way. [VII]	Yes ☐ No ☐ Can't say ☐
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed? [VIII]	
1.9	All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). [IX]	Yes ☐ No ☐ Can't say ☐ Does not apply ☐
1.10	Where the study is carried out at more than one site, results are comparable for all sites. [X]	Yes ☐ No ☐ Can't say ☐ Does not apply ☐

SECTION 2: OVERALL ASSESSMENT OF THE STUDY

2.1	***How well was the study done to minimise bias?*** ***Code as follows:*** [XI]	High quality (++) ☐ Acceptable (+) ☐ Unacceptable – reject 0 ☐
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?	
2.3	Are the results of this study directly applicable to the patient group targeted by this guideline?	
2.4	**Notes.** Summarise the authors' conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above.	

SUMMARY FOR PARTICIPANT

[I] Unless a clear and well-defined question is specified, it will be difficult to assess how well the study has met its objectives or how relevant it is to the question you are trying to answer on the basis of its conclusions.

[II] Random allocation of patients to receive one or the other of the treatments under investigation, or to receive either treatment or placebo, is fundamental to this type of study.

[III] Allocation concealment refers to the process used to ensure that researchers are unaware of which group the patients are being allocated to at the time they enter the study. Research has shown that where allocation concealment is inadequate, investigators can overestimate the effect of interventions by up to 40%.

[IV] Blinding refers to the process whereby people are kept unaware of which treatment an individual patient has been receiving when they are assessing the outcome for that patient. It can be carried out to up to three levels. Single-blinding is where patients are unaware of which treatment they are receiving. In double-blind studies, neither the clinician nor the patient knows which treatment is being given. In very rare cases studies may be triple-blinded, where neither patients, clinicians, nor those conducting the analysis are aware of which patients received which treatment. The higher the level of blinding, the lower the risk of bias in the study.

[V] Patients selected for inclusion in a trial must be as similar as possible. The study should report any significant differences in the composition of the study groups in relation to gender mix, age, stage of disease (if appropriate), social background, ethnic origin, or co-morbid conditions. These factors may be covered by inclusion and exclusion criteria, rather than being reported directly. Failure to address this question, or the use of inappropriate groups, should lead to the study being downgraded.

[VI] If some patients received additional treatment, even if of a minor nature or consisting of advice and counselling rather than a physical intervention, this treatment is a potential confounding factor that may invalidate the results. **If groups were *not* treated equally, the study should be rejected unless no other evidence is available.** If the study is used as evidence it should be treated with caution.

[VII] The primary outcome measures used should be clearly stated in the study. **If the outcome measures are not stated, or the study bases its main conclusions on secondary outcomes, the study should be rejected.** Where outcome measures require any degree of subjectivity, some evidence should be provided that the measures used are reliable and have been validated prior to their use in the study.

[VIII] The number of patients that drop out of a study should give concern if the number is very high. Conventionally, a 20% drop-out rate is regarded as acceptable, but this may vary. Some regard should be paid to why patients dropped out, as well as how many. It should be noted that the drop-out rate may be expected to be higher in studies conducted over a long period of time. A higher drop-out rate will normally lead to downgrading, rather than rejection of a study.



[IX] In practice, it is rarely the case that all patients allocated to the intervention group receive the intervention throughout the trial, or that all those in the comparison group do not. Patients may refuse treatment, or contraindications arise that lead them to be switched to the other group. If the comparability of groups through randomisation is to be maintained, however, patient outcomes must be analysed according to the group to which they were originally allocated irrespective of the treatment they actually received. (This is known as intention-to-treat analysis.) If it is clear that analysis was not on an intention-to-treat basis, the study may be rejected. If there is little other evidence available, the study may be included but should be evaluated as if it were a non-randomised cohort study.

[X] In multi-site studies, confidence in the results should be increased if it can be shown that similar results were obtained at the different participating centres.

[XI] Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++): Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+): Most criteria met. Some flaws in the study with an associated risk of bias. Conclusions may change in the light of further studies. **Low quality** (0): Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

Notes on Methodology Checklist 2: Controlled Trials

The top part of the form identifies the study and links it to the particular guideline and key question to which it relates. It includes reminders of factors you should consider before deciding whether it is worth progressing to a full appraisal of the paper concerned.

Section 1	This section makes a series of statements about aspects of the systematic review process that affect the internal validity of the review and asks you to assess how well the review addresses each issue. The objective is to assess how well the authors have dealt with the risk of bias in their methods. If you would like more information on randomised controlled trials, their characteristics and weaknesses then please refer to Greenhalgh T. How to read a paper: the basics of evidence-based medicine. 3rd edition. Oxford: Blackwell;2006. Section 3.3 Page 44. *Note that the "Response" column is for guidance only. You may opt for a different rating depending on how information is presented in any given review.*

Statement 1.1	**The study addresses an appropriate and clearly-focused question**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	Unless a clear and well-defined question is specified, it will be difficult to assess how well the study has met its objectives or how relevant it is to the question you are trying to answer on the basis of its conclusions.	Always applies	**YES** If elements of the research question are present in the text. {Note that this does not have to be exactly in the PICO format, but all the elements must be present}. **NO** If there is no clear question in the text. **CAN'T SAY** If you think there is insufficient detail to allow an assessment to be made.

Statement 1.2	**The assignment of subjects to treatment groups is randomised**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	Random allocation of patients to receive one or the other of the treatments under investigation, or to receive either treatment or placebo, is fundamental to this type of study.	Always applies	**YES** If a good randomisation method is used such as computer generated off-site allocation. If a poor randomisation method is used such as a coin-flip then mark as 'yes', but mention in notes that the randomisation method was poor. **NO** If deterministic methods such as day of the week, birth date, day of arrival at the clinic, etc. These studies can then be assessed as controlled clinical trials instead of RCTs. **CAN'T SAY** If randomisation is mentioned, but method not specified.



Statement 1.3	An adequate concealment method is used		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	Allocation concealment refers to the process used to ensure that researchers are unaware of which group the patients are being allocated to at the time they enter the study. Research has shown that where allocation concealment is inadequate, investigators can overestimate the effect of interventions by up to 40%.	Always applies	**YES** If centralised allocation, computerised allocation systems, or the use of coded identical containers. **NO** If method of concealment used is regarded as poor, or relatively easy to subvert. Mark as 'no' if no concealment method is reported. **CAN'T SAY** If concealment is mentioned, but not described.
Statement 1.4	**Subjects and investigators are kept 'blind' to treatment allocation**		
	Blinding refers to the process whereby people are kept unaware of which treatment an individual patient has been receiving when they are assessing the outcome for that patient. It can be carried out to up to three levels. Single-blinding is where patients are unaware of which treatment they are receiving. In double-blind studies neither the clinician nor the patient knows which treatment is being given. In very rare cases, studies may be triple-blinded, where neither patients, clinicians, nor those conducting the analysis are aware of which patients received which treatment. The higher the level of blinding, the lower the risk of bias in the study.	When blinding is possible	**YES** If the blinding levels are single-, double- or triple-blinded where possible **NO** If the study could have been blinded, but was not. **CAN'T SAY** If the presence of blinding is not clear.
Statement 1.5	**The treatment and control groups were similar at the start of the trial**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	Patients selected for inclusion in a trial must be as similar as possible. The study should report any significant differences in the composition of the study groups in relation to gender mix, age, stage of disease (if appropriate), social background, ethnic origin,	Always applies	**YES** If the patient groups look reasonably similar. In some trials a p value will be given for each factor considered. These values should ideally all be >0.05. This is very good practice, but its absence should not affect your assessment of study quality.

