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MaHTAS
Malaysian Health Technology Assessment Section

Kami Sedia Membantu
KEMENTERIAN KESIHATAN MALAYSIA

MANUAL ON DEVELOPMENT AND IMPLEMENTATION OF EVIDENCE-BASED CLINICAL PRACTICE GUIDELINES

FOREWORD
BY DIRECTOR GENERAL OF HEALTH MALAYSIA

Clinical practice guidelines (CPG) development has always been a collaborative effort between the Ministry of Health and the Academy of Medicine Malaysia, and it is my sincere hope that this endeavour will be brought to greater heights in the future.

To improve the quality of clinical practice we must provide medical professionals with tools that they need to do their job and make the best decisions in each case. Hence, CPG is one of the means that helps to minimise inappropriate variation in clinical practice and to improve the effectiveness, efficiency and safety of clinical decisions.

The previous manual launched in 2003, introduced and briefly captured the necessary steps to develop an evidence-based CPG. Updating this manual is timely aid to further improve methodologically the quality of the evidence-based CPG, its dissemination and implementation strategies.

It is my fervent hope that this manual will greatly assist all those involved in the development and implementation of an evidence-based CPG towards delivering high quality healthcare to the community. I would like congratulate the Malaysian Health Technology Assessments Section (MaHTAS), Medical Development Division for their effort in developing this manual.

DATUK DR NOOR HISHAM ABDULLAH
DIRECTOR GENERAL OF HEALTH MALAYSIA

PREFACE

This Manual on Development and Implementation of Evidence-based Clinical Practice Guidelines by Ministry of Health (MoH) Malaysia is an update to the Guidelines for Clinical Practice Guidelines 2003.[1] The manual outlines the key elements of development and implementation process used in all CPGs developed by MaHTAS. It is also useful for any CPG developers and implementers in the country. The decision to include both development and implementation aspects of a CPG reflects that both process are heavily interdependent.[2]

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1. INTRODUCTION

Aims of Chapter:

- to introduce the definition of Clinical Practice Guidelines (CPG)
- to describe the role CPG in improving health care
- to provide background of CPG development in Malaysia

CPG has been **defined** as statements that include recommendations intended to optimise patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options.[3] The statements are developed systematically to assist practitioner's and patient's decisions about appropriate healthcare for specific clinical circumstances.[4] CPG is designed to help the healthcare professionals managing patients (clinical decision making) in an appropriate and effective way based on the best and current available evidence. This is especially so when variation of practice and inefficient use of resources exist in a particular clinical issue. In addition, CPG can play an important role in health policy formation and have evolved to cover topics across the healthcare continuum such as health promotion, screening, diagnosis, treatment and prevention. The ultimate aim of CPG development is to improve the quality of healthcare. Thus, CPG developers need to understand factors that promote the usability of the CPG to optimise their impact in clinical practice.

CPG is a decision tool to close gaps between current and best practice.[5] It is one of the elements of good medical decision making which take account of clinicians' values and experiences, patients' values and preferences, and availability of resources. CPG development, implementation and review should be seen not as linear process, but cycles of interdependent activities which complement each other (refer to **Figure 1**). The research circle produces evidence of different levels to be used as the basis of evidence-based CPG development. On the other hand, the practice circle implements recommendations stipulated in the CPG. This translates evidence into practice which will be monitored through standards and eventually promotes clinical excellence.[2] The effectiveness of each recommendations performed in any healthcare setting can be evaluated and improvised through further research. In short, CPG acts a bridge between research and clinical domains.

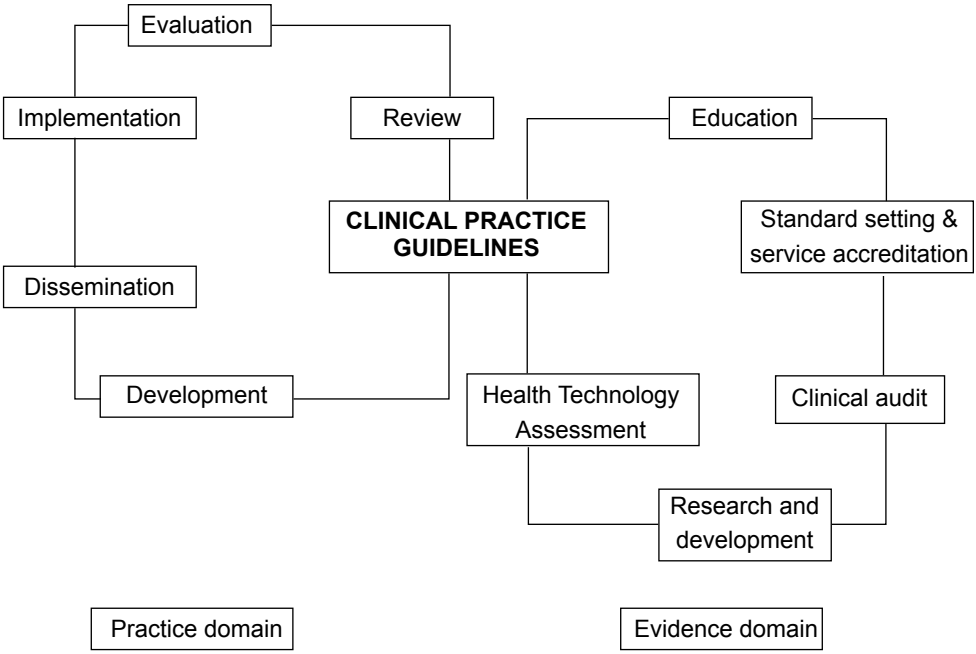

Figure 1. CPG bridging evidence and practice domains

Modified: Scottish Intercollegiate Guidelines Network. SIGN 50 A guideline developer's handbook. Edinburgh: SIGN; 2008

Traditionally, guidelines are developed using experts' consensus methodology. They are easy to be developed but lack in supporting evidence that may lead to biased conclusions. They also lack in the involvement of target user (perspectives of stakeholders) in their development. Expert opinion does not always reflect the state of current knowledge. There is now growing recognition that CPG should be based on best available scientific evidence. Thus, MaHTAS only develops evidence-based CPG using a standard systematic review methodology. The methodology used by MaHTAS is consistent with other international guidelines developers as reported by World Health Organization (WHO) Contractual Partner in her **Technical Report 2007**.[6]

The Academy of Medicine of Malaysia started to develop guidelines since 1992. In April 2001, CPG development came under purview of MaHTAS and has since then been coordinated by the CPG Unit of MaHTAS. The unit acts as a secretariat of CPG development under MoH as well as providing methodological

advice in the development of such documents to all guideline developers in the country. The CPGs produced by MaHTAS are evidence-based and involve multidisciplinary development groups (DG). It is relevant to clinicians, clinical support staffs, academicians, public health personnel as well as the patients and their carers. The CPGs will be reviewed at various levels of stakeholders before they are finally endorsed and disseminated. In 2008, MaHTAS started to develop implementation strategies such as quick reference (QR), training module and patient information leaflet. Since the inception of the CPG programme, the CPG and the QR are printed by the MoH and disseminated free to target users mainly from MoH healthcare facilities. In some instances, development of CPG and the relevant documents are done together with other divisions in the MoH and professional body. The CPG still need to be endorsed by MoH before they are listed as national evidence-based CPG.

In Malaysia, CPGs are developed by MaHTAS, professional societies and Oral Health Division. The topic of CPG developed by MaHTAS will be determined by the CPG Technical Advisory Committee (TAC) while the professional societies have the liberty of developing CPG of their interest. MaHTAS will brief the work process of CPG development and implementation to the latter on their request and assist them wherever possible after that. Ensuring the quality of such critically important process before the CPG endorsed by Health Technology Assessment (HTA) and CPG Council poses a challenge to MaHTAS.

2. PRINCIPLES OF CPG

Aims of Chapter:

- to describe the principles of CPG development and implementation

2.1 Definition

CPG is defined as statements that include recommendations intended to optimise patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options.[3]

2.2 Goal

The goal of a CPG is to improve the quality of care. The CPG is intended as an aid to clinical judgement and not to replace it. The ultimate decision on clinical management will depend on the individual patient's condition, local circumstances, patient's choices and the clinical judgement of the healthcare team involved. The CPG should allow healthcare providers and patients to use their own judgement when choosing from the available options.[1]

2.3 Evidence-based CPG

An evidence-based CPG should indicate the methodology in obtaining the evidence, strength of the evidence and the specific evidence upon which a conclusion (recommendation) is formulated. In some important clinical issues where evidence is limited, the recommendation may be made based on expert opinion. This should also be indicated for potential users aware that it represents current best practice. All ethical issues should be considered in drawing up the CPG.[1]

There **three key elements in the methodology** of an evidence-based CPG are:[7]

a. development should be carried out by a multidisciplinary group
b. systematic review should be conducted to identify scientific evidence
c. recommendation formulated should be explicitly linked to the supporting evidence and graded according to the strength of the evidence

2.4 Informed Decision Making

Using the CPG, the healthcare providers and patients will be able to perform informed decision-making through education and communication. This can reduce or avoid inappropriate decision making.[1]

A good CPG changes healthcare process, improves patients outcomes and ensures efficient use of healthcare resources. It can be used to further develop standard for healthcare, educate healthcare professionals and help in shared decision-making between patients and healthcare professionals.[8] Guidelines that have recommendations based on evidence are considered to be of greater value to practitioners and consumers because the decisions are likely to result in improved consumer outcomes. They are more used than those that were not.[9]

2.5 Attributes

CPG should be valid, clear, reliable and reproducible. It should also be clinically applicable, flexible with multidisciplinary involvement. The development process and scheduled review should be clearly documented.[1]

A CPG is not intended to be a “menu-driven’ or “cook book” where the healthcare provider does not use discretion in managing the patient. It is also not a medical textbook that provide in-depth background clinical knowledge of a health problem. However, the development of a CPG is a rigorous process requiring extensive expertise and resources to ensure a high-quality outcome. Thus, resource requirements needed to carry out a CPG development and implementation should be considered as an investment.[10]

For a CPG to be well accepted and adopted to the intended users, they should play a part in both the conception and development of the document. The recommendations in the CPG should be formulated on the best available evidence in well-designed research. In doing so, not only the effectiveness aspect should be considered, but also the harm, cost and other relevant aspects should be taken into account.

3. CPG GOVERNANCE FRAMEWORK

Aim of Chapter:

- to describe the organisational structure of CPG Programme in MoH Malaysia

The process of developing CPG should include participation by representatives of key groups and affected disciplines.[2] Diversity is an essential feature of a multidisciplinary guideline team in order to ensure all management aspects of a health condition are being covered in the CPG.[5] The **multidisciplinary composition** will also facilitate ownership of both the CPG development process and the resulting recommendations.[11] The relevant stakeholders can involve in different stages of CPG development but remains as collaborative network in the CPG Programme.

