# **Meeting report**

Consultation on the Development of Guidance on How to Incorporate

the Results of Modelling into WHO Guidelines,

Geneva, Switzerland, 27-29 April 2016



#### WHO/HIS/IER/REK/2017.2

#### © World Health Organization 2017

Some rights reserved. This work is available under the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 IGO licence (CC BY-NC-SA 3.0 IGO; https://creativecommons.org/licenses/by-ncsa/3.0/igo).

Under the terms of this licence, you may copy, redistribute and adapt the work for non-commercial purposes, provided the work is appropriately cited, as indicated below. In any use of this work, there should be no suggestion that WHO endorses any specific organization, products or services. The use of the WHO logo is not permitted. If you adapt the work, then you must license your work under the same or equivalent Creative Commons licence. If you create a translation of this work, you should add the following disclaimer along with the suggested citation: "This translation was not created by the World Health Organization (WHO). WHO is not responsible for the content or accuracy of this translation. The original English edition shall be the binding and authentic edition".

Any mediation relating to dispute arising under the licence shall be conducted in accordance with the mediation rules of the World Intellectual Property Organization.

**Suggested citation.** Consultation on the Development of Guidance on How to Incorporate the Results of Modelling into WHO Guidelines. Geneva: World Health Organization; 2017 (WHO/HIS/IER/REK/2017.2). Licence: CC BY NC-SA 3.0 IGO

Cataloguing-in-Publication (CIP) data. CIP data are available at http://apps.who.int/iris.

**Sales, rights and licensing.** To purchase WHO publications, see http://apps.who.int/bookorders. To submit requests for commercial use and queries on rights and licensing, see http://www.who.int/about/licensing.

**Third-party materials.** If you wish to reuse material from this work that is attributed to a third party, such as tables, figures or images, it is your responsibility to determine whether permission is needed for that reuse and to obtain permission from the copyright holder. The risk of claims resulting from infringement of any third-party-owned component in the work rests solely with the user.

**General disclaimers.** The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by WHO in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by WHO to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility or the interpretation and use of the material lies with the reader.

In no event shall WHO be liable for damages arising from its use.

## **Table of Contents**

2.   3.	- Meeting objectives	
<b>3</b> .		
	Participants	
<b>1.</b> :	Scope and aims of the meeting	
5. node	Guideline development at WHO and the need for guidance on the use of mathem elling	ati
5.	Review of mathematical modelling	
7.	Internet-based expert survey	
3.	Surveys of the use of mathematical modelling in WHO and other guidelines	
<b>)</b> .	Examples of the use of mathematical modelling in WHO guidelines	••••
LO.	Guidelines for Accurate and Transparent Health Estimates Reporting	••••
L1.	Assessing quality and risk of bias in mathematical modelling studies	••••
L2.	Breakout session	
L3.	Overview of GRADE and key terms and definitions	••••
L4. cervi	Examples of the use of modelling in GRADE: treatment of MDR-TB, screening for cal pre-cancer	)r
L5.	Screening for aneurysms to prevent subarachnoid haemorrhage	••••
L6.	Antiretroviral combination therapy to reduce HIV transmission	••••
L7.	Final discussion and summary conclusions	••••
L8.	Next steps	••••
L9.	References	••••
Anne	x 1. Meeting Agenda	
ultati Guic	on on the development of guidance on how to incorporate the results of modelling delines	; in 
- 29	April 2016, Large Library Meeting Room, World Health Organization, Avenue Appia	20

#### Acknowledgements

The GRC Secretariat is grateful to Professors Helen Ward and Tom Trikalinos who chaired this consultation in Geneva, Switzerland on 26-29 April 2016, and to all who participated in the meeting. Ms Myriam Felber kindly provided technical assistance at the meeting and in the preparation of this report.

#### Funding

The work reported in this article and the meeting in Geneva was funded by the UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (WHO/TDR).

The consultation took place at World Health Organization headquarters, Avenue Appia 20, Geneva, Switzerland on 26-29 April 2017 and was chaired by **Professors Helen Ward**, Imperial College London, UK and **Thomas Trikalinos**, Brown University, Providence, USA. The agenda of the meeting is found in the Annex.

#### 1. Background

WHO guidelines cover a wide range of public health, health system and clinical topics and are developed using processes and methods to ensure they are of high-quality and contain credible recommendations. Increasingly WHO staff are faced with decisions regarding whether to include the results of modelling in the evidence base used to inform recommendations, and if so, how to evaluate the results of models and to integrate those results with primary data to inform a recommendation. Currently there are no widely agreed-upon methods for accomplishing this, either at WHO or in the international community of guideline developers.

Modelling studies are increasingly performed to address questions about the effectiveness of interventions for specific population groups and settings, which differ from the carefully controlled conditions in which randomized controlled trials (RCTs) are typically conducted. Modelling studies are also used to assess long term outcomes and to bridge the gap between efficacy and (long-term) effectiveness, thus obtaining "real world evidence" (1-4). Mathematical modelling is relevant to infections for which population-level effects such as herd immunity are not captured by trials of individuals, and to assess the epidemic potential of new outbreaks (5, 6). Modelling may also be useful in the context of prioritising and planning clinical trials (7). Finally, mathematical modelling has been used in economic evaluations of clinical and public health interventions (5). The WHO Handbook for Guideline Development (8) recognizes the role of modelling in economic evaluations that inform recommendations and mathematical modelling studies have been incorporated into WHO guidelines.

This consultation was part of a project funded by WHO to develop technical guidance on if, when and how to incorporate the results of modelling into WHO guidelines and to develop training materials for WHO staff and for members of WHO-sponsored guideline panels.