Statement 1.5	**The treatment and control groups were similar at the start of the trial**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	or co-morbid conditions. These factors may be covered by inclusion and exclusion criteria, rather than being reported directly. Failure to address this question, or the use of inappropriate groups, should lead to the study being downgraded.	Always applies	**NO** If the patient groups have important differences in factors that may influence the outcomes. **CAN'T SAY** If the patient groups have not been adequately described.
Statement 1.6	**The only difference between the groups is the treatment under investigation**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	If some patients received additional treatment, even if of a minor nature or consisting of advice and counselling rather than a physical intervention, this treatment is a potential confounding factor that may invalidate the results. **If groups were *not* treated equally, the study should be rejected unless no other evidence is available.** If the study is used as evidence it should be treated with caution.	Always applies	**YES** If there appears to be no important differences between treatment groups other than the treatment being studied. **NO** If there appears to be an important difference between the two groups. **CAN'T SAY** If there is no description of groups.
Statement 1.7	**All relevant outcomes measured in a standard, valid and reliable way**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	The primary outcome measures used should be clearly stated in the study. **If the outcome measures are not stated, or the study bases its main conclusions on secondary outcomes, the study should be rejected.** Where outcome measures require any degree of subjectivity, some evidence should be provided that the measures used are reliable and have been validated prior to their use in the study.	Always applies	**YES** If there are clearly described outcome measures. **NO** If measures are entirely subjective and based on human judgement with no validation. **CAN'T SAY** If measures are unclear.
Statement 1.8	**What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	The number of patients that drop out of a study should give concern if the number is very high.	Always applies	{Enter percentage}

	Conventionally, a 20% drop-out rate is regarded as acceptable, but this may vary. Some regard should be paid to why patients dropped out, as well as how many. It should be noted that the drop-out rate may be expected to be higher in studies conducted over a long period of time. A higher drop-out rate will normally lead to downgrading, rather than rejection of a study.		
Statement 1.9	**All the subjects are analysed in the groups to which they were randomly allocated (intention-to-treat analysis)**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	In practice, it is rarely the case that all patients allocated to the intervention group receive the intervention throughout the trial, or that all those in the comparison group do not. Patients may refuse treatment, or contraindications arise that lead them to be switched to the other group. If the comparability of groups through randomisation is to be maintained, however, patient outcomes must be analysed according to the group to which they were originally allocated irrespective of the treatment they actually received. (This is known as intention-to-treat analysis.) If it is clear that analysis was not on an intention-to-treat basis, the study may be rejected. If there is little other evidence available, the study may be included but should be evaluated as if it were a non-randomised cohort study.	Always applies	**YES** If ITT (intention-to-treat) is mentioned in the text. 'modified' ITT is acceptable if an explanation is provided. **NO** If ITT is not mentioned in the text. **CAN'T SAY** If 'modified' ITT is indicated without any explanation. **NOT APPLICABLE** If all participants are accounted for and none are lost to follow-up.
Statement 1.10	***Where the study is carried out at more than one site, results are comparable for all sites.***		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	In multi-site studies, confidence in the results should be increased if it can be shown that similar results	In a multi-centre trial	**YES** If there is no marked difference in the site data reported or if there is no difference in the centres that can be determined.

Statement 1.10	***Where the study is carried out at more than one site, results are comparable for all sites.***		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	were obtained at the different participating centres.		**NO** If there are one or more sites that have markedly worse or better data than the others. Or if the sites have different characteristics such as community treatment against hospital in-patient treatment. **CAN'T SAY** If no site-specific data is given. **NOT APPLICABLE** If there is only one site.
Section 2	**Section 2** relates to the overall assessment of the paper. It starts by rating the methodological quality of the study based on your responses in Section 1 and using the following coding system. This section is very important and your rating will appear in the evidence table. PLEASE FILL IN.		
Statement 2.1	How well was the study done to minimise the risk of bias or confounding?		
	++	High quality (++): Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research.	
	+	Acceptable (+): Most criteria met. Some flaws in the study with an associated risk of bias. Conclusions may change in the light of further studies.	
	0	Low quality (0): Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.	
Statement 2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?		
	This is your clinical judgement of the study.		
Statement 2.3	Are the results of this study directly applicable to the patient group targeted by this guideline?		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	Does this study make sense in the Scottish context? Consider whether it is appropriate to extrapolate from other countries or healthcare systems.	Always applies	Yes ☐ No ☐
Statement 2.4	**Notes.** Summarise the authors' conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This is a very important part of the evaluation and will feature in the evidence table. PLEASE FILL IN.		

Methodology Checklist 3: Cohort Studies

Study identification *(Include author, title, year of publication, journal title, pages)*

Guideline topic:	Key Question No:	Reviewer:

Before completing this checklist, consider:

1. Is the paper really a cohort study? If in doubt, check the study design algorithm available from SIGN and make sure you have the correct checklist.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO REJECT (give reason below). IF YES complete the checklist.

Reason for rejection: ☐ 1. Paper not relevant to key question ☐ 2. Other reason (please specify):

Please note that a retrospective study (ie a database or chart study) cannot be rated higher than +.

Section 1: Internal validity

	In a well-conducted cohort study:	**Does this study do it?**		
1.1	The study addresses an appropriate and clearly-focused question[I].	Yes ☐	No ☐	Can't say ☐
	Selection of subjects			
1.2	The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation[II].	Yes ☐	No ☐	Can't say ☐ Does not apply ☐
1.3	The study indicates how many of the people asked to take part did so, in each of the groups being studied[III].	Yes ☐	No ☐	Does not apply ☐
1.4	The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis[IV].	Yes ☐	No ☐	Can't say ☐ Does not apply ☐
1.5	What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed[V].			
1.6	Comparison is made between full participants and those lost to follow-up, by exposure status[VI].	Yes ☐	No ☐	Can't say ☐ Does not apply ☐

ASSESSMENT			
1.7	The outcomes are clearly defined[VII].	Yes ☐ Can't say ☐	No ☐
1.8	The assessment of outcome is made blind to exposure status. If the study is retrospective this may not be applicable[VIII].	Yes ☐ Can't say ☐	No ☐ Does not apply ☐
1.9	Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome[IX].	Yes ☐ Can't say ☐	No ☐
1.10	The method of assessment of exposure is reliable[X].	Yes ☐ Can't say ☐	No ☐
1.11	Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable[XI].	Yes ☐ Can't say ☐	No ☐ Does not apply ☐
1.12	Exposure level or prognostic factor is assessed more than once[XII].	Yes ☐ Can't say ☐	No ☐ Does not apply ☐
CONFOUNDING			
1.13	The main potential confounders are identified and taken into account in the design and analysis[XIII].	Yes ☐ Can't say ☐	No ☐
STATISTICAL ANALYSIS			
1.14	Have confidence intervals been provided?[XIV]	Yes ☐	No ☐
Section 2: OVERALL ASSESSMENT OF THE STUDY			
2.1	How well was the study done to minimise the risk of bias or confounding?[XV]	High quality (++) ☐ Acceptable (+) ☐ Unacceptable (–) ☐ reject (0) ☐	
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, do you think there is clear evidence of an association between exposure and outcome?	Yes ☐ Can't say ☐	No ☐
2.3	Are the results of this study directly applicable to the patient group targeted in this guideline?	Yes ☐	No ☐
2.4	**Notes.** Summarise the authors' conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above.		



[I] Unless a clear and well-defined question is specified in the report of the review, it will be difficult to assess how well it has met its objectives or how relevant it is to the question you are trying to answer on the basis of the conclusions.

[II] This relates to **selection bias.*** It is important that the two groups selected for comparison are as similar as possible in all characteristics except for their exposure status, or the presence of specific prognostic factors or prognostic markers relevant to the study in question.

[III] This relates to selection **bias.*** The participation rate is defined as the number of study participants divided by the number of eligible subjects, and should be calculated separately for each branch of the study. A large difference in participation rate between the two arms of the study indicates that a significant degree of selection bias* may be present, and the study results should be treated with considerable caution.

[IV] If some of the eligible subjects, particularly those in the unexposed group, already have the outcome at the start of the trial the final result will be subject to **performance bias**.* A well-conducted study will attempt to estimate the likelihood of this occurring, and take it into account in the analysis through the use of sensitivity studies or other methods.

[V] This question relates to the risk of **attrition bias**.*The number of patients that drop out of a study should give concern if the number is very high. Conventionally, a 20% drop-out rate is regarded as acceptable, but in observational studies conducted over a lengthy period of time, a higher drop-out rate is to be expected. A decision on whether to downgrade or reject a study because of a high drop-out rate is a matter of judgement based on the reasons why people dropped out, and whether drop-out rates were comparable in the exposed and unexposed groups. Reporting of efforts to follow up participants that dropped out may be regarded as an indicator of a well-conducted study.

[VI] For valid study results, it is essential that the study participants are truly representative of the source population. It is always possible that participants who dropped out of the study will differ in some significant way from those who remained part of the study throughout. A well-conducted study will attempt to identify any such differences between full and partial participants in both the exposed and unexposed groups. This relates to the risk of **attrition bias**.* Any unexplained differences should lead to the study results being treated with caution.