There are four levels in the organisational structure of CPG Programme in MoH (refer to **Figure 2**). MaHTAS acts as the secretariat in the meetings and discussions at all levels.

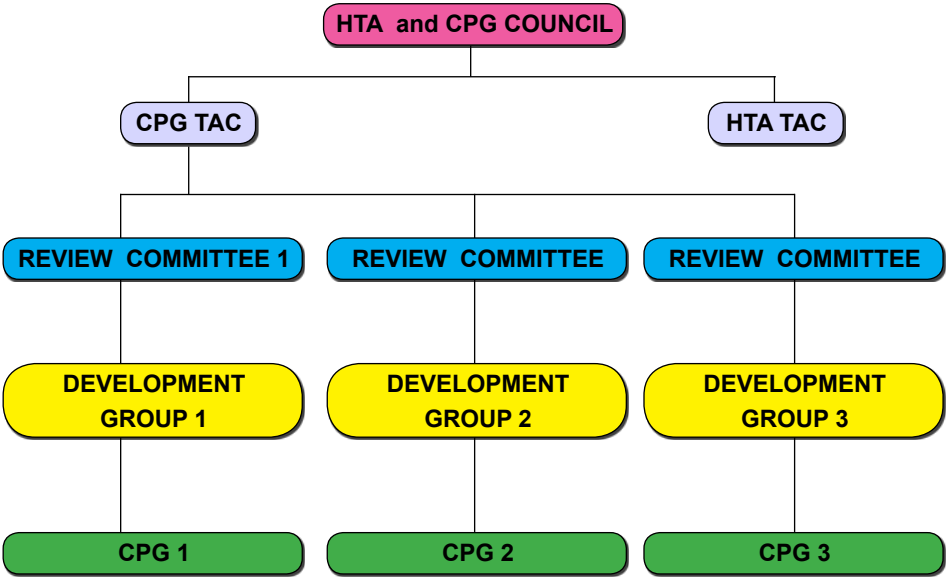

Figure 2. Organisational structure of CPG Programme in MoH

3.1 CPG Development Group*

CPG DG is the working group of a CPG. It is set up specifically for each CPG topic and the members are essentially multidisciplinary in nature. Geographical representative may be considered. The chairman of new CPG is normally chosen by the relevant National Head of Clinical Service while the former chairman may continue to be the chairman for a revised (new edition) CPG. The chairman of a CPG has the liberty to select other members of the DG with the advice from MaHTAS. The primary role of the chairman is to facilitate discussion and consensus. The person should have general knowledge of the topic but does not need to be a topic expert to avoid preconceived opinion/ bias.[12] The DG is responsible for constructing the CPG i.e. from setting up the protocol/clinical questions to preparing the final draft of the CPG. These are done according to the systematic review methodology and guided by MaHTAS. The group will also have to develop suggested implementation strategies such as a QR, a training module and a patient information leaflet. Refer to **Appendix 1** on Terms of Reference (TOR) for DG.

3.2 CPG Review Committee*

CPG Review Committee (RC) comprises of (senior) consultants in public healthcare facilities, private consultants, patients/carers/non-governmental organisation members and other relevant stakeholders from different discipline and experience background. The members of RC will assist the DG by providing technical input and expert guidance throughout the development of CPG. Refer to **Appendix 2** on TOR for RC.

*All members of DG and RC will have to fill up the Agreement of Appointment **(PTK-BOR-04)** form and **Disclosure (Declaration of Interest) form** (refer to **Appendix 3**). The tenure of DG and RC is throughout the development of CPG and its implementation strategies. The DG and RC meet three times i.e. during presentation of CPG protocol, summary of evidence and CPG draft.

3.3 CPG TAC[1]

The CPG TAC is an 11-member multidisciplinary committee that oversees the running of CPG Programme. The members are nominated by National Head of Clinical Services or Head of Programme and appointed by Deputy Director-General of Health (Medical) for a 2-year tenure. They provide technical input on matters relating to CPG including its implementation and thus determine the overall direction of CPG Programme. Other important task of the TAC is evaluating methodological quality of evidence-based CPGs according to Appraisal of Guidelines Research and Evaluation (AGREE) II criteria. Once

accepted by the TAC, a CPG can be presented to the HTA and CPG Council for final approval. The CPG TAC also conducts prioritisation exercise for new CPG topics for MaHTAS every two years.

3.4 HTA and CPG Council[1]

The HTA and CPG Council is chaired by the Director-General of Health Malaysia and is made up high ranking officers in MoH and representatives from the main universities, Academy of Medicine and relevant societies. Members are appointed by post in the MoH or nominated by the university or society. The Council is the highest level in hierarchy of the CPG organisational structure and has overall responsibility in both the HTA and CPG Programme in the country. The Council is responsible for endorsement of newly-developed (including new edition) CPG which will be listed as national evidence-based CPG. Only after this will the CPG be printed and distributed to the healthcare facilities and posted in the websites of MoH and Academy of medicine.

4. CPG WORK PROCESS

Aim of Chapter:

- to give an overview of CPG work process
- to describe in details each step of CPG development by MaHTAS

Development of CPG involves several steps that can each be conducted with different degree of rigor,[12] with resource constraints taken into consideration.[13] Other guiding principles on CPG development include planning the dissemination and implementation, evaluating its usefulness and impact, and updating it regularly.[5]

The extent to which a CPG may improve health outcomes depends on the quality of evidence it uses and effectiveness of its implementation. To achieve the latter, the CPG should not be a stand-alone document but rather incorporated fully in the healthcare system such as quality assurance activities. It is a great challenge to develop a system that can support the development, implementation and evaluation of CPG as part of mainstream healthcare delivery.[13]

Challenges in CPG development and implementation include:[10]

- variation in definition of "quality of care" by different stakeholders
- complexity of clinical practice to be captured in CPG
- difficulty in translating research results into daily practice
- difficulty in implementing a CPG
- resource constraint in updating a CPG

MaHTAS has outlined **12-steps work process** in its CPG development which are:

1. Define CPG topic
2. Develop DG/RC and CPG protocol
3. Determine mode of formulation of CPG
4. Retrieve evidence
5. Critically appraise evidence
6. Analysis and synthesis of evidence
7. Write CPG draft
8. Review CPG draft by peer/external reviewers, TAC CPG, and HTA and CPG Council
9. Disseminate CPG
10. Develop implementation strategies
11. Monitor and evaluate CPG
12. Update CPG

The work process can be illustrated in **Figure 3** below:-

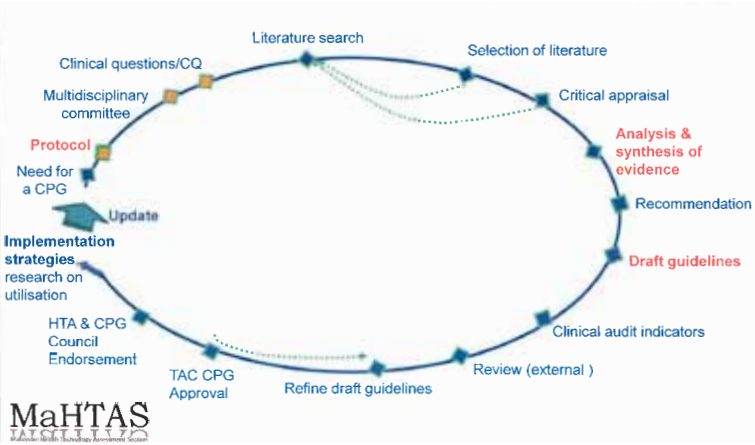

Figure 3. Work process of CPG development and implementation of MaHTAS

The red-coloured steps are where the meeting between DG and RC are conducted. Each 12 steps in the work process will be further elaborated in the following sections. The duration of CPG development varies depending on whether it is a new project, full update or minor revision. TAC CPG states that it should **not be more than two years**.

The CPG methodology should be transparent that the potential biases of its development have been adequately addressed and the recommendations are valid internally and externally, and feasible for practice.[2, 5] A clear description of the development process should accompany all CPG, either within the CPG or in a separate, referenced document.[12] The CPG methodology has evolved significantly worldwide and MaHTAS has tried to improve its CPG development so as to be consistent with international standard taking into consideration of local context. It is based on internationally acceptable criteria of quality, as detailed in the AGREE II instrument.

4.1 Selection of Topics

A CPG should address specific healthcare needs to improve quality of patient care or demonstrate significant changes in outcomes. This is supported by robust evidence (valid scientific studies) of effective practice on which its recommendations is based.[2, 5] Due to limited resources, selection of appropriate topics for CPG development is crucial.[2, 11]

New topics of CPG to be developed are requested by MaHTAS through a biennial formal invitation to the National Heads of Clinical Services, Master of Academy of Medicine and Deans of Medical Faculty. The request form (**PTK-BOR-03 Pin. 1/2009**), which is available online (http://www.moh.gov.my/), has to be filled in by the CPG requestor. It consists of:

- summary of clinical problem and outcome
- brief background on clinical topic to be addressed
- evidence of variation in practice
- likely benefits of developing and implementing the CPG
- size and strength of evidence on the topic (citing key references)
- aspects of management of the clinical condition to be focused on
- any related existing guidelines or protocols

Topic selection (suitability screening) is performed to ensure that investing in a CPG for a particular topic would be worthwhile.[5] As MaHTAS has limited resources in CPG development, proposed CPG topics received following the above requests are **prioritised** by the TAC CPG members. These are done on the basis of the following weighted criteria:

- burden of disease
- variation in practice
- resource impact
  - cost impact on health service
  - cost-effectiveness
  - effective treatment proven and mortality or morbidity can be reduced
  - likelihood that change can be implemented and measured in health outcomes, practice, prescribing patterns, number of procedures or interventions, or changes in resource utilisation/cost
- timeliness or urgency for CPG to be produced
- supporting evidence

Informal requests for CPG development are also received from time to time. If the requesters want MaHTAS to coordinate their project, their requests will undergo similar prioritisation process together with the formal requests. Currently, only three new CPG topics will be developed by MaHTAS each year. Thus, the six highest ranking of new topics in the prioritization will be taken in for CPG development by MaHTAS. The results of the prioritisation exercise will be made known to all requesters. The selected new topics will be presented to HTA-CPG Council for their acknowledgement.

New topics that fail to be in the top six rankings can either be developed by the requester (with the professional societies) or resend for the next round of prioritisation. Any society that wishes to develop a CPG on its own are advised to acknowledge MaHTAS about it for monitoring purpose. The societies should allow MaHTAS to brief them on the CPG work process and to consult for advices during their CPG development from time to time.