### 2. Meeting objectives

The objectives of the consultation were to develop general guidance for WHO staff who are not experts in modelling on if, when and how to consider and integrate the results of mathematical modelling into the body of evidence upon which recommendations in WHO guidelines are based. Specifically:

- When it is appropriate to consider modelling studies as part of the evidence that supports a guideline?
- How should the quality and risk of bias in mathematical modelling studies be assessed?
- Can the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach be adapted to assess the quality of a body of evidence and for formulating recommendations to include the results of modelling?

## 3. Participants

The following people participated in the consultation at WHO headquarters in Geneva:

Name	Affiliation	Country	Remarks	
Tom Trikalinos	Brown University	USA	Chair	
Helen Ward	Imperial College London	United Kingdom	Chair	
Christian Althaus	University of Bern	Switzerland		
Patrick Bossuyt	University of Amsterdam	The Netherlands	28-29 April only	
Matthias Egger	University of Bern	Switzerland		
David Fisman	University of Toronto	Canada		
Gordon Guyatt	McMaster University	Canada		
Tim Hallett	Imperial College London	United Kingdom		
Mark Helfand	Oregon Health & Science University	USA		
Rodney Jackson	University of Auckland	New Zealand		
Leigh Johnson	University of Cape Town	South Africa		
Nicola Low	University of Bern	Switzerland		
Veena Manja	McMaster University	Canada		
Georgia Salanti	University of Bern	Switzerland		
Anna Schöni	University of Bern	Switzerland		
Holger Schünemann	McMaster University	Canada		
Julie Ann Simpson	University of Melbourne	Australia		
Christopher Dye	World Health Organization	Switzerland	27 April only	
Philippa Easterbrook	World Health Organization	Switzerland	29 April only	
Nathan Ford	World Health Organization	Switzerland		
Daniel Hogan	World Health Organization	Switzerland		
Susan Norris	World Health Organization	Switzerland		
Gretchen Stevens	World Health Organization	Switzerland		

This meeting report summarizes the presentations made at the meeting and the discussions that followed. Some key slides shown at the meeting are reproduced in the report, the slides for each presentation, and other key documents are available via the hyperlinks in the text.

## Wednesday 27 April 2016

#### 4. Scope and aims of the meeting

**CHRISTOPHER DYE**, Director of Strategy, Office of the Director-General welcomed everyone to the meeting on behalf of Margaret Chan, Director General and stressed the importance of this consultation. After a round of introductions and the review of declarations of interest and code of conduct for WHO experts, **SUSAN NORRIS** (<u>slides</u>) summarized the scope and aims of the meeting: to develop guidance for WHO staff on: (i) when it is appropriate to consider modelling studies as part of the evidence that supports a guideline; (ii) how to assess the quality and risk of bias in mathematical modelling studies; and (iii) how to adapt the GRADE approach for assessing the quality of a body of evidence and for formulating recommendations to include the results of modelling. The project output will be a guidance document for WHO staff, which will address the points listed in **Figure 1**.

Figure 1 - Project output: Guidance document for WHO staff

- Background
  Scope, purpose, objectives
  Definitions: types of models, key terms related to modelling
  Types of questions that can be answered with modelling and where modelling is not indicated
   Principles underlying high-quality models
   Assessing the quality of individual models: model calibration and validation
   Optimal reporting of models
   Limitations of models
   How to incorporate the results of models into GRADE for assessing quality (certainty) of evidence
  - 10. Results of models and the formulation of recommendations

# 5. Guideline development at WHO and the need for guidance on the use of mathematical modelling

**SUSAN NORRIS** (<u>slides</u>) gave an overview of WHO and of **guideline development at WHO**. The primary role of WHO is to direct and coordinate international health within the UN system, and provide guidance in the areas of: (i) health systems; (ii) promoting health through the life course; (iii) non-communicable diseases; (iv) communicable diseases; and (v) preparedness, surveillance and response.

A WHO guideline is defined as "any document, whatever its title, that contains WHO recommendations about health interventions, whether they be clinical, public health or policy interventions."

A recommendation "provides information about what policy makers, health care providers or patients should do. It implies a choice between different interventions that have an impact on health and that have ramifications for the use of resources."

Following the article of Oxman et al. in 2007 (9) on the use of evidence in WHO guidelines which concluded that WHO guidelines relied heavily on expert opinion and that systematic reviews were rarely used for developing recommendations, a standard process for guideline development at WHO was put in place. The WHO Guidelines Review Committee (GRC) was established to develop and implement procedures to ensure that WHO guidelines are consistent with internationally accepted best practices, appropriately based on evidence and transparent. The WHO Handbook for Guidelines was revised (link) and standards for guideline development were implemented, including a process for development and approval and reporting of evidence and recommendations. This 9-step process includes: (1) formulation of a clear definition of scope and target audience; (2) setting up a broad and representative guideline development group; (3) declaration of interests and management of conflicts of interests; (4) development of key questions for systematic reviews using PICO format (Patients, Intervention, Comparison, Outcome); (5) conduct of one or more systematic reviews, and quality assessment and synthesis of the body of evidence for each question; (6) formulation of recommendations based on the evidence and other explicit considerations; (7)

development of a plan for implementation and updating; (8) impact evaluation; and (9) updating (**Figure 2**).



**Figure 2** – Guideline development at WHO (8)

GRADE, Grading of Recommendations Assessment, Development and Evaluation GRC, Guidelines Review Committee

WHO guidelines use the GRADE approach which provides an explicit approach to assessing the quality of the evidence across studies and outcomes, and translating evidence to recommendations. The members of the Guideline Development Group (GDG) formulate recommendations and approve the final guideline. They are supported by the WHO Steering

## 预览已结束,完整报告链接和二维码如下:



https://www.yunbaogao.cn/report/index/report?reportId=5 27027