[VII] This relates to the risk of **detection bias**.* Once enrolled in the study, participants should be followed until specified end points or outcomes are reached. In a study of the effect of exercise on the death rates from heart disease in middle aged men, for example, participants might be followed up until death, or until reaching a predefined age. **If outcomes and the criteria used for measuring them are not clearly defined, the study should be rejected.**

[VIII] This relates to the risk of detection bias.* If the assessor is blinded to which participants received the exposure, and which did not, the prospects of unbiased results are significantly increased. Studies in which this is done should be rated more highly than those where it is not done, or not done adequately.

[IX] This relates to the risk of **detection bias**.* Blinding is not possible in many cohort studies. In order to asses the extent of any bias that may be present, it may be helpful to compare process measures used on the participant groups - e.g. frequency of observations, who carried out the observations, the degree of detail and completeness of observations. If these process measures are comparable between the groups, the results may be regarded with more confidence.

[X] This relates to the **risk of detection bias**.* A well-conducted study should indicate how the degree of exposure or presence of prognostic factors or markers was assessed. Whatever measures are used must be sufficient to establish clearly that participants have or have not received the exposure under investigation and the extent of such exposure, or that they do or do not possess a particular prognostic marker or factor. Clearly-described, reliable measures should increase the confidence in the quality of the study.

[XI] This relates to the risk of **detection bias**.* The primary outcome measures used should be clearly stated in the study. **If the outcome measures are not stated, or the study bases its main conclusions on secondary outcomes, the study should be rejected.** Where outcome measures require any degree of subjectivity, some evidence should be provided that the measures used are reliable and have been validated prior to their use in the study.

[XII] This relates to the risk of **detection bias**.* Confidence in data quality should be increased if exposure level is measured more than once in the course of the study. Independent assessment by more than one investigator is preferable.

[XIII] Confounding is the distortion of a link between exposure and outcome by another factor that is associated with both exposure and outcome. The possible presence of confounding factors is one of the principal reasons why observational studies are not more highly rated as a source of evidence. The report of the study should indicate which potential confounders have been considered, and how they have been assessed or allowed for in the analysis. Clinical judgement should be applied to consider whether all likely confounders have been considered. If the measures used to address confounding are considered inadequate, the study should be downgraded or rejected, depending on how serious the risk of confounding is considered to be. **A study that does not address the possibility of confounding should be rejected.**

[XIV] Confidence limits are the preferred method for indicating the precision of statistical results, and can be used to differentiate between an inconclusive study and a study that shows no effect. Studies that report a single value with no assessment of precision should be treated with extreme caution.

[XV] Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++): Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+): Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0): Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.



SIGN

Notes on Methodology Checklist 3: Cohort Studies

The studies covered by this checklist are designed to answer questions of the type "What are the effects of this exposure?", It relates to studies that compare a group of people with a particular exposure with another group who either have not had the exposure, or have a different level of exposure. Cohort studies may be prospective (where the exposure is defined and subjects selected before outcomes occur), or retrospective (where exposure is assessed after the outcome is known, usually by the examination of medical records).

Section 1

Section 1 identifies the study, the reviewer, the guideline for which the paper is being considered as evidence, and the key question(s) it is expected to address. The reviewer is asked to consider a series of aspects of cohort study design and to make a judgement as to how well the current study meets this criterion. Each relates to an aspect of methodology that research has shown to be likely to influence the conclusions of a study.

Because of the potential complexity and subtleties of the design of this type of study, there are comparatively few criteria that automatically rule out use of a study as evidence. It is more a matter of increasing confidence in the strength of association between exposure and outcome by identifying how many aspects of good study design are present, and how well they have been tackled. A study that fails to address or report on more than one or two of the questions addressed below should almost certainly be rejected.

If you would like more information on cohort studies, their characteristics and weaknesses then please refer to Greenhalgh T. How to read a paper: the basics of evidence-based medicine. 3rd edition. Oxford: Blackwell;2006. Section 3.4 Page 49.

Retrospective studies or single-cohort studies are generally regarded as a weaker design, and should not receive a rating higher than "+".

Definitions for terms marked with a * can be found in the Cochrane Handbook.

{Note that the "Response" column is for guidance only. You may opt for a different rating depending on how information is presented in any given review.}

Statement 1.1	**The study addresses an appropriate and clearly-focused question**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	Unless a clear and well-defined question is specified in the report of the review, it will be difficult to assess how well it has met its objectives or how relevant it is to the question you are trying to answer on the basis of the conclusions.	Always applies	**YES** If elements of the research question are present in the text. **NO** If there is no clear question in the text. **CAN'T SAY** If you think there is insufficient detail to allow an assessment to be made.

Statement 1.2	The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation.		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	This relates to **selection bias.*** It is important that the two groups selected for comparison are as similar as possible in all characteristics except for their exposure status, or the presence of specific prognostic factors or prognostic markers relevant to the study in question.	Only when there is a comparison group	**YES** Where characteristics of the populations from which participants were selected are summarised (preferably in a table). **NO** Where there is no indication of how groups were selected, or what the relevant population characteristics were. **CAN'T SAY** Where source populations are identified, but no specific characteristics are tabulated. **NOT APPLICABLE** Where there is no comparison group.
Statement 1.3	**The study indicates how many of the people asked to take part did so, in each of the groups being studied.**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	This relates to **selection bias**. * The participation rate is defined as the number of study participants divided by the number of eligible subjects, and should be calculated separately for each branch of the study. A large difference in participation rate between the two arms of the study indicates that a significant degree of **selection bias*** may be present, and the study results should be treated with considerable caution.	Only in prospective, multiple-cohort studies	**YES** Where the participation rate per group is clearly defined. **NO** Where authors do not indicate the actual participation rate. **NOT APPLICABLE** Where there is no comparison group.



Statement 1.4	The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis?		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	If some of the eligible subjects, particularly those in the unexposed group, already have the outcome at the start of the trial the final result will be subject to **performance bias.*** A well-conducted study will attempt to estimate the likelihood of this occurring, and take it into account in the analysis through the use of sensitivity studies or other methods.	Almost always applies	**YES** Where sensitivity analyses are carried out to assess the impact of this occurring. **NO** Where no mention is made of this possibility. **CAN'T SAY** Where the possibility is acknowledged, but no estimate of actual impact is made. **NOT APPLICABLE** Where the study relates to the long-term effects of an existing condition.
Statement 1.5	**What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed?**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	This question relates to the risk of **attrition bias.*** The number of patients that drop out of a study should give concern if the number is very high. Conventionally, a 20% drop-out rate is regarded as acceptable, but in observational studies conducted over a lengthy period of time a higher drop-out rate is to be expected. A decision on whether to downgrade or reject a study because of a high drop-out rate is a matter of judgement based on the reasons why people dropped out, and whether drop-out rates were comparable in the exposed and unexposed groups. Reporting of efforts to follow up participants that dropped out may be regarded as an indicator of a well-conducted study.	In prospective studies	**Percentage**

Statement 1.6	Comparison is made between full participants and those lost to follow-up, by exposure status.		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	For valid study results, it is essential that the study participants are truly representative of the source population. It is always possible that participants who dropped out of the study will differ in some significant way from those who remained part of the study throughout. A well-conducted study will attempt to identify any such differences between full and partial participants in both the exposed and unexposed groups. This relates to the risk of **attrition bias.*** Any unexplained differences should lead to the study results being treated with caution.	Prospective, multiple-cohors studies	**YES** Where there has been some follow-up of drop-outs, with explanation provided. **NO** Where there is no indication that this factor has been considered. **CAN'T SAY** Where drop-out rates are mentioned, but no follow-up information is provided. **NOT APPLICABLE** Retrospective or single group studies.
Statement 1.7	**The outcomes are clearly defined**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	This relates to the risk of **detection bias.*** Once enrolled in the study, participants should be followed until specified end points or outcomes are reached. In a study of the effect of exercise on the death rates from heart disease in middle aged men, for example, participants might be followed up until death, or until reaching a predefined age. **If outcomes and the criteria used for measuring them are not clearly defined, the study should be rejected.**	Always applies	**YES** Where endpoints or outcomes are clearly specified and used in the analysis. **NO** Where outcomes and measurement criteria are not discussed. **CAN'T SAY** Where definitions of outcomes and/or methods of measuring them are unclear.