4.2 Preparation

i. Appointment of CPG Development Group and Review Committee

A guidelines development panel should include diverse and relevant stakeholders.[12] When a topic of a CPG has been selected, DG and RC will be set up. Convening an effective DG is one of the most important stages in producing a CPG.[8] The DG is the **working group** who help to draw up the CPG whereas the RC provides technical input in relation to the CPG. Members are multidisciplinary in nature and the exact composition of the teams should be tailored to the topic covered by the CPG.[2, 5, 8, 12, 13] They may consists of relevant stakeholders such as:

- healthcare providers from various disciplines (including primary care, pharmacy, allied health), public/academic/private healthcare institutions and all sectors/geographical locations
- public health specialists/programme managers/experts in research methodology (biostatician, health economists, etc.)
- representatives of professional groups e.g. Academy of Medicine/ professional societies
- patients and/or carers

Establishing **multidisciplinary** DG and RC is important to ensure that:[2, 5, 8, 13]

- all relevant groups are represented and will be able to provide expertise from all stages in the patient's journey of care
- all relevant scientific evidence will be located and critically evaluated
- practical problems with using the CPG will be identified and well-addressed
- credibility of the CPG is seen by relevant stakeholder groups and their ownership of the document will help in the CPG implementation

Chairman will be identified in both DG and RC to lead a CPG development and implementation. The role of a chairman is crucial to ensure that the group functions effectively and achieves its aims. The chairman helps the DG to work collaboratively, ensuring a balanced contribution from all members.[8] Members of the DG and RC in turn should give full commitment in accomplishing the tasks

given to them and be responsible to indicate areas of concern to the chairman. All members of DG and RC should also bear in mind that they represent a specialty/profession or stakeholder group. Thus they must be prepared to consult with their fraternity to ensure that the widest possible range of views is being considered in the CPG development. The chairman should ensure that each DG member is able to present his/her views and that the discussions are open and constructive. New member may be recruited in the CPG development if this is deemed very necessary. DG members need to make collective decisions throughout the development of a CPG. In most cases, this is done through a process of informal consensus. However, people who are not DG members but who have relevant expertise may be asked to attend CPG development meetings to take part in specific discussions.[8]

A letter of appointment as members of DG and RC will be sent to the selected members together with TOR (refer to **Appendix 1 and 2)** and agreement of appointment form/**PTK–BOR–04**. As emphasised earlier, declaration of competing interests/conflicts of interest will have to be done by all members in a written statement[2, 5, 8, 13] using a format as shown in **Appendix 3**. This is important as it describes funding, sponsorship, employment relationships and memberships or affiliations that may be perceived to have had some influence on CPG development especially in the recommendations.[5] Those who hold significant share or position in a pharmaceutical firm should not be members of the groups.

ii. Training of DG and briefing to RC

Members of the DG will be provided with training and support in some technical areas of CPG development so that they can carry out their role effectively. The official and annual training is called Systematic Review on Evidence-based CPG Development and Implementation. It consists of lectures and practical sessions and covers topics on CPG work process, literature search, critical appraisal, AGREE II instrument, analysis and synthesis of evidence, and implementation strategies. Relevant articles and CPGs related to the CPG topic to be developed are used in the training. As for the RC, they will be briefed on the CPG work process in the first meeting with DG.

iii. Development of CPG protocol/clinical questions

Preparing the scope is the first step in developing a CPG as it determines the shape of the review work.[8] Prior to the start of a CPG project, a **protocol** will be developed to describe the scope of the CPG. The protocol statements are mainly developed in a consensus manner and were often multidisciplinary in nature.[5]

It gives an overview and framework of what the CPG will include, and what will not be covered. Thus, it provides information to healthcare professionals, stakeholders and the public about the expected content of the CPG.[8] They consists of the title of the CPG ,objectives, target users and population, and also clinical questions covered in the CPG. It will also explain the methodology of the CPG development, proposed clinical audit indicators for quality management and disclosure conflict of interest. Deciding on the clinical questions is entirely the responsibility of the DG.[11]

The CPG protocol is prepared using format **PTK-FM-03** (refer to **Appendix 4**) by MaHTAS initially. It will then be discussed among the DG and then presented to the RC in the first meeting between them. This is mainly to ensure that clinical issues identified by the DG are relevant and appropriate. The DG will finalise the protocol based on the comments received. Both the DG and RC have to agree to the final protocol before work on the CPG can be started. The clinical questions are formulated based on the clinical issues addressed in the protocol. These questions must be clear, focused and closely define the boundaries of the CPG topic. They are important both as the starting point for the systematic literature review and as a guide for the development of recommendations by the DG.[2, 8] The exact number of clinical questions for each CPG depends on the topic and the breadth of the scope. However, the number of clinical questions should be manageable for the DG and within the agreed timescale for CPG completion. Usually, a total of between 15 and 20 clinical questions is considered a reasonable number.

4.3 Mode of Development and Appraisal of Guidelines Research and Evaluation II

One way to achieve consistent, appropriate and high quality healthcare within available resources is via development and implementation of CPG. However, the benefits and successful uptake of CPG are only as good as the quality of CPG themselves.[14]

The quality of CPG is defined as the confidence that potential biases of their development have been addressed adequately and that recommendations are both internally and externally valid, and feasible for practice. They can be evaluated through:[14]

- methods used to develop the CPG
- content of the final recommendations
- factors linked to the CPG uptake

In the mid-90s, there was a need to establish an international methodology of conducting CPG. This led to the development of AGREE II instrument in 2001 which were later published in 2003. This validated instrument is a generic tool designed primarily to help CPG developers and users assess the methodological quality of the document. It addresses issue of variability in CPG quality specifically its methodological rigour and transparency. Many DGs use the AGREE II instrument, with or without modification, as the major screening source for selection of CPG. However, it does not assess clinical content, quality of supporting evidence or impact on patients' outcomes of a CPG. It can be used by healthcare providers, CPG developers, policy makers and educators for slightly different purposes.[15] AGREE project has led to the development of Guidelines International Network (G-I-N) in 2002. It has a mission to lead, strengthen and support collaboration and work within the guideline development, adaptation and implementation community.[16] MaHTAS is a member of G-I-N since 2004.

Before applying AGREE II, an appraiser should:

- read the CPG carefully and in full
- identify all information about the CPG development process

This is because the relevant information may be contained in a separate document. It is recommended that the assessment is done by at least two appraisers but preferably four to increase its reliability.[17]

The original AGREE instrument has been refined and resulted in the development of AGREE II. The new instrument guides on what and how information should be reported in the CPG and changes in terms, renumbering and deleted/included item. In summary, AGREE II contains 23 key items which are categorised in six domains (capturing a separate dimension of CPG quality) i.e.:[17]

- Scope and purpose
- Stakeholder involvement
- Rigour of development
- Clarity and presentation
- Applicability
- Editorial independence

Each item is scored on a 7-point Likert scale based on criteria and considerations. There are also two global rating assessments (overall quality and recommendation) at the end of the assessment. Domain scores are calculated by summing up all scores of individual items in a domain and standardised

the total as a percentage of the maximum possible score for that domain. The overall assessment requires the appraisers to make a subjective judgement on the quality of the CPG and decide as to whether or not to use/recommend a CPG.[17] MaHTAS uses AGREE mainly for:

- assessment of relevant CPG for references prior to embarking into a new CPG project
- self-assessment (checklist tool) during and after development of a new CPG project so that the quality of CPG is ensured
- assessment by TAC CPG prior to the CPG being presented to the HTA and CPG Council

Refer to **Appendix 9** for related AGREE II instrument (**PTK-FM-04 Pin.1/2015**). The methodology in CPG development of MaHTAS **complies with the criteria used by AGREE II**.

Sometimes, DG faces a choice between adopting/adapting an existing CPG or creating a new one. De novo production of high quality evidence-based CPG requires a lot of resources in terms of experienced personals, long working hours and others. Apart from de novo development, a CPG can be developed using adaptation methodology. Unnecessary duplication of effort could be avoided if existing guidelines were adapted rather than developed de novo. Adaptation can be achieved through a scientific process for the customisation of high quality evidence-based CPGs.[18] The recommendations in a CPG may be used although there are differences in cultural and organisational aspects between two or more guideline developers including those from different countries.

Adaptation is **defined** as a systematic approach to considering the endorsement or modification of guidelines produced in one setting for application and implementation in another. In doing so, modifications are allowed. It may range from minor alterations (e.g. translation of a guideline from the original language to the language of the user or adapting a guidelines format) to the creation of a customised guideline (e.g. built on recommendations pulled from a number of guidelines with each recommendation modified to fit the context of the users). One or more guidelines can be adapted at one time. The two key elements in the adaptation process are:[19]

- transparent and explicitness in process (sufficient detail in methodology)
- appropriate referencing and acknowledgment to source documents

There are three main phases in CPG adaptation:[19]

- Set-up Phase – Identify necessary resources and skills, with timeline of adaptation work
- Adaptation Phase – Assessing existing guidelines in terms of quality, currency, content, consistency, acceptability and applicability with eventual decision on adaptation
- Finalisation Phase – External review, consultation with endorsement bodies and finally consultation and acknowledgement to the source guidelines developers

Further details of the adaptation process can be obtained in the **Manual on Adaptation of Evidence-based Clinical Practice Guidelines (version 1.1)**.[19] A summary of the adaptation process is shown below in **Figure 4**. MaHTAS has received training on this by an expert with the assistance of WHO.

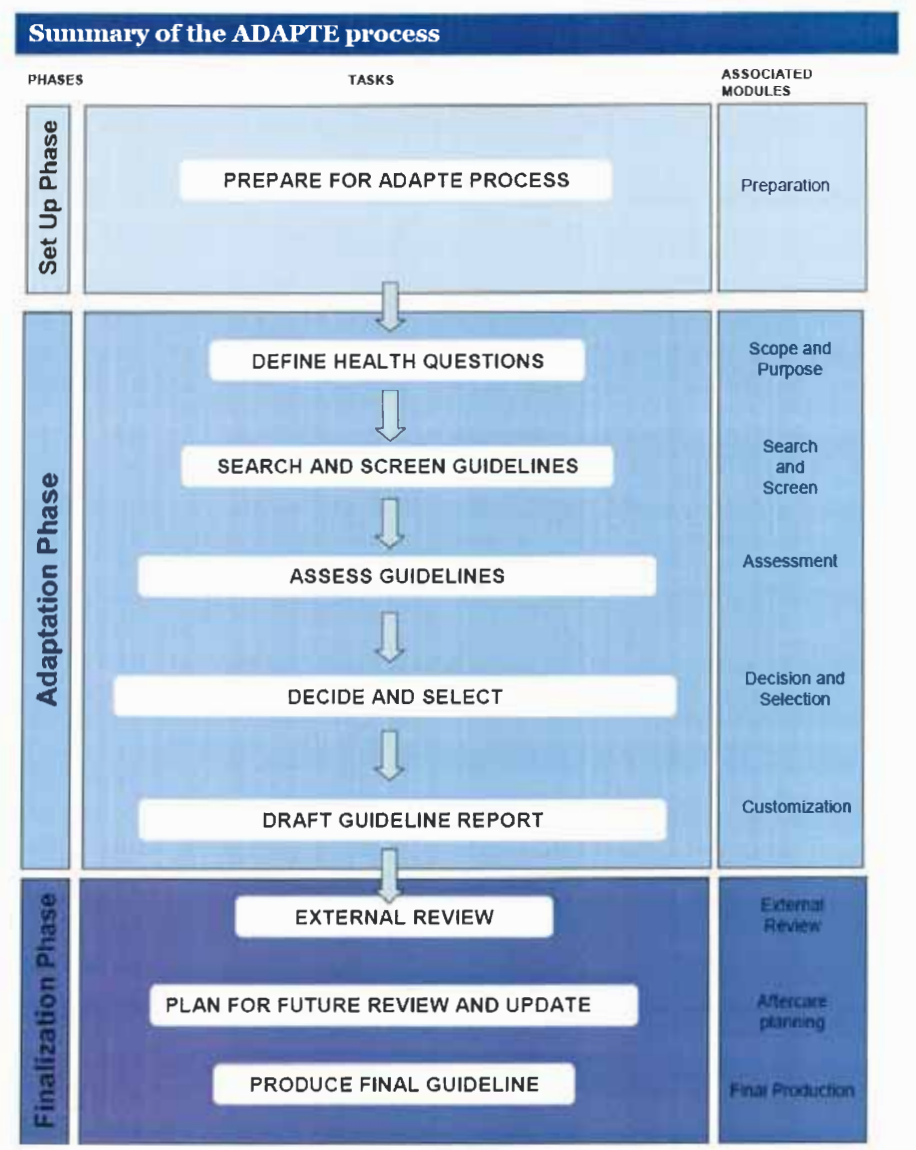

Figure 4. Summary of adaptation process

4.4 Retrieval of Literature

Introduction

An evidence-based CPG is based, to a great extent, on existing knowledge from published and unpublished studies. The systematic identification of

evidence is an essential step in CPG development. Systematic literature searches undertaken should be **thorough, transparent and reproducible**. These searches will minimise biases such as publication bias and database bias that may affect the validity of the CPG that being developed.[20, 21] However, it is necessary to strike a balance between striving for comprehensiveness and maintaining relevance when developing a search strategy. The quality of literature searches is extremely important especially for a systematic review.[21]

Ideally, all evidence should be accessed but in practical point, attempt should be concentrated to retrieve only the best available evidence. There are two types of evidence i.e. primary and secondary. The former is first-hand/direct/ original evidence while the latter is interpretation of findings reported in primary sources. Problems in retrieval of evidence can arise from database, search terms, time and publication issues. In the development of CPG coordinated by MaHTAS, systematic review of evidence is undertaken by trained DG of each CPG and guided by MaHTAS. MaHTAS has received training on search strategy by an expert (research librarian) with the assistance of WHO.

In this manual and especially in this section, literature, article and evidence are used interchangeably. The literature retrieval in developing a CPG is basically divided into three parts:-

i. Formulation of clinical/health questions
ii. Search strategy
iii. Documentation of search

Steps in searching for clinical evidence

i. Formulation of clinical/health questions

A clearly defined and answerable question is the foundation of a good, systematic literature search.[21] Development of a set of clear and focused clinical questions is fundamental to the successful completion of a CPG project. Effective and efficient CPG development involves asking and answering clinical questions using research evidence wherever possible. Well-developed questions help the DG to focus on evidence that is relevant to the CPG that is being developed. The literature search must focus on the best available evidence addressing each question. The DG has also to be realistic on the number of questions that can be addressed in a single CPG. A set of 20 questions is usually within manageable capacity of a CPG development. The DG is also responsible in listing down the questions based on their knowledge and experience in managing the health condition addressed in the CPG.

There are several key components to a well-formulated question. A clearly defined question should specify the type of population (patient/problem), intervention or exposure, and outcome that are of interest. A well-known acronym used in this context is **PICO (population, intervention, comparator and outcome)**. A PICO is a model which is not a rigid and may be revised (refer to an example in **Table 1**). In addition, the types of studies that are relevant to answering the question should be specified[8] as different domain of questions are usually addressed by different study design. It is not always essential to search for every concept of PICO. Population and intervention are often only appropriate to be searched for.[21]

Table 1. An example of a focused question

PICO	Patient or Problem	Intervention (a cause, prognostic factor, treatment, etc.)	Comparison Intervention (if necessary)	Outcome
Example	"In patients with heart failure from dilated cardiomyopathy who are in sinus rhythm ..."	"... would adding anticoagulation with warfarin to standard heart failure therapy ..."	"... when compared with standard therapy alone ..."	"...lead to lower mortality or morbidity from thromboembolism. Is this enough to be worth the increased risk of bleeding?"

*Appropriate study design = randomised controlled trial (RCT)

ii. Search strategy

a. Translating a clinical/health question into search terms

Constructing an effective combination of search terms for searching in electronic databases requires a structured approach. One such approach involves breaking down the clinical question into 'facets' (PICO) and filtering with study design. From this, identify the search terms in each 'facet'/concept which best capture the subject. The search terms should include subject indexing terms (Medical SubHeading [MeSH]) that are assigned by the database producer and a range of text words (free text) in the title and abstract of studies.[21] The final search strategy

is an iterative process in which groups of terms are used in several permutations to identify the combination of terms that seems most sensitive in identifying relevant studies. This requires skilled adaptation of search strategies based on knowledge of the subject matter, the subject headings and the combination of 'facets' which best capture the topic.[8]

Example:
Clinical question: In patients undergoing hip replacement, what is the extent of risk reduction in post-operative infection by antimicrobial prophylaxis?
Break down of the question into 'facets':

- Population/problem - (patients undergoing) hip replacement
- Intervention - antimicrobial prophylaxis
- Control - nil
- Outcome - (reduction) post-operative infection
- Study design - RCT

Refer to **Table 2** for the related terms.

Table 2. Search terms (MeSH and text words) for post-operative infection

Free text terms	*Medical Subject Headings (MeSH)*
Bacterial infection	Bacterial infections
Post-operative complication(s)	Post-operative complications
Wound infection	Surgical wound infection
Septicaemia	Sepsis
Bacterial contamination	Infection control

It is important to consider all possible alternative terms for each elements used and advice from experts can be sought on this matter. Once the search term have been defined, the Boolean operators (AND, OR, NOT) to link facets within a search and various search features (e.g. truncation/wild cards, proximity operators, limits, etc.) available in the databases can be used. Search filters may be used to retrieve specific types of literatures.[21]

b. Locating the information sources

The clinical question should be used as a guide to develop search strategy. In order to minimise bias and ensure adequate coverage of relevant literatures, the search must cover a range of minimum databases/platforms which include Medline, Cochrane Library and Pubmed for electronic searches. Because subject headings differ from a database to another, individual search strategies should be developed for each database. Text word searches should be identical.[2]

It is very important to document the databases, dates, search terms and filters (limits) used in any particular search. Other sources can be accessed to identify relevant evidence such as reference lists (cross-references), conference proceedings, dissertations, technical reports, research registries, grey literature, study authors, field experts, manufacturers, general search engine and hand-searching. Practically, multiple searches using different databases and different search strategies are conducted with priority given on high level evidence.[8]

The period of search coverage will depend on the clinical topic under consideration. The date range for the search should be agreed upon by the DG. For a rapidly developing field, a 5- or 10-year limit to the search may be appropriate, whereas in other areas a much longer time frame might be necessary.[2, 22]

c. Bibliographic management

Electronic records of the references retrieved by searches should be stored using bibliographic reference management software (BRMS) such as EndNote, Reference Manager and ProCite. Records can be exported from bibliographic databases such as Medline and imported automatically into the software using import features. Additional details or new references can also be added manually. Bibliographic reference management software is a tool for managing information.[22]

BRMS assists the CPG development process in four main ways i.e. retrieval, organisation and storage of references and incorporation of references into CPG using a specific citation style. References are entered manually or downloaded into a BRMS database file where they can be stored and later integrated into the CPG to create properly formatted bibliographies. Most BRMS packages interface directly with the word processing software used for report writing. Bibliographies can be dynamically generated and updated in a variety of styles as required.[22]

d. Retrieval of full text article

A large proportion of articles are only available through journal subscriptions or direct purchases.[21] Full text of potentially useful article selected from databases, hand searching and reference lists need to be obtained and appraised. This can be done with the help from CPG coordinators/secretariat, information professionals or librarians.[23]

e. Updating searches

The searches undertaken for each clinical/health question need to be re-run to identify any further evidence that has been published.[21] The final re-run of searches should be done 6 – 8 weeks before consultation on the CPG draft. This can be done either by using database and website automatic alerting systems on each search or by executing re-runs of searches at one or two time points before the consultation.[22]

iii. Documenting the search

The process of developing CPG should be replicable and transparent. For users to evaluate the thoroughness of the search for potentially relevant studies, the search process should be documented in adequate detail that it can be reproduced.[8, 21] Each search conducted will have to be listed in a **Search Strategy Table** as shown in **Appendix 5**. Such documentation should allow searches to be repeated or modified when the CPG is updated.

4.5 Critical Appraisal of Literature

All literatures retrieved from a systematic search and relevant to the clinical questions need to be critically appraised for their quality. The methodology used in the selected literatures must be assessed to ensure its validity. The assessment will affect the level of evidence assigned to the appraised literatures, which will in turn influence the grade of recommendation that they support.[2]

Assessment of the evidence is essentially critical appraisal, a process of critically looking at clinical research studies and asking questions.[5] The assessment will also identify the most appropriate data to address the clinical questions and to ensure that the CPG recommendations are based on the best available evidence. To conduct such assessment, a systematic review process should be used that is explicit, transparent and able to identify potential problems such as bias within the studies.[5, 8]

The methodological assessment focuses on the conduct of the study that affects the validity of its results and conclusion drawn. In study of clinical effectiveness, the study quality can be defined as the degree of confidence about the estimate of a treatment effect. For diagnostic study, questions about diagnosis are concerned with the performance of a diagnostic test. Studies about patient experience are likely to be qualitative studies or cross-sectional surveys.[8] Assessment of CPG is dealt in the section on AGREE II in this manual (refer to **Section 4.3**).