Statement 1.8	The assessment of outcome is made blind to exposure status		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	This relates to the risk of **detection bias.*** If the assessor is blinded to which participants received the exposure, and which did not, the prospects of unbiased results are significantly increased. Studies in which this is done should be rated more highly than those where it is not done, or not done adequately.	In studies with more than one group	**YES** Where assessors are blinded to exposure status. **NO** Where assessors could have been blinded, but were not. **CAN'T SAY** If randomisation is mentioned, but method not specified. **NOT APPLICABLE** Where there is only one group being studied.
Statement 1.9	**Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome.**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	This relates to the risk of **detection bias.*** Blinding is not possible in many cohort studies. In order to assess the extent of any bias that may be present, it may be helpful to compare process measures used on the participant groups - e.g. frequency of observations, who carried out the observations, the degree of detail and completeness of observations. If these process measures are comparable between the groups, the results may be regarded with more confidence.	Always applies	**YES** Where process measures are detailed across groups, and are the same or similar for each. **NO** Where there is no indication of if or how measures were managed. **CAN'T SAY** Where there is insufficient information to decide how comparable measures were across groups.

Statement 1.10	The measure of assessment of exposure is reliable.		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	This relates to the risk of **detection bias.*** A well-conducted study should indicate how the degree of exposure or presence of prognostic factors or markers was assessed. Whatever measures are used must be sufficient to establish clearly that participants have or have not received the exposure under investigation and the extent of such exposure, or that they do or do not possess a particular prognostic marker or factor. Clearly-described, reliable measures should increase the confidence in the quality of the study.	Always applies	**YES** Where measures used are clearly defined and have a known degree of accuracy. **NO** Where measures are not defined. **CAN'T SAY** Where it is unclear which measures were used, or how they were defined.
Statement 1.11	**Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable.**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	This relates to the risk of **detection bias.*** The primary outcome measures used should be clearly stated in the study. **If the outcome measures are not stated, or the study bases its main conclusions on secondary outcomes, the study should be rejected.** Where outcome measures require any degree of subjectivity, some evidence should be provided that the measures used are reliable and have been validated prior to their use in the study.	Whenever any kind of subjective measure is used.	**YES** Where clearly-identified primary outcome measures are used in the analysis. If measures are subjective, justification for their use should be provided (e.g. validation of an assessment tool). **NO** Where outcome measures are not defined, or the analysis is based on secondary outcomes. **CAN'T SAY** Where subjective measures are described, but no indication given of how they were validated. **NOT APPLICABLE** Where measures used are completely objective.



Statement 1.12	Exposure level or prognostic factor is assessed more than once		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	This relates to the risk of **detection bias.*** Confidence in data quality should be increased if exposure level is measured more than once in the course of the study. Independent assessment by more than one investigator is preferable.	Prospective studies only.	**YES** Where it is clearly stated that exposure level is measured more than once. **NO** Where it is clear that exposure was only checked once. **CAN'T SAY** Where there is no indication of when exposure was measured. **NOT APPLICABLE** In retrospective studies.
Statement 1.13	**The main potential confounders are identified and taken into account adequately in the design and analysis**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	Confounding is the distortion of a link between exposure and outcome by another factor that is associated with both exposure and outcome. The possible presence of confounding factors is one of the principal reasons why observational studies are not more highly rated as a source of evidence. The report of the study should indicate which potential confounders have been considered, and how they have been assessed or allowed for in the analysis. Clinical judgement should be applied to consider whether all likely confounders have been considered. If the measures used to address confounding are considered inadequate, the study should be downgraded or rejected, depending on how serious the risk of confounding is considered to be. **A study that does not address the possibility of confounding should be rejected.**	Always applies	**YES** Where the main potential confounders are discussed and sensitivity analyses carried out to see if and to what extent they may have affected results. **NO** Where there is no mention of confounding. **CAN'T SAY** Where confounding is mentioned, but no comment on or analysis of potential impact on results.

Statement 1.14	Confidence intervals are provided		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	Confidence limits are the preferred method for indicating the precision of statistical results, and can be used to differentiate between an inconclusive study and a study that shows no effect. Studies that report a single value with no assessment of precision should be treated with extreme caution.	Always applies	**YES** ☐ **NO** ☐



Section 2	**SECTION 2** relates to the overall assessment of the paper. It starts by rating the methodological quality of the study, based on your responses in Section 1 and using the following coding system. The code allocated here, coupled with the study type, will decide the **level of evidence** that this study provides. The aim of the other questions in this section is to summarise your view of the quality of this study and its applicability to the patient group targeted by the guideline you are working on.		
Statement 2.1	**How well was the study done to minimise the risk of bias or confounding, and to establish a causal relationship between exposure and effect?**		
	++	High quality (++): Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research.	
	+	Acceptable (+): Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies.	
	0	Low quality (0): Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.	
Statement 2.2	**Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, do you think there is clear evidence of an association between exposure and outcome?**		
	What does this statement mean?		
	This is your clinical judgement of the study		
Statement 2.3	**Are the results of this study directly applicable to the patient group targeted in this guideline?**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	Does this study make sense in the Scottish context?	Always applies	**YES** ☐ **NO** ☐
Statement 2.4	**Notes.** Summarise the authors' conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This section is very important and will appear on the evidence table. **PLEASE FILL IN.**		

SIGN

Methodology Checklist 4: Case-Control Studies

Study identification *(Include author, title, year of publication, journal title, pages)*

Guideline topic: | Key Question No: | Reviewer:

Before completing this checklist, consider:

1. Is the paper really a case-control study? If in doubt, check the study design algorithm available from SIGN and make sure you have the correct checklist.
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO, REJECT (give reason below). IF YES, complete the checklist.

Reason for rejection: ☐ 1. Paper not relevant to key question ☐ 2. Other reason (please specify):

	In an well-conducted case-control study:	*Does this study do it?*
SECTION 1: INTERNAL VALIDITY		
1.1	The study addresses an appropriate and clearly-focused question[I].	Yes ☐ No ☐ Can't say ☐
SELECTION OF SUBJECTS		
1.2	The cases and controls are taken from comparable populations[II].	Yes ☐ No ☐ Can't say ☐
1.3	The same exclusion criteria are used for both cases and controls[III].	Yes ☐ No ☐ Can't say ☐
1.4	What percentage of each group (cases and controls) participated in the study[IV]?	Case: Controls:
1.5	Comparison is made between participants and non-participants to establish their similarities or differences [V].	Yes ☐ No ☐ Can't say ☐
1.6	Cases are clearly defined and differentiated from controls [VI].	Yes ☐ No ☐ Can't say ☐
1.7	It is clearly established that controls are non-cases [VII].	Yes ☐ No ☐ Can't say ☐
ASSESSMENT		
1.8	Measures will have been taken to prevent knowledge of primary exposure influencing case ascertainment [VIII].	Yes ☐ No ☐ Can't say ☐
1.9	Exposure status is measured in a standard, valid, and reliable way [IX].	Yes ☐ No ☐ Can't say ☐
CONFOUNDING		
1.10	The main potential confounders are identified and taken into account in the design and analysis [X].	Yes ☐ No ☐ Can't say ☐
1.11	Confidence intervals are provided [XI].	Yes ☐ No ☐
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	How well was the study done to minimise the risk of bias or confounding [XII]?	High quality (++) ☐ Acceptable (+) ☐ Unacceptable (–) ☐ Reject (0) ☐
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, do you think there is clear evidence of an association between exposure and outcome?	Yes ☐ No ☐ Can't say ☐
2.3	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes ☐ No ☐ Can't say ☐
2.4	**Notes.** Summarise the authors' conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above.	

[I] Unless a clear and well-defined question is specified in the report of the review, it will be difficult to assess how well it has met its objectives or how relevant it is to the question you are trying to answer on the basis of the conclusions.

[II] Study participants may be selected from the target population (all individuals to which the results of the study could be applied), the source population (a defined subset of the target population from which participants are selected), or from a pool of eligible subjects (a clearly-defined and counted group selected from the source population. **If the study does not include clear definitions of the source population, it should be rejected.**

[III] All selection and exclusion criteria should be applied equally to cases and controls. Failure to do so may introduce a significant degree of bias into the results of the study.

[IV] Differences between the eligible population and the participants are important, as they may influence the validity of the study. A participation rate can be calculated by dividing the number of study participants by the number of eligible subjects. It is more useful if calculated separately for cases and controls. If the participation rate is low, or there is a large difference between the two groups, the study results may well be invalid due to differences between participants and non-participants. In these circumstances, the study should be downgraded, and rejected if the differences are very large.

[V] Even if participation rates are comparable and acceptable, it is still possible that the participants selected to act as cases or controls may differ from other members of the source population in some significant way. A well-conducted case-control study will look at samples of the non-participants among the source population to ensure that the participants are a truly representative sample.

[VI] The method of selection of cases is of critical importance to the validity of the study. Investigators have to be certain that cases are truly cases, but must balance this with the need to ensure that the cases admitted into the study are representative of the eligible population. **The issues involved in case selection are complex, and should ideally be evaluated by someone with a good understanding of the design of case-control studies. If the study does not comment on how cases were selected, it is probably safest to reject it as a source of evidence.**

[VII] Just as it is important to be sure that cases are true cases, it is important to be sure that controls do not have the outcome under investigation. Control subjects should be chosen so that information on exposure status can be obtained or assessed in a similar way to that used for the selection of cases. If the methods of control selection are not described, the study should be rejected. **If different methods of selection are used for cases and controls the study should be evaluated by someone with a good understanding of the design of case-control studies.**

[VIII] If there is a possibility that case ascertainment can be influenced by knowledge of exposure status, assessment of any association is likely to be biased. A well-conducted study should take this into account in the design of the study.

[IX] The primary outcome measures used should be clearly stated in the study. **If the outcome measures are not stated, or the study bases its main conclusions on secondary outcomes, the study should be rejected.** Where outcome measures require any degree of subjectivity, some evidence should be provided that the measures used are reliable and have been validated prior to their use in the study.

[X] Confounding is the distortion of a link between exposure and outcome by another factor that is associated with both exposure and outcome. The possible presence of confounding factors is one of the principal reasons why observational studies are not more highly rated as a source of evidence. The study should indicate which potential confounders have been considered, and how they have been allowed for in the analysis. Clinical judgement should be applied to consider whether all likely confounders have been considered. If the measures used to address confounding are considered inadequate, the study should be downgraded or rejected. A study that does not address the possibility of confounding should be rejected.

[XI] Confidence limits are the preferred method for indicating the precision of statistical results, and can be used to differentiate between an inconclusive study and a study that shows no effect. Studies that report a single value with no assessment of precision should be treated with extreme caution.

[XII] Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++): Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+): Most criteria met. Some flaws in the study with an associated risk of bias. Conclusions may change in the light of further studies. **Low quality** (0): Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.



SIGN

Notes on Methodology Checklist 4: Case-Control Studies

The studies covered by this checklist are designed to answer questions of the type "What are the factors that caused this event?", and involve comparison of individuals with an outcome with other individuals from the same population who do not have the outcome. These studies start after the outcome of an event, and can be used to assess multiple causes of a single event. They are generally used to assess the causes of a new problem, but may also be useful for the evaluation of population-based interventions such as screening.

Section 1	**SECTION 1** identifies the study, the reviewer, the guideline for which the paper is being considered as evidence, and the key question(s) it is expected to address. The reviewer is asked to consider a series of aspects of cohort study design and to make a judgement as to how well the current study meets this criterion. Each relates to an aspect of methodology that research has shown makes a significant difference to the conclusions of a study. Case-control studies need to be very carefully designed, and the complexity of their design is often not appreciated by investigators, leading to many poor-quality studies being conducted. The questions in this checklist are designed to identify the main features that should be present in a well-designed study. There are few criteria that should, alone and unsupported, lead to rejection of a study. However, a study that fails to address or report on more than one or two of the questions addressed below should almost certainly be rejected. If you would like more information on case-control studies, their characteristics, and weaknesses then please refer to Greenhalgh T. How to read a paper: the basics of evidence-based medicine. 3rd edition. Oxford: Blackwell;2006. Section 3.5 Page 50. Definitions for terms marked with a * below can be found in the Cochrane Handbook. *{Note that the "Response" column is for guidance only. You may opt for a different rating depending on how information is presented in any given review.}*		
Statement 1.1	**The study addresses an appropriate and clearly-focused question**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	Unless a clear and well-defined question is specified in the report of the review, it will be difficult to assess how well it has met its objectives or how relevant it is to the question you are trying to answer on the basis of the conclusions.	Always applies	**YES** If elements of the research question are present in the text. **NO** If there is no clear question in the text. **CAN'T SAY** If you think there is insufficient detail to allow an assessment to be made.
Statement 1.2	**The cases and controls are taken from comparable populations**		
	Study participants may be selected from the target population (all individuals to which the results of the study could be applied), the source population (a defined subset of the target population from which participants are selected),	Always applies	**YES** Where all populations are clearly defined. **NO** Where it is unclear on what bases the cases and controls were selected.

Statement 1.2	**The cases and controls are taken from comparable populations**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	or from a pool of eligible subjects (a clearly-defined and counted group selected from the source population). **If the study does not include clear definitions of the source population, it should be rejected.**		**CAN'T SAY** Where there is some discussion of which populations cases and controls were selected from, but no clarity about how each group was selected.
Statement 1.3	**The same exclusion criteria are used for both cases and controls**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	All selection and exclusion criteria should be applied equally to cases and controls. Failure to do so may introduce a significant degree of bias into the results of the study.	Always applies	**YES** Where selection and exclusion criteria are explicitly stated for both cases and controls. **NO** Where there is evidence that selection and exclusion criteria were different for cases and controls. **CAN'T SAY** Where selection and/or exclusion criteria, or their application, are not clearly specified.
Statement 1.4	**What percentage of each group (cases and controls) participated in the study?**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	Differences between the eligible population and the participants are important, as they may influence the validity of the study. A participation rate can be calculated by dividing the number of study participants by the number of eligible subjects. It is more useful if calculated separately for cases and controls. If the participation rate is low, or there is a large difference between the two groups, the study results may well be invalid due to differences between participants and non-participants. In these circumstances, the study should be downgraded, and rejected if the differences are very large.	Always applies	Percentage cases: Percentage controls:

Statement 1.5	**Comparison is made between participants and non-participants to establish their similarities or differences**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	Even if participation rates are comparable and acceptable, it is still possible that the participants selected to act as cases or controls may differ from other members of the source population in some significant way. A well-conducted case-control study will look at samples of the non-participants among the source population to ensure that the participants are a truly representative sample.	Always applies	**YES** Where data is presented on the key characteristics of a sample of people from the source population that were not included in the study. **NO** Where no information on the characteristics of the source population is available. **CAN'T SAY** Where the issue is discussed, but detailed information is not provided.
Statement 1.6	**Cases are clearly defined and differentiated from controls**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	The method of selection of cases is of critical importance to the validity of the study. Investigators have to be certain that cases are truly cases, but must balance this with the need to ensure that the cases admitted into the study are representative of the eligible population. **The issues involved in case selection are complex, and should ideally be evaluated by someone with a good understanding of the design of case-control studies. If the study does not comment on how cases were selected, it is probably safest to reject it as a source of evidence.**	Always applies	**YES** Where methods used to define and identify cases are clearly described. **NO** Where there is no discussion of how cases were identified. **CAN'T SAY** Where the methods used to define or identify cases are mentioned, but no details or justification are provided.
Statement 1.7	**It is clearly established that controls are non-cases**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	Just as it is important to be sure that cases are true cases, it is important to be sure that controls do not have the outcome under investigation. Control subjects should be chosen so that information on exposure	Always applies	**YES** Where methods used to define and identify controls are clearly described. **NO** Where there is no discussion of how controls were identified.