The retrieved articles will be appraised individually by two appraisers. The **subjective nature** of critical appraisal makes double checking essential to minimise bias and ensure consistency.[11] The checklists used for the assessment differs between study designs. Thus, it is important to determine the study design so that the appropriate assessment can be applied in the appraisal. There are many checklists that can be used and currently MaHTAS uses the **Oxford Critical Appraisal Skilled Programme (CASP) checklist** in its critical appraisal (refer to **Appendix 6** for an example of a modified checklist, full list available at http://www.casp-uk.net/#!casp-tools-checklists/c18f8). Any differences arising from the appraisal should be discussed fully at the DG meetings.

The DG should know the characteristics of data to be extracted from the appraised literatures for inclusion in an **evidence table (ET)**. ET helps to identify the similarities and differences between studies, including the key characteristics of the study population, interventions and outcome measures. This provides a basis for comparison.[8] More about ET is discussed in the next section.

4.6 Analysis and Synthesis of Evidence

A CPG should describe the process used to reach consensus (formal or informal) among the working group members and this should be established before the start of its development.[12] Studies identified during literature searches need to be reviewed to identify the most appropriate evidence to address the clinical questions and to ensure that the recommendations are based on the best available evidence. As mentioned earlier, one of the three core principles in CPG methodology is the formulation of recommendations which are explicitly linked to the supporting evidence.[7] The recommendations will be graded according to a pre-determined grading system.

i. Analysis of evidence

Analysis of evidence should be done in an explicit and structured approach. This is to ensure that it is easily understood and helps to make well-informed decisions by the target users. After appraising evidence, an appraiser will have to consider its **level (grade)** and **quality**. The relevant information will then be extracted into ET for presentation.

Grading of evidence is classification of the evidence into different levels based on type of study design. In any hierarchical grading system of research design, a clinical trial sits at top level, followed by observational studies, expert opinions

and laboratory-based studies (refer to **Figure 5**). However, a good systematic review/meta-analysis of the primary papers is regarded as higher evidence because it give a more reliable and precise estimate of an outcome than one study alone.[23]

Figure 5. Hierarchy of evidence

There are many grading system of evidence available such as US/Canadian Preventive Task Force (USPTF), Catalonian Agency for Health Technology Assessment and Research Spain, Scottish Intercollegiate Guidelines Network, Oxford Centre for Evidence Based Medicine, etc. MaHTAS uses **US/CPTF** as it is easy to be applied (refer to **Table 3**). Whatever grading system being used in a CPG, the DG must use similar system which should be explicitly indicated in the document. The level of evidence will influence the grade of recommendation.

Table 3. Level of evidence of US/CPSTF

Level	Study design
I	Evidence from at least one properly randomised controlled trial
II -1	Evidence obtained from well-designed controlled trials without randomisation
II-2	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or group
II-3	Evidence from multiple time series with or without intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence
III	Opinions of respected authorities based on clinical experience; descriptive studies and case reports; or reports of expert committees

Source: Harris RP, Helfand M, Woolf SH, et al. Current methods of the US Preventive Services Task Force: a review of the process. Am J Prev Med. 2001;20(3 Suppl):21-35.

Quality of evidence looks at how well a study has been carried out in terms of methodology, data analysis, conclusions, etc. (check on its validity). Assessment of the evidence is essentially critically appraising it. The methodological assessment is based on a number of key questions on the study design. Once the study design has been determined, assessment using appropriate checklist for the critical appraisal. A common checklist should be used by the DG for consistency of the assessment is conducted. MaHTAS has based its assessment on CASP checklist of Centre for Evidence Based Medicine Oxford.[24] There is no objective scoring system available and thus the evidence is rated as good, fair or poor subjectively. DG can use information in the comment column in an ET for the rating. Good quality study meets all design-specific criteria well while a poor study has at least one design-specific “fatal flaw”, or an accumulation of lesser flaws to the extent that the results of the study are not able to inform recommendations.[25] The quality can also be based on number of criteria from the checklist that being fulfilled and also whether unfulfilled criteria are thought to alter the conclusions of the study or review.[7] It has to be emphasised that in minimising any potential bias in the assessment, each evidence must be evaluated independently by at least two individuals.

An ET provides a summary/key information of critical appraisal on studies appraised relating to each clinical question (refer to **Appendix 7**). DG should use one table per clinical question. ET also provides a basis for comparison between studies including the key characteristics of the study population, interventions and outcome measures. All ET should be presented to the DG who will then decide admissibility of the evidence for the CPG. There are a number of ways to decide on this; MaHTAS uses the consensus approach. The ET is important as it will be referred to in the meeting with RC, when recommendations are being drawn and CPG being drafted. It is a record of transparency in a CPG development.

ii. Synthesis of evidence

Synthesis of evidence is the **combination of evidence** under a clinical question into a single or unified statement/s (as opposed to analysis). It usually done based on an intervention or outcome point of view. Technical and methodological knowledge of DG helps the synthesis process.

Factors to be considered in this stage of CPG development are:

i. quantity of evidence i.e. volume of evidence, type (design) of study and number of study subjects
ii. consistency of evidence i.e. statistical measurement including heterogeneity, reasonable explanation for inconsistency, conclusion of each studies, etc.
iii. generalisability of evidence i.e. whether the evidence is directly applicable or extrapolated to the target population
iv. clinical impact of evidence i.e. benefit/harm of an intervention under consideration likely to have on patients (statistical and clinical significance) and balance between benefit against harm

From the synthesis of evidence, recommendations can be formulated for the CPG.

4.7 Writing the Draft

Writing the CPG is important but **most difficult task** in CPG development

i. Principles of Writing

Writing the CPG is important in order to get the message across **clearly** and **effectively**. This is especially so when communicating complex and technical information to a wide range of readers and also when enhancing utilisation/ implementation of recommendations in CPGs is the utmost aim. Clarity of definitions, language and formats are important in the adoption of a CPG.[2]

To achieve the above aims, the DG should know the principles of effective writing:[26]

- Principle 1 – Know who the target readers are as it will affect the level of writing and what needed for readers to do with the information provided.
- Principle 2 – Plan ahead on what to be written and put the key points in logical manner which include the best structure for the CPG. For example, subheadings will help readers navigates through the CPG and find needed information easily.
- Principle 3 – Keep the writings short and clear. This includes using short sentences (ideally 15 – 20 words), varying the sentences and restricting to one main idea per sentence/paragraph.
- Principle 4 – Use active sentences to tell readers what to do as such sentences sound more direct, concise and professional. However, passive sentence can be useful if it is not clear who is doing the action, if rewording would be longer, or if it simply sounds better.
- Principle 5 – Use plain English and avoid jargon which may lead to misunderstanding.
- Principle 6 – Be consistent in style and as succinct as possible in writing. Writing draft as a group can be challenging and requires prior agreement about the consistent use of terminology, tables/figures and use of statistics.

Many CPG users may not have time to read the full document, and thus would want to focus only on the recommendations and algorithms. It is therefore vital that recommendations are clear and understood by those who have not read the full.[8] Taking the evidence of whatever level, quality and relevancy, and turning it into a clinically useful recommendation depends on the experience and judgment of CPG developers.[2]

Recommendations are series of guiding statements that propose a course of action to the target users. They should progress through a logical manner in the CPG. Writing recommendations is one of the most important steps in developing a CPG. Users will not put the CPG into practice if they are not sure what is being recommended. Formulating recommendations is perhaps the most difficult part of CPG development and requires the exercise of judgment based on experience as well as knowledge of the evidence and the methods used to generate it.[5, 12] Evidence is necessary, but may not be sufficient when making a recommendation. If a recommendation is based on expert opinion, it has to be clearly spelled out in the text.

Recommendations must be linked to evidence taking into account their grade and quality. All the accepted evidence need to be considered giving greater weight to studies of higher quality. Each recommendation should advise a course of action (action-oriented manner) and followed by an indication of the strength of the recommendation.[5] They must also be carefully worded based on levels of certainty by using the words “should” and “may”. They should also be concise, clear/specific and practical while considering different level of local healthcare delivery and current resources. It is rare for evidence to show clearly what course of action to be recommended for any given question.[2, 12]

When recommendations formulated are not agreed upon unanimously by the DG, formal consensus methods can be used for agreeing the final recommendations. The methodology on how disagreements are resolved should be written clearly. Where robust evidence is lacking, DG can recommend for research in it.[2] MaHTAS considers management options available locally when formulating any recommendations.

ii. Grading recommendations, assessment, development and evaluation

A CPG should use a rating system to communicate the quality and reliability of both evidence and the strength of its recommendations. This would increase its trustworthiness and implementation.[12] Judgments on evidence and related recommendations in healthcare are complex issues, which are impeded by resource limitation. However, the shortcomings of many grading systems in CPG development need to be addressed to facilitate systematic reviewers and guideline developers in using a logical, systematic and transparent framework in their work process.

A new grading system called Grading of Recommendations Assessment, Development and Evaluation (GRADE) has been introduced in 2004. It aims

to create a **highly structured, transparent** and **informative system** for rating quality of evidence to support the development of recommendations.[27] This can minimise bias in formulating recommendations and aid in interpretation of guidelines thereafter.[28]

In GRADE, clinical questions are generated with outcomes categorised as critical, important and not important. Evidence on the first two categories is searched for.

The GRADE method involves five distinct steps:[28]

STEP 1
Assign a priority ranking of "high" to RCTs and "low" to observational studies. RCTs are initially assigned a higher grade because they are usually less prone to bias than observational studies.

STEP 2
Then **"downgrade"** or **"upgrade"** the studies from initial ranking. Downgrading occurs because identifiable bias. Observational studies can be upgraded when multiple high-quality studies show consistent results.

STEP 3
Assign final grade for the quality of evidence as "high", "moderate", "low" or "very low" for all the critically important outcomes. Refer to **Table 4** for ranking of evidence.

Table 4. Final GRADE ranking

Final GRADE ranking	
High ⨁⨁⨁⨁	Confident that the effect of the study reflects the actual effect
Moderate ⨁⨁⨁	Quite confident that the effect in the study is close to the true effect, but it is also possible that it is substantially different
Low ⨁⨁	The true effect may differ significantly from the estimate
Very low ⨁	The true effect is likely to be substantially different from the estimated effect

Summary of the evidence are tabulated in **GRADE evidence profile** (refer to **Appendix 8**).

STEP 4

Consider other factors that impact on the strength of recommendation for a course of action because high quality evidence does not always imply a strong recommendation (refer to **Table 5**).

Table 5. Factors that impact on the strength of recommendation

Factor	Comments
Balance between desirable and undesirable effects	The larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted. The narrower the gradient, the higher the likelihood that a weak recommendation is warranted.
Quality of evidence	The higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted.
Values and preferences	The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak recommendation is warranted.
Costs (resource allocation)	The higher the costs of an intervention and the greater the resources consumed cause the lower the likelihood that a strong recommendation is.

STEP 5

The quality of evidence reflects the extent of confidence that the estimates of an effect are adequate to support a particular recommendation. GRADE classifies recommendations as **"strong"** or **"weak"**:

- Strong recommendations mean that most informed patients would choose the recommended management and that clinicians can structure their interactions with patients accordingly.
- Weak recommendations mean that patients' choices will vary according to their values and preferences, and clinicians must ensure that patients' care is in keeping with their values and preferences.

Clear balance of consequences brings out 'strong recommendation' and the words 'should or should not' are used in the recommendation. In less clear or probable consequences, a 'weak recommendation' will be formulated using the words 'may or may not'. In circumstances where there is lack of good evidence but in view of clinical importance of an issue, strong recommendation is justifiable.[11]

MaHTAS has received training on GRADE by an expert with the assistance of WHO. As many guideline developers have used GRADE, MaHTAS have decided **to adapt** the principles of GRADE in its work process. This adoption of GRADE will undoubtedly occur in the future once MaHTAS have the capacity and ready to do so.

iii. CPG Layout

Having well developed and defined template of presentation on the final CPG is important to facilitate its development process. MaHTAS has a style of writing which can be summarised in three parts. In general, the font used is Arial of size 11, single spacing and justified alignment.

At the time of printing, the layout of the CPG developed is as follow:-

i. Front part
   - Statement of intent/disclaimer, procedure of updating, address of CPG Secretariat and URL addresses to access the CPG online
   - Level of evidence of US/CPTF and principles of GRADE
   - CPG development and objectives/scope (a brief description of the systematic methodology used)

ii. Body
   - Evidence on all clinical questions mentioned in the CPG protocol
     - The sequence may not follow the protocol
     - Explicit link between the recommendations and their supporting evidence will be ensured
   - **Boxes** – light yellow for important points/general principles that need to be highlighted and light blue for recommendations
   - Algorithms
   - A discussion on facilitators, barriers and potential resource implications in applying CPG recommendations
   - Proposed clinical audit indicator for quality management

   iii. End part
      - References (Vancouver's style)
      - Appendices of search terms, clinical questions, medication table, etc.
      - Others such as list of abbreviations, acknowledgement, disclosure statement and source of funding

The CPG Unit will act as the secretariat to all CPGs that it is coordinating including attending all DG meetings in the CPG development.

4.8 Technical and Methodological Review

Consultation with stakeholders is an integral part of CPG development process. It is a vital part of the quality-assurance and peer-review processes. For this reason, all CPGs should be scrutinised on their methodological and technical contents.[12] Experts in both methodology and technical fields should be invited to review the CPG draft. Each comment received must be compiled, addressed and recorded.[11] All of these will lead to the acceptance of the documents and hence their utilisation by the intended users. A description of the methodology used to conduct the review should be presented, which include a list of the reviewers and their affiliation.

MaHTAS has developed a strategy to check on its CPG development at various stages. At the outset, DG will be taught on developing an evidence-based CPG in a related workshop. In line with its role, RC will do **technical reviews** at least three times throughout the development of a particular CPG as mentioned earlier (refer to **Figure 2)**. This is to ensure comprehensiveness and accuracy in interpretation of scientific evidence by DG. At each stage, all comments received from RC will be documented and addressed appropriately. Further review will be conducted independently by selected external (peer) reviewers from relevant disciplines both locally and abroad. The CPG draft will also be posted on the MoH website for a limited duration for interested parties to give their constructive feedback on it.

Methodological review will be conducted by MaHTAS continuously throughout the CPG development. However, an independent review will also be done by TAC CPG using AGREE II instrument on the first draft of the CPG (**PTK-FM-04 Pin.1/2015**, refer to **Appendix 9**). When a CPG passes this evaluation, it will be submitted and presented to HTA and CPG Council for final endorsement. The presentation will highlight and summarise the key information of the CPG. Once endorsed, the CPG can be published, disseminated and listed as national evidence-based CPG. It will also be uploaded in official websites of MoH, Academy of Medicine, relevant society, GIN and others so that it accessible easily by larger number of target users.

In summary, each comment received on the CPG draft must be acknowledged and answered as fully and as factually as possible. Responses and changes must be made with the agreement of the whole DG prior to publication of the CPG. Consultation with stakeholders will generate a sense of ownership over the CPG across disciplinary boundary. It enhances the validity of the final CPG and increase the likelihood that it will be successfully into local practice.[2]

4.9 Printing of CPG (and QR)

Prior to the printing of a CPG, MaHTAS will conduct a proofreading exercise on the documents together with the DG. This has to be done as soon as the approval of the CPG is attained as the CPG should be printed within three months after that. During proofreading, major changes should be avoided unless they are deemed necessary by the DG collectively. The DG is also encouraged to discuss on implementation strategies of the CPG during this time. Once a QR being developed, it will undergo a small pre-test on its content.

Since the inception of the CPG programme, the CPG (and later its QR) developed by MaHTAS is printed by MoH (funded wholly) and disseminated free of charge to target users mainly in the MoH healthcare facilities. Funding from professional societies as part of their corporate social responsibility is welcomed. The number of CPG and QR to be printed is based upon existing healthcare facilities, medical faculties/allied health colleges and other listed recipients. The printing of hardcopies is limited due to financial constraints. While waiting for the printing and dissemination of the CPG and QR to be completed, the documents will be uploaded and made available at the MoH and Academy of Medicine websites.

As the CPG and its QR are now available in mobile app for Android and IOS platform (**MyMaHTAS**) since 2014, the printing of the documents will be **reduced gradually** from time to time as the documents are freely and easily accessible at real time anywhere.

4.10 Dissemination of CPG (and QR)

CPG must be made available and accessible as widely as possible in order to facilitate its implementation. However, passive dissemination of the printed documents alone is ineffective in achieving change in clinical practice. Thus it has to be accompanied with other effective implementation activities such as QR, training module (active dissemination) and patient information leaflet.

The development of CPG and QR involves substantial resources and this necessitates a good plan on their dissemination. There should be local co-coordinators/champions looking into the dissemination of the documents. An evaluation of barriers at different stages of dissemination should be considered. They can be in the form of financial resources, organisational structure, work culture, etc.[5]

Financial and logistic constraints have let to limited printing of CPG and QR to all healthcare providers in Malaysia. In view of that, a **facility-based approach** is used to print and disseminate the documents. The CPG produced by MaHTAS will be disseminated to all public healthcare facilities while the QR to both public and private facilities. In principle, the bigger the facility, the more number of CPG and QR will be sent to them. The final number of CPG and QR to be received by the healthcare facilities is subject to change based on number of facilities, and printed number of CPG and QR. Individual acquisition of the CPG and QR can be achieved via the soft-copy of the documents that are posted in both websites of MoH, Academy of Medicine and some professional societies.

The CPG and QR will be delivered to healthcare facilities in packages which will include letter of receipt ("Surat Akuan Penerimaan"). The letter is meant for monitoring the receipt of the documents by the recipients.

For MoH healthcare facilities, MaHTAS will contact each State Health Department to collect the packages for dissemination in their respective state. The State Health Deputy Directors (Medical) will be responsible on the dissemination of the CPG and QR to all hospital and health clinic in their states. Representatives from State Health Department in Peninsular Malaysia will have to come and collect the packages themselves (delivery by hand). While State Health Departments in Sabah, Sarawak and Labuan will receive the documents through courier service (delivery by post).

For public non-MoH healthcare facilities (including teaching hospitals), Academy of Medicine, private hospitals, private clinics and others, they will receive the CPG and/or QR directly by mailing post. A flow chart on dissemination is illustrated in **Appendix 10**. Professional societies which develop CPG and QR on their own can seek help from MaHTAS to disseminate their products but will have to pay the pre-packing and mailing expenses. Once the process of dissemination is in progress, the CPG and QR will be uploaded in the MoH and Academy of Medicine websites for greater accessibility. The dissemination of CPG and QR has to be done efficiently with the aim of reaching target users safely and as quickly as possible.

4.11 Implementation Strategies

It is important not only to develop valid CPG using a strong methodology, but also to ensure the implementation of the evidence-based recommendations stipulated in the CPG. Although a CPG aims to assist healthcare providers in practicing best clinical practice, there is often a gap between the development and implementation into practice of the document.[2]

Simple dissemination of CPG is likely to have no impact at all on implementation. The aim of any implementation strategy of a CPG is to encourage the uptake of its recommendations. Before conducting a strategy, it is important to identify barriers to a CPG utilisation. The barriers can be divided into two i.e. those internal to the CPG itself and those external to it (related to clinical environment and local circumstances). The former is dealt with systematic, transparent and comprehensive methodology in the CPG development. The external barriers are such as organisational factors, peer group factors and individual factors and dealt individually.[2] On a systematic review of 76 articles on why physicians do not follow CPG, there were many barriers to physician adherence identified. These include lack of awareness and familiarity of the CPG, lack of agreement with the CPG or its concept and characteristics of the CPG of being not user-friendly.[29] CPG implementation which is not planned according to the needs of target users will lead to unsuccessful uptake of the document.[5]

Implementation of a CPG should be a local responsibility. There should be team work and co-operation between primary and secondary/tertiary care on it. MaHTAS facilitates the implementation at national level via a number of approaches. These include at the outset a wide and free dissemination of the CPG hardcopies to the healthcare facilities (facility-based dissemination). Apart from that the CPG is uploaded in the relevant websites (to improve its availability and accessibility) and will be officially launched at national level (to create awareness of its existence).

CPG implementation has to take into account evidence on effectiveness of different strategies (evidence-based implementation). Each implementation strategy is effective under different circumstances and a multifaceted approach is most likely to achieve change. An approach should be tailored to suit local circumstances and address local barriers.[2] During CPG development, the DG should identify 'key priorities for implementation' (recommendations which have the biggest impact on patient care and outcome).[8] This will help the development of implementation strategy.