Statement 1.7	**It is clearly established that controls are non-cases**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	status can be obtained or assessed in a similar way to that used for the selection of cases. If the methods of control selection are not described, the study should be rejected. **If different methods of selection are used for cases and controls the study should be evaluated by someone with a good understanding of the design of case-control studies.**		**CAN'T SAY** Where the methods used to define or identify controls are mentioned, but no details or justification are provided.
Statement 1.8	**Measures will have been taken to prevent knowledge of primary exposure influencing case ascertainment**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	If there is a possibility that case ascertainment can be influenced by knowledge of exposure status, assessment of any association is likely to be biased. A well-conducted study should take this into account in the design of the study.	Nearly always applies	**YES** Where assessors are blinded to exposure status. **NO** Where no blinding of assessors takes place. **CAN'T SAY** Where it is not possible to fully blind assessors (eg where assessors talk directly to participant or if the study is retrospective ie database or chart). **NOT APPLICABLE** Where studies are based on analysis of medical charts or databases.
Statement 1.9	**Exposure status is measured in a standard, valid and reliable way**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	The primary outcome measures used should be clearly stated in the study. **If the outcome measures are not stated, or the study bases its main conclusions on secondary outcomes, the study should be rejected.** Where outcome measures require any degree of subjectivity, some evidence should be provided that the measures used are reliable and have been validated prior to their use in the study.	Always applies	**YES** Where outcome measures are clearly identified and are either objective or use a validated evaluation tool. **NO** Where outcome measures are subjective, and are not based on a validated tool. **CAN'T SAY** Where outcome measures are not described in detail.



Statement 1.10	**The main potential confounders are identified and taken into account in the design and analysis**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	Confounding is the distortion of a link between exposure and outcome by another factor that is associated with both exposure and outcome. The possible presence of confounding factors is one of the principal reasons why observational studies are not more highly rated as a source of evidence. The study should indicate which potential confounders have been considered, and how they have been allowed for in the analysis. Clinical judgement should be applied to consider whether all likely confounders have been considered. If the measures used to address confounding are considered inadequate, the study should be downgraded or rejected. **A study that does not address the possibility of confounding should be rejected.**	Always applies	**YES** Where confounders are discussed, identified, and allowed for in the analysis. **NO** Where confounding is not discussed. **CAN'T SAY** Where confounding is mentioned, but not discussed in detail.
Statement 1.11	**Confidence intervals are provided**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	Confidence limits are the preferred method for indicating the precision of statistical results, and can be used to differentiate between an inconclusive study and a study that shows no effect. Studies that report a single value with no assessment of precision should be treated with extreme caution.	Always applies	**Yes** ☐ **No** ☐
Section 2	**SECTION 2 relates to the overall assessment of the paper. It starts by rating the methodological quality of the study, based on your responses in Section 1 and using the following coding system:**		
Statement 2.1	**How well was the study done to minimise the risk of bias or confounding?**		

SIGN

Methodology Checklist 5: Economic Evaluations

This checklist is based on the BMJ requirements for authors submitting economic studies for publication in that journal. Drummond M, Jefferson TO. Guidelines for authors and peer reviewers of economic submissions to the BMJ. BMJ 1996:313;275

Study identification *(Include author, title, year of publication, journal title, pages)*

Guideline topic:	Key Question No:	Reviewer:

Before completing this checklist, consider:

1. Is the paper an economic study (ie assessing the **cost-effectiveness** of something), or is it just a study of costs? REJECT IF THE LATTER IS TRUE.
2. Is the paper relevant to the key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO, REJECT (give reason below). IF YES, complete the checklist.

Reason for rejection: ☐ 1. Not an economic study ☐ 2. Paper not relevant to key question ☐ 3. Other reason (please specify):

SECTION 1: INTERNAL VALIDITY

	In a well-conducted RCT study...	*Does this study do it?*
1.1	The study addresses an appropriate and clearly-focused question	Yes ☐ No ☐ Can't say ☐
1.2	The economic importance of the question is clear	Yes ☐ No ☐ Can't say ☐
1.3	The choice of study design is justified	Yes ☐ No ☐ Can't say ☐
1.4	All costs that are relevant from the viewpoint of the study are included and are measured and valued appropriately	Yes ☐ No ☐
1.5	The outcome measures used to answer the study question are relevant to that purpose and are measured and valued appropriately	Yes ☐ No ☐ Can't say ☐ Not applicable ☐
1.6	If discounting of future costs and outcomes is necessary, it has been performed correctly	Yes ☐ No ☐ Can't say ☐ Not applicable ☐
1.7	Assumptions are made explicit and a sensitivity analysis has been performed	Yes ☐ No ☐ Can't say ☐
1.8	The decision rule is made explicit and comparisons are made on the basis of incremental costs and outcomes	Yes ☐ No ☐
1.9	The results provide information of relevance to policy-makers	Yes ☐ No ☐

SECTION 2: OVERALL ASSESSMENT OF THE STUDY

2.1	*How well was the study conducted?*	High quality (++) ☐ Acceptable (+) ☐ Unacceptable – reject (0) ☐
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	Yes ☐ No ☐
2.4	**Notes.** Summarise the authors' conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above.	



Notes on Methodology Checklist 5: Economic Evaluations

The top part of the form identifies the study and links it to the particular guideline and key question to which it relates. It includes reminders of factors you should consider before deciding whether it is worth progressing to a full appraisal of the paper concerned.

Section 1	**SECTION 1** identifies the study and asks a series of questions aimed at establishing the internal validity of the study under review - i.e. making sure that it has been carried out carefully, and that the results are likely to be reliable and useful. Each question covers an aspect of study design that is known to make a significant difference to the conclusions of a study. ***Note*** *that the "Response" column is for guidance only. You may opt for a different rating depending on how information is presented in any given review.{}*		
Statement 1.1	**The study addresses an appropriate and clearly-focused question**		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	As with clinical evaluations, a clearly-defined question is essential to allow the user to assess how well the study has met its objectives or how relevant it is to the guideline recommendation to which the results might be applied. For an economic evaluation, the question should contain information on the alternatives under comparison, the viewpoint, and (ideally) the form of economic evaluation being used and the resulting decision rule.	Always applies	**YES** If elements of the research question are present in the text. {Note that this does not have to be exactly in the PICO format, but all the elements must be present}. **NO** If there is no clear question in the text. **CAN'T SAY** If you think there is insufficient detail to allow an assessment to be made.
Statement 1.2	**The economic importance of the question is clear**		
	Not all economic evaluations are equally relevant or important. A comparison between different drugs available to treat the same condition, for example, could influence the choice of drug and possibly the overall cost of treatment. A study of drug therapy versus psychotherapy, on the other hand, could have major implications for the range, type, and extent of resources required to deliver good quality healthcare in a specific area.	Always applies	**YES** Where information is provided on the potential impact of the study results on the delivery of healthcare in the area to which it relates. **NO** Where no information is provided on the potential impact of study results. **CAN'T SAY** Where impact is discussed, but not in enough detail to allow conclusions to be drawn.

Statement 1.3	The choice of study design is justified		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	The design of the study can have a big impact on the results derived from it. It is therefore important that the study design is clearly identified, and its limitations made clear. Each study design has its own strengths and weaknesses and each may be appropriate under different settings. The main types of study used for economic evaluations are: **• Economic evaluation alongside randomised controlled trial.** In some respects this is a good model as cost and benefit data can be collected in parallel with the clinical data, and is therefore likely to be relevant and applicable. On the other hand, a number of factors are likely to make study results unrepresentative of real practice. More resources are likely to be available in a study setting than in normal practice; patient compliance may be higher than normal; there is unlikely to be scope for economies of scale; etc. The overall result is likely to be higher costs and better outcomes in the trial than are achievable once the treatment is provided on a broader basis. **• Before and after studies.** A "before and after study" compares costs and outcomes before the introduction of a new therapy, and after it has been provided for some time. The major problem with this type of study design is the difficulty of attributing any changes purely to the new treatment (high risk of confounding).	Always applies	**YES** Where the reason why the design was chosen is provided, and comments made on potential weaknesses and how they are addressed. **NO** Where no justification is offered. **CAN'T SAY** Where the choice of design is mentioned, but there is little or no discussion of the justification or how potential problems are addressed.



Statement 1.3	The choice of study design is justified		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	• **Comparative studies.** Two systems are compared in these studies – one with the new intervention, and one that does not have the new intervention but is similar in all other respects. This design is often used in areas where randomised trials are impractical or unethical. The main difficulty is in finding two directly comparable locations or systems and eliminating the possibility of confounding. In some studies comparisons may be made between a real location and an economic model. In all such studies use of sensitivity analysis to assess the reliability of results is essential, and such analyses are particularly important where model comparisons have been used. • **Modelling of routine data sets.** For major policy issues, econometric modelling based on data sets such as mortality or health service utilisation can be used to estimate the effect of changes. The general lack of suitable data sets makes this a difficult option to apply in a UK context. • **Secondary economic evaluations.** In these evaluations local data is applied to the results of published studies to produce economic evaluations that can be applied in the local context. The scope for applying such methods is limited by the range of published economic studies. Again, the effective use of sensitivity analysis is an essential part of a well-designed study.	Always applies	**YES** Where the reason why the design was chosen is provided, and comments made on potential weaknesses and how they are addressed. **NO** Where no justification is offered. **CAN'T SAY** Where the choice of design is mentioned, but there is little or no discussion of the justification or how potential problems are addressed.

Statement 1.4	All costs that are relevant from the viewpoint of the study are included and are measured and valued appropriately		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	This is a key aspect of study design. Any study that fails to adequately detail how cost information was obtained or estimated should not be used as evidence. All costs relevant to the study have to be identified, measured, and valued. What constitutes "relevant costs" will depend on the viewpoint of the study. A study looking at the subject from the point of view of the health service, for example, will cover all treatment and related costs. A study taking a societal view will take into account additional costs such as lost working days. Ideally, opportunity costs (i.e. the extent to which an opportunity to use resources for some other purpose has been given up) should be used and not purely financial costs. Costs are defined as any change (either increase or decrease) in resource use as a result of the study intervention, and measured in appropriate units. Realistically, many studies will rely on cost data. Likely sources of such data include the financial systems of service providers, scales of charges for provision of services by the private sector, and published cost studies. All sources of cost data have weaknesses, and a well-conducted study will indicate how possible uncertainties or weaknesses in the data have been addressed.	Always applies	**YES** Where all cost information is detailed along with the source(s) and how any estimates are made. **NO** Where cost information is absent or estimates are presented without justification.



Statement 1.5	The outcome measures used to answer the study question are relevant to that purpose and are measured and valued appropriately		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	This is a key aspect of study design. Any study that fails to adequately detail how outcomes were measured and (where appropriate) valued should not be used as evidence. All outcomes should be explicitly identified and measured, even if they are not the prime focus of the study. If, for example, a comparison of two treatment programmes showed no difference in cost-effectiveness in terms of life years gained between two treatments, measurement of other factors such as long-term pain or quality of life could help choose between them.	Applies in cost-benefit analyses and other cases where costs and outcomes are measured and valued in comparable units	**YES** Where all outcomes are explicitly measured and valued. **NO** Where the basis of measurements and values is not reported. **CAN'T SAY** Where the basis of measurements or values are reported but not discussed (including discussion of any uncertainties) in detail. **NOT APPLICABLE** Where the study design does not require direct comparison of outcomes in comparable units, or where none of the options are dominant (i.e. none is clearly better and cheaper, or worse and more expensive, than the others).

<table>
<tr><td>Statement 1.6</td><td colspan="3">If discounting of future costs and outcomes is necessary, it has been performed correctly</td></tr>
<tr><td></td><td>What does this statement mean?</td><td>When does this statement apply?</td><td>Response:</td></tr>
<tr><td></td><td>In many economic studies some costs or outcomes may not arise at the time of the study, but in the future. A transplant patient, for example, may be able to resume a full life following transplant but will require lifelong drug therapy and periodic follow-up visits to hospital. These future costs and benefits must be taken into account, but should be valued at a lower level than immediate costs and benefits. This is normally done through a process of discounting at a fixed rate per annum. Take the example of the transplant patient, and assume that following surgery he is going to be permanently reliant on drugs that currently cost £20,000 per annum. Assume also that though the actual amount paid each year remains constant, the value of this amount will decline by 6% per annum. We can now calculate how much the drug will cost in each future year, based on present day values.

<table>
<tr><th>Year</th><th>Future value</th><th>Discount factor</th><th>Present value</th></tr>
<tr><td>0</td><td>£20,000</td><td>1</td><td>£20,000</td></tr>
<tr><td>1</td><td>£20,000</td><td>0.943</td><td>£18,860</td></tr>
<tr><td>2</td><td>£20,000</td><td>0.89</td><td>£17,800</td></tr>
<tr><td>3</td><td>£20,000</td><td>0.84</td><td>£16,800</td></tr>
<tr><td>4</td><td>£20,000</td><td>0.793</td><td>£15,860</td></tr>
</table>

The discount factor is calculated by working out the value of £1 less the decrease in value over the year, so in year one it is 1/1.06, in year 2 it is 0.943/1.06, and so on.
Looking at the table, it is clear that working out the cost of the drugs at a fixed rate per annum will give a very different answer to one based on the discounted rate. This is a rather simplified example, but for the purposes of study evaluation it is not necessary to evaluate such calculations in detail – just to be sure that they have been done if the interventions have long-term effects, and that there is some justification for the selected discount rate.</td><td>Applies where there are long-term effects from the intervention being studies</td><td>YES Where discounting has taken place, and the discount rate is reported and justified.
NO Where discounting is appropriate but has not been done.
CAN'T SAY Where discounting has been done, but the rate and/or justification are missing.
NOT APPLICABLE Where discounting is not appropriate/required.</td></tr>
</table>



Statement 1.7	Assumptions are made explicit and a sensitivity analysis has been performed		
	What does this statement mean?	**When does this statement apply?**	**Response:**
	Economic evaluation requires assumptions to be made, but if studies are to be useful to others and comparable with other work the assumptions made must be explicit. **If a study appears to make assumptions that are not identified or explained it should not be used as evidence.** Wherever assumptions have been made, sensitivity analyses should be carried out to see what difference variations in the assumptions would make to the final outcome. Where such analyses are not included in a study, the results should be treated with great caution.	Always applies	**YES** Where all assumptions are explicitly identified and justified, and sensitivity analyses are carried out. **NO** Where there is no discussion of any assumptions that may have been made. **CAN'T SAY** Where assumptions are identified but no justification or sensitivity analysis is included.
Statement 1.8	**The decision rule is made explicit and comparisons are made on the basis of incremental costs and outcomes**		
	The decision rule specifies the basis on which a decision about the intervention will be made – e.g. the most cost-effective option will be selected. The results of an economic evaluation are normally expressed as the additional cost per additional unit of outcome. If the results are presented in some other way, the study may not be a true economic evaluation but a form of cost study. *Note that this information provides a basis for decision-making, but does not represent a decision in itself: the final decision (like the recommendations based on these studies) is likely to be influenced by other factors as well as the economic case.*	Always applies	**YES** Where results are presented in a way that allows for a decision to be made on the basis of differences in cost-per-unit outcome. **NO** Where results are presented in some other way.

Section 2	**Section 2** relates to the overall assessment of the paper. It starts by asking a fundamental question about the nature of the study, and whether it is a true economic evaluation. If the paper is a cost study, it will be of little or no value as a source of evidence for guideline recommendations**.**			
Statement 2.1	**How well was the study conducted?**			
	++	**High quality (++):** Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research.		
	+	**Acceptable (+):** Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies.		
	0	**Low quality (0):** Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.		
Statement 2.2	***The results of this study directly applicable to the patient group targeted by this guideline?***			
	What does this statement mean?		**When does this statement apply?**	**Response:**
	Does this study make sense in the Scottish context? Consider the comparisons made, the context, and whether the costs, valuations, and judgements made in the study can reasonably be extrapolated to the NHS in Scotland.		Always applies	Yes ☐ No ☐
Statement 2.3	**Notes.** Summarise the authors' conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above. This section is very important and will appear on the evidence table. **PLEASE FILL IN.**			

7. TEMPLATES FOR THE PARTICIPANTS

1. SEARCH PROCESS AND RESULTS FORM

- **Name of the Working Group:**
- **Date:**

During the process of identification and collection of studies, this form has to be filled to keep a record of the search process and search results for the critical and important criteria.