There are many effective implementation strategies of CPG. However, it has to be noted that none of these approaches on transferring evidence to practice is superior to all changes in all situations.[30, 31] Reminders, audit, educational outreach/interactive educational workshops, patient-directed interventions and multi-faceted interventions have moderate to large effectiveness in CPG implementation.[2, 5, 31, 32] Most effective implementation strategies are those that have a direct effect on consultation between patient and healthcare professional. In other words, the CPG will become part of the process of care or embedded in many different aspects of the healthcare system.[13]

In 2007, in collaboration with WHO, an independent guidelines expert was invited to review and provide recommendation on the current strategies used in the formulation and implementation of evidence-based CPG in Malaysia. Among others, implementation strategies were recommended to be implemented and given a priority by MoH.[6] In 2008, MaHTAS conducted a workshop to develop the first implementation activities based on CPG on Major Depressive Disorder. Since then, implementation of CPG has been part of TOR for the DG. An **implementation strategy** will be developed after the CPG has been approved by HTA-CPG Council and will include either one and/or more of the following:-

- QR for healthcare providers
- Training module for healthcare providers
- Patient information leaflet
- Launching of the CPG
- Publication of the CPG
- Others

MaHTAS works with various agencies and individuals in developing the implementation strategies. The documents will be uploaded and accessible freely in the websites of MoH and Academy of Medicine Malaysia.

In order to evaluate the impact of the CPG implementation strategies, it is necessary to collect data on who has seen, is familiar with as well as actually use them.[5] For MaHTAS, a QR utilisation survey will be conducted biannually. As for the training module, a national training of core trainers based on it will be conducted. Cascade or echo training at state level and subsequent level of healthcare following it will then be monitored annually. In the third strategy, patient/carer and non-governmental organisations will be invited to develop patient information leaflet together with the DG. MaHTAS also attempts implementing the CPG via publication either in electronic journal or mass media.

4.12 Monitoring and Evaluation

Development, dissemination and implementation of a CPG should be monitored and evaluated.[2] The evaluation process is intended to assess the validity of a CPG and the effectiveness of its dissemination and implementation, thus measuring the efficiency of the CPG programme. It requires data on processes, practices and outcomes and these requirements should be taken into account when the CPG is being developed.

Measuring the application of CPG recommendations can facilitate their ongoing use.[17] The DG should identify key points in the implementation of the CPG as the basis in developing **clinical audit indicators** for quality management. These are recommendations that are likely to have the biggest impact on patient care and patient outcomes.[8] The indicators developed should be specific, measurable and attainable with a goal of achieving the best outcome. Preferably, they use minimum data sets of which are being collected in MoH.

Impact of a programme could be measured at short, immediate and long term interval. Adherence to the guidelines recommendation may be reflected in the outcomes measured according to the developed indicators. Continuous quality improvement requires a regular working method of measuring adherence in order to monitor effectiveness. Self-reported utilisation or adherence has been considered among the method of choice for use following its feasibility, low cost, etc.

Information obtained from the clinical audit in a CPG can be used for standard setting and service accreditation. The audit will assist organisations in monitoring and reviewing their practice against the key priorities/recommendations in the CPG.[2, 8] This will hopefully improve the quality of healthcare. All CPG developed by MaHTAS, present with proposed monitoring and/ or auditing criteria. Research and survey can be conducted for the purpose.

As mentioned earlier, MaHTAS are regularly monitoring on utilisation of QR and conduct of echo training using the CPG training module. Related evaluations are also done from time to time with other interested parties on the adherence of the CPGs.

4.13 Updating

CPG should be kept up-to-date. Thus when a CPG is developed, a date and strategy should be set for its timely revision. In a study of 17 CPG published by the US Agency for Healthcare Research and Quality, the point at which

no more than 90% of the CPG were still valid was 3.6 years (95% CI, 2.6 to 4.6).[33] The current practice of MaHTAS is to review or update existing CPGs in **minimum four years** time or in the advent/emergence of any significant change in management of patient.

A CPG may require full or selective review/update.[2, 8] A full review after a fixed time is not always appropriate as new evidence is published at different rates in different fields. A selective update focuses on identified chapters in the original CPG that need to be updated.[2] Any decision to update a CPG should balance the need to reflect changes in the evidence against the need for stability. This is because frequent changes to CPG recommendations would make implementation difficult.[8] As for MaHTAS, updating a CPG needs to be set against the competing priorities of new CPG topics taking account of the capacity of the CPG programme. A full review of any particular CPG is advocated so that each aspect of the CPG will be updated at one time and thus avoiding possible confusion among target users. A CPG that is not updated in the suggested time frame may not be accessible from the MoH and Academy of Medicine websites.

A CPG may be considered automatically withdrawn four years after publication or once an update or revision has been issued, unless otherwise specified in the individual CPG. Users should keep in mind that evidence-based CPG are only as current as the evidence that supports them and new evidence can supercede recommendations made in the CPG.

The responsibility for updating a CPG rests on the chairman and/or DG of the CPG. Update of CPG is suggested if there is new evidence supporting changes in:-

- new benefits/harms including on resources
- new outcomes
- new interventions/technology

The DG should also assess what has been learnt from the evaluation of the dissemination and implementation strategies and incorporate suggested improvements in the update process.[4]

The chairman of the earlier edition of the CPG will be formally contacted by MaHTAS on the need to update the CPG. A new DG will be formed and MaHTAS will assist them in the updating work. Update process involves scoping and searching for evidence based on key questions and search strategies used in the original CPG. The scope of the CPG may be revised to include or withdraw certain clinical questions. The new DG may be similar to the DG of the earlier edition or otherwise.

Measures are taken to ensure that errors in the collection, synthesis, interpretation or presentation of the evidence are avoided as much as possible throughout the CPG development. However, on rare occasions errors may be found after publication of a CPG. Most of the times, they do not warrant changes to the CPG. However if changes are necessary such as error in recommendation, an erratum or corrigendum will be issued and notified to target users by conventional and electronic mail/message.

5. OTHER RELATED ISSUES

Aim of Chapter:

- to discuss on issues pertaining to CPG development

Issues that are frequently encountered in CPG development are pharmaceutical involvement and medico-legal.

5.1 Pharmaceutical Involvement

Pharmaceutical involvement is an issue mainly in the CPG developed externally (by the society). This is because the funding of the CPG development may come from pharmaceutical companies. Apart from that, such companies may act as the secretariat of the CPG development as well. To minimise bias in CPG development, all members of the DG and RC are required to fill in a Disclosure Form.

Any pharmaceutical companies' involvement is **required to follow** the following conditions:

- They are allowed to fund CPG development but source of funding must be mentioned in the CPG.
- Involvement of more than one company is preferred.
- They are **strictly not allowed** to act as secretariat e.g. writing, editing or even being a member of the development or working group.
- There should be an explicit statement saying that views and interests of funding body will not influence final recommendations.
- Company logo must not appear in the CPG.

5.2 Medico-legal

Frequently, CPG developers and users show concern on potential medico-legal implications of CPG to medical practitioners if the patient does not receive treatment specified in the CPG. A simple answer to the question is that there is **no legal binding** to the CPG.

Standard of care required by law derives from customary and accepted practice rather than from imposition of practices through CPG. The CPG will not be introduced as a substitute for expert testimony. However, it could be produced as evidence of such customary and accepted practice in the court of law or when medical practitioner's duty of care had been breached.[2, 13]

Thus, healthcare providers may need to justify as why they do not follow the endorsed national evidence-based CPG. CPG developers are unlikely to be held liable for any negative consequences of implementation of the CPG, particularly if the processes of preparation and the limitations of the guidelines are clearly described.[13]

5. 3 Standards of Practice

Standards of practice depend on resources available but should be aimed to achieve as set in the CPG.

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TERMS OF REFERENCE

CPG DEVELOPMENT GROUP

- Identify and recommend members with regards to committee ensuring that is multidisciplinary
- Review and provide technical input on CPG protocol developed by HTA Section
- Retrieve evidence systematically according to assigned sections/aspects in CPG protocol (assisted by the HTA Section)
- Analyse and synthesise evidence retrieved by developing evidence tables
- Prepare draft report from evidence tables according to assigned sections
- Submit draft report to HTA Section for merging
- Review final draft report of CPG
- Do necessary amendments/modifications on final report as recommended or suggested by the TAC CPG (assisted by HTA Section)
- The development group is responsible to complete the final report of the CPG topic
- Consider implementation strategies that include developing a quick reference, a training module and a consumer leaflet

TERMS OF REFERENCE

CPG REVIEW COMMITTEE

- Review the CPG protocol developed by development group
- Review and provide technical input when evidence is being presented by the development group
- Assist and provide input when drawing recommendations based on the evidence
- Provide expert advice and guidance when reviewing draft guidelines

POLICY OF DECLARATION OF COMPETING INTEREST

Clinical practice guidelines (CPG) are designed to help practitioners assimilate, evaluate and implement the ever increasing amount of evidence and opinion based on the **best available evidence.** The clinical questions about the management are compiled by a multidisciplinary development group by means of a systematic review and critical appraisal of the relevant articles. Where there is little or no evidence with regards to the clinical question being addressed, the development group together with the review committee will make recommendations based on their own clinical experience. However, all the recommendations being drawn should be set in the local context as far as possible and reflect local practice.

There will also be situations, where sponsoring and financial support for the guidelines work is welcome. For example, the development group received funding for printing the guidelines from pharmaceutical companies. This funding was recorded and a declaration was made stating that "the printing and dissemination of this guideline has been assisted by funding from XXXXXXX". However, the logo of the pharmaceutical companies is not permitted to be printed on the guidelines.

In keeping with the desire to be free from bias or the perception of bias, brand names for pharmaceuticals or other products should not appear in the guidelines published by the Ministry of Health Malaysia or endorsed by Ministry of Health Malaysia. Only generic names should be used.

All members of our guidelines development group and review committees are required to complete a declaration of competing interest detailing the sources of funding, and other possible conflicts of interest. An explicit statement regarding the above is made at the end of published CPG.

DECLARATION OF COMPETING INTEREST*

I understand that this declaration will be retained by the HTA Unit Administrator and made available on inspection at the HTA Unit, Ministry of Health Malaysia.

1. Have you in the **last three years** accepted the following from any pharmaceutical and medical device industries that may in any way gain or lose financially from the results of your work (in relation to developing this CPG):
   - A fee for speaking?
   - Fund support for research?
   - Funding for publication?
   - Consultancies?

If so, please declare the occasion or event and the organisation that provided you with financial support.

Organisation	Event

2. Have you, during **last three years**, been employed by an organisation that may in any way gain or lose financially from the results or conclusion of this guideline or systematic review?
   If so, please declare the organisation and the nature of your relationship with that organisation.

Organisation	Event

3. Do you have any competing financial interests such as investments or directorships? If so specify.

Organisation	Interest

4. Do you belong to a political party, special interest group or hold deep personal or religious convictions that may have affected what you have written and that readers should be aware of when reading your paper?

Organisation/personal beliefs that could be perceived as influencing your work

5. List the source(s) of funding for the development of this CPG

Signature: .....

Name: .....

Work place: .....

Title of CPG that you have contributed: .....

.....

Date: .....

* *The Ministry of Health Malaysia requires all members of the guideline development group or review committee to fill in this form.*

Appendix 4

PTK – FM – 03

CLINICAL PRACTICE GUIDELINES (CPG) PROTOCOL

TITLE:

1. **INTRODUCTION/BACKGROUND INFORMATION**

2. **OBJECTIVES**

3. **SCOPE OF GUIDELINES**
   a. Target population (inclusion & exclusion criteria)
   b. Target users
   c. Healthcare settings

4. **CLINICAL QUESTIONS**
   a. Epidemiology and clinical diagnosis
   b. General treatment and management plan
   c. Pharmacological treatment, non-pharmacological treatment and prevention
   d. Resource implications/organisational barriers

5. **ALGORITHM**

6. **PROPOSED CLINICAL AUDIT INDICATORS FOR QUALITY MANAGEMENT**

7. **DICLOSURE CONFLICT OF INTEREST**

8. **STRATEGY**

9. **METHODOLOGY**

SEARCH STRATEGY TABLE

Clinical Question:

Date	Database	Keywords	Year of publication	Other limit	No. of search	No. of relevant title	No. of relevant abstract	No. of full article used	Notes
				Language: Study: Age: Sex: Journal: Publication Type:					
6/12/10	Pubmed	"breast cancer" AND vitamins AND survival	2005 - 2008	English	6	4	2	2	
6/12/10	Cochrane library via OVID	"breast cancer" AND vitamins AND benefit	2005 - 2008	English	18				
8/12/10	CRD databases	"breast cancer" AND (dietary OR nutrition) AND recurrent	2005 - 2008	English	20				

CASP FOR SYSTEMATIC REVIEW

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? ☐ Yes ☐ Can’t tell ☐ No
   HINT: An issue can be ‘focused’ In terms of
   - The population studied
   - The intervention given
   - The outcome considered

2. Did the authors look for the right type of papers? ☐ Yes ☐ Can’t tell ☐ No
   HINT: ‘The best sort of studies’ would
   - Address the reviews question
   - Have an appropriate study design (usually RCTs for papers evaluating interventions)

(B) Is it worth continuing?

Detailed questions

3. Do you think all the important, relevant studies were included? ☐ Yes ☐ Can't tell ☐ No
   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

4. Did the review's authors do enough to assess the quality of the included studies? ☐ Yes ☐ Can't tell ☐ No
   HINT: The authors need to consider the rigour of the studies they have identified. Lack of rigour may affect the studies' results.

5. If the results of the review have been combined, was it reasonable to do so? ☐ Yes ☐ Can't tell ☐ No
   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

(C) 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

(D) Will the results help locally?

8. Can the results be applied to the local population? ☐ Yes ☐ Can't tell ☐ No
   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

9. Were all important outcomes considered? ☐ Yes ☐ Can't tell ☐ No
   HINT: Consider whether is there other information you would like to have seen

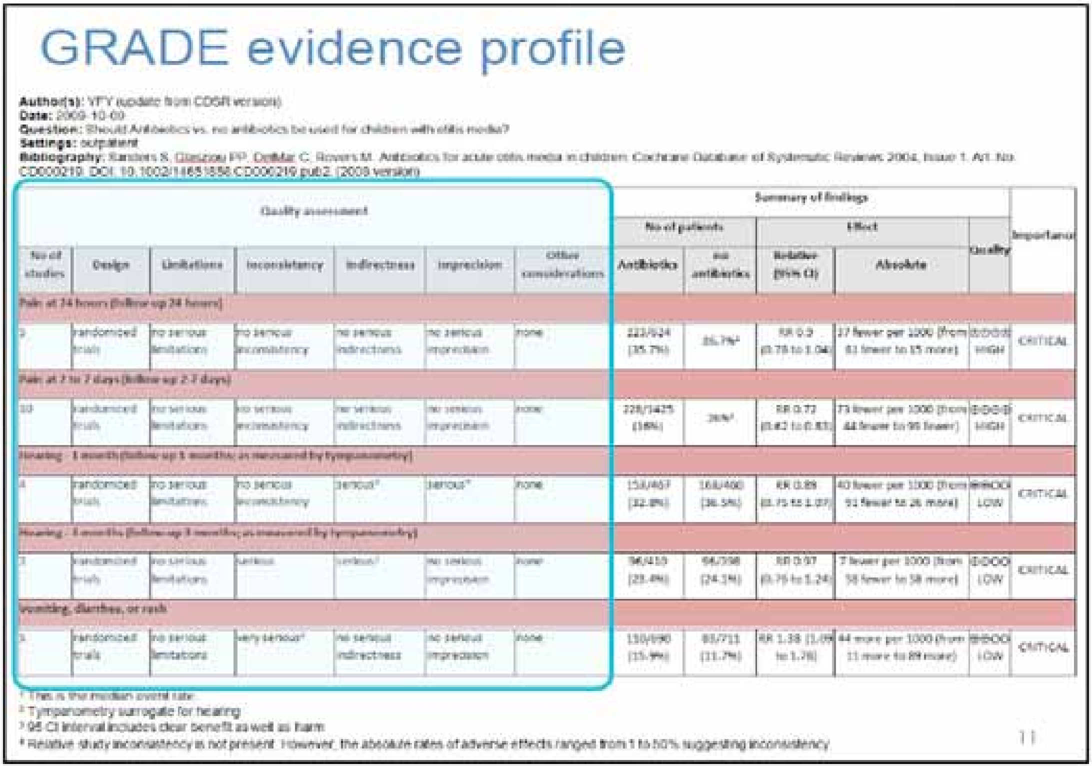
10. Are the benefits worth the harms and costs? ☐ Yes ☐ Can't tell ☐ No
    HINT: Consider even if this is not addressed by the review, what do you think?

Modified: Critical Appraisal Skills Programme (available at http://www.casp-uk.net/#!casp-tools- checklists/c18f8)

EVIDENCE TABLE

No.	Author Title Journal Year Volume Issue Page number (Use proper citation)	Type of Study Aim Sample size Population/setting Intervention Follow-up	Outcome (Primary and Secondary) Results (with statistics) Conclusion	Grade and Quality of Evidence	Comments (by appraiser)

GRADE EVIDENCE PROFILE



GRADE evidence profile

Author(s): YFY (update from CDSR version)
Date: 2009-10-09
Question: Should Antibiotics vs. no antibiotics be used for children with otitis media?
Settings: outpatient
Bibliography: Sanders S, Glasziou PP, DelMar C, Rovers M. Antibiotics for acute otitis media in children. Cochrane Database of Systematic Reviews 2004, Issue 1. Art. No. CD000219. DOI: 10.1002/14651858.CD000219.pub2. (2009 version)

Quality assessment							Summary of findings					Importance
							No of patients		Effect		Quality	
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Antibiotics	no antibiotics	Relative (95% CI)	Absolute		
Pain at 24 hours (follow-up 24 hours)												
5	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	223/624 (35.7%)	35.7%[1]	RR 0.9 (0.78 to 1.04)	37 fewer per 1000 (from 81 fewer to 15 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Pain at 2 to 7 days (follow-up 2-7 days)												
10	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	228/1425 (16%)	26%[1]	RR 0.72 (0.62 to 0.83)	73 fewer per 1000 (from 44 fewer to 99 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Hearing - 1 month (follow-up 1 months; as measured by tympanometry)												
4	randomized trials	no serious limitations	no serious inconsistency	serious[2]	serious[3]	none	150/457 (32.8%)	168/460 (36.5%)	RR 0.89 (0.75 to 1.07)	40 fewer per 1000 (from 91 fewer to 26 more)	⊕⊕OO LOW	CRITICAL
Hearing - 3 months (follow-up 3 months; as measured by tympanometry)												
3	randomized trials	no serious limitations	serious	serious[2]	no serious imprecision	none	96/415 (23.4%)	94/398 (24.3%)	RR 0.97 (0.76 to 1.24)	7 fewer per 1000 (from 58 fewer to 58 more)	⊕⊕OO LOW	CRITICAL
Vomiting, diarrhea, or rash												
5	randomized trials	no serious limitations	very serious[4]	no serious indirectness	no serious imprecision	none	110/690 (15.9%)	83/711 (11.7%)	RR 1.38 (1.09 to 1.76)	44 more per 1000 (from 11 more to 89 more)	⊕⊕OO LOW	CRITICAL

[1] This is the median control rate
[2] Tympanometry surrogate for hearing
[3] 95 CI interval includes clear benefit as well as harm
[4] Relative study inconsistency is not present. However, the absolute rates of adverse effects ranged from 1 to 50% suggesting inconsistency

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APPRAISAL OF GUIDELINES FOR RESEARCH & EVALUATION II (AGREE II) INSTRUMENT

DOMAIN 1 : SCOPE & PURPOSE

1. The overall objective(s) of the guideline is (are) specifically described.

1 Strongly disagree	2	3	4	5	6	7 Strongly agree

Comments :

2. The health question(s) are covered by the guideline is (are) specifically described.

1 Strongly disagree	2	3	4	5	6	7 Strongly agree

Comments :

3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.

1 Strongly disagree	2	3	4	5	6	7 Strongly agree

Comments :

DOMAIN 2 : STAKEHOLDER INVOLVEMENT

4. The guideline development group includes individuals from all relevant professional groups.

1 Strongly disagree	2	3	4	5	6	7 Strongly agree

Comments :

5. The views and preferences of the target population (patients, public, etc.) have been sought.

1 Strongly disagree	2	3	4	5	6	7 Strongly agree

Comments :

6. The target users of the guideline are clearly defined.

1 Strongly disagree	2	3	4	5	6	7 Strongly agree

Comments :

DOMAIN 3 : RIGOUR OF DEVELOPMENT

7. Systematic methods were used to search for evidence.

1 Strongly disagree	2	3	4	5	6	7 Strongly agree

Comments :

8. The criteria for selecting the evidence are clearly described.

1 Strongly disagree	2	3	4	5	6	7 Strongly agree

Comments :

9. The strengths and limitations of the body of evidence are clearly described.

1 Strongly disagree	2	3	4	5	6	7 Strongly agree

Comments :

10. The methods for formulating the recommendations are clearly described.

1 Strongly disagree	2	3	4	5	6	7 Strongly agree

Comments :

11. The health benefits, side effects and risks have been considered in formulating the recommendations.

1 Strongly disagree	2	3	4	5	6	7 Strongly agree

Comments :

12. There is an explicit link between the recommendations and the supporting evidence.

1 Strongly disagree	2	3	4	5	6	7 Strongly agree

Comments :

13. The guideline has been externally reviewed by experts prior to its publication.

1 Strongly disagree	2	3	4	5	6	7 Strongly agree

Comments :

14. A procedure for updating the