TABLE 1: Search process

Search No.	Element of the recommendation	Specific data	Database/ Date accessed	Search terms	Language restriction

TABLE 2: Search result

Search no.	Element of the recommendation	Criteria for inclusion/ exclusion	No. of reviewers	No. of studies identified before screening of titles and abstracts	No. of unique studies identified after screening of titles and abstracts	No. of studies retrieved in full text

TABLE 3: Search outcome

Search no.	Element of the recommendation	No. of studies retrieved in full text	No. of full studies found relevant	Tools used to assess quality of study	No. of studies utilised after assessing quality of evidence

TABLE 4: Rating of studies

Search no.	Element of the recommendation	Journal article	Author	Type of study	Rating tool used	Total score

2. STUDY CHARACTERISTICS SHEET TEMPLATE

Study		
Vaccine		
Objectives		
Study period		
Study site		
Methods		
Participants	Number: Vaccine group: Control group: Inclusion: Exclusion:	
Intervention	1. Vaccine: 2. Comparator: Description:	
Outcomes	**1-** **2-**	
Funding		
Risk of bias	**Assessment**	**Description**
Adequate sequence generation		
Allocation concealment		
Blinding		
Missing output data		
Other bias		

SECTION B

DEVELOPMENT OF AN EVIDENCE-BASED RECOMMENDATION NOTE



FOR
PARTICIPANT

SUMMARY FOR PARTICIPANT

LEARNING OBJECTIVES

- Learn the steps for writing a recommendation note
- Understand the principles for making a judgement from the evidence collected
- Understand the processes of deliberation and decision concerning the proposed recommendation

1. STEPS IN THE DEVELOPMENT OF A RECOMMENDATION NOTE

After the type of evidence needed to issue the recommendation has been identified and the quality of evidence assessed and summarised in a document, the information is then analysed and discussed to provide a recommendation for or against a particular vaccination issue. **The strength of the quality of evidence alone cannot justify a strong recommendation. Other factors need to be considered** besides the quality of evidence.

1.1 ANALYSIS (JUDGEMENT) OF THE BODY OF EVIDENCE

1.1.1 Judgement on the intervention and its outcome(s)

A systematic review of the literature on the intervention's outcome is the driver of an evidence-based recommendation. Considerable resources (time, finance, varied expertise in the team, including in bio-statistics) are utilised in performing a systematic review. NITAGs may instead consider using already available systematic reviews of good quality (WHO, Cochrane Collaboration).

A separate section on systematic review methodology using the GRADE approach is included in Training 4.

Experts may consider the following elements to make a judgement about an intervention's outcomes:

Desirable outcomes	Undesirable outcomes
Reduction in morbid events	Short-term minor side effects
Improved quality of life	Long-term rare serious adverse events
Decreased resource use	Increased resource use
	Inconvenience

1.2.2 Judgement on evidence on the other elements identified in the recommendation framework

These elements will depend on the specific topic being considered for the recommendation. Nevertheless, factors that are likely to be included in the decision-making process are related to the health system and to the environment in which the recommendation will be implemented. Judgement on issues around health system and context will consider the confidence in the evidence of:

- Organisation and leadership
- Infrastructure
- Human and financial resources
- Quality of care
- Quality of data
- Enabling implementation factors: physical, socio-cultural environment, and political



1.2 OUTLINE OF A DRAFT RECOMMENDATION NOTE

1. Executive summary

It is drafted after the finalisation of the recommendation note.

2. Introduction

2.1 Context of the question

Who included the topic in the NITAG agenda?

- Was it included in the annual work plan, suggested by the Ministry of Health or a NITAG member? Further clarification should be enquired if needed,
- If the topic was added to the NITAG agenda per official request from the Ministry, it should be mentioned and the letter should be joined to the report.

Why was the topic added to the agenda?

- Opportunity of introduction of a new vaccine, ongoing epidemic, new data on vaccine efficacy or disease burden?

2.2 General information on the subject

Brief description of the problem identified.

3. Methodology

In developing an evidence-based recommendation, NITAG members should always describe the research process which needs to be transparent and accessible to policy-makers and a wide range of stakeholders who are mostly unfamiliar with the language of research. The methodology section should clarify the following points:

Does the recommendation note employ systematic and transparent methods to identify, select, and assess research evidence?

- Describe the recommendation framework (i.e. the PICO questions on the intervention and other identified elements taken into account).
- Describe how research evidence was identified, selected, and assessed in ways that are easily understood. This objective can be achieved by using techniques such as explanatory 'boxes' within the note to clarify or highlight particular concepts, or through the inclusion of additional appendices. The methods should be systematic in nature and reported in a transparent yet understandable way.

How was the recommendation developed?

- Was a Working Group established?
- How was the discussion organised and the recommendation adopted?
- Was the recommendation note reviewed for both scientific quality and system relevance?

4. Analysis of the evidence

This section will include and discuss:

- The intervention outcomes from systematic reviews (if NITAG performed a systematic review, the summary of the evidence quality assessment should be included in summary tables)
- Health systems and context issues which were taken into account in the recommendation framework. Given that recommendation notes are typically context-specific, a recommendation note would also ideally discuss the evidence on local applicability and equity considerations of the findings

5. Conclusion and recommendation formulation

This section refers back to the evidence of each element of the decision-making framework and the judgement presented in the previous section to draw conclusions on:

- Potential benefits and harms of the intervention compared to the alternative
- Possible options
- Cost and cost-effectiveness of each option
- Implementation of each option: efficiency, local applicability, acceptability (by different stakeholders), equity, feasibility (expertise and human resources available? budget available? timeline for implementation suitable?), potential barriers, sustainability

Recommendation options are clearly formulated and links to the available evidence are well demonstrated. **NB:** Whatever format is chosen, the minimum that a recommendation note should contain is a list of key messages, a report, and a reference list for those who wish to read more. Furthermore, in general, when there are options, it is preferable to present recommendations in favour of a particular management approach rather than against an approach.

The recommended formulations of a recommendation are: "We recommend that"; "Policy-makers should/ should not". The recommendation should avoid wording such as: "We suggest" or "Policy-makers might"

The Canadian National Advisory Committee on Immunisation has the following standard language for the methodology section (Canada Communicable Disease Report January 2009-vol 35 ACS-1)

NACI reviewed the draft work plan of the X Working Group and the key questions for the proposed literature review, including such considerations as the burden of illness of the disease to be prevented and the target population(s), safety, immunogenicity, efficacy, effectiveness of the vaccine(s), vaccine schedules, and other aspects of the overall immunisation strategy.

The knowledge synthesis was performed by <name(s)>, and supervised by the Working Group. Following critical appraisal of individual studies, summary tables with ratings of the quality of the evidence using NACI's methodological hierarchy (Table X) were prepared, and proposed recommendations for vaccine use developed.

The Working Group Chair and PHAC medical specialist presented the evidence and proposed recommendations to NACI on <date(s)>.

Following thorough review of the evidence and consultation at the NACI meetings of <date> and <date>, the committee voted on specific recommendations.
The description of relevant considerations, rationale for specific decisions, and knowledge gaps are described in the text.
The full knowledge synthesis is maintained by the PHAC at the following url:< >. PHAC maintains documentation of these processes throughout knowledge synthesis and recommendation development.

The NACI formulation of recommendations is shown in the table below:

A	NACI concludes that there is **good evidence to recommend** immunisation.
B	NACI concludes that there is **fair evidence to recommend** immunisation.
C	NACI concludes that the existing evidence is **conflicting and does not allow a recommendation to be made for or against** immunisation, however other factors may influence decision-making.
D	NACI concludes that there is **fair evidence to recommend** against immunisation.
E	NACI concludes that there is **good evidence to recommend** against immunisation.
F	NACI concludes that there is **insufficient evidence (in either quantity and/or quality) to make a recommendation**, however other factors may influence decision-making.

2. DELIBERATION AND DECISION CONCERNING THE PROPOSED RECOMMENDATION

The NITAG Working Group/Secretariat presents the proposed recommendations for discussion and deliberation to NITAG members.

The NITAG members should discuss the following:

- What are the options being proposed?
- Are they confident in the evidence supporting these options?
- What are their opinions on the balance between the benefits and harms of each option?
- Does each option fit the organisational (infrastructure, human resource, and organisation of the health system) and socio-environmental context (demographic and geographic patterns)?
- What are the potential barriers (political, financial, logistical, socio-cultural, etc.) to the implementation of each option? What are the potential solutions to these barriers?
- Who are the potential supporters and opponents of each option? Refer to Training 2 for more details on how to deal with potential opponents (patient associations, anti-vaccine lobbies, finance ministries, etc.)

NITAG members should decide which option will be recommended to the government. The decision can be made by vote or consensus according to the NITAG's mode of operation[1].
If no recommendation is issued, the NITAG has to specify the rationale for this decision, this could be:

- Confidence in effect estimates is so low that the NITAG feels that the issue of a recommendation is too speculative
- The trade-offs between benefit and harm are closely balanced, and the values, preferences, and resource implications not known or too variable

(1) Fretheim A, S.H., Oxman AD., Improving the use of research evidence in guideline development: 5. Group processes. Health Res Policy Syst., 2006.4 (17).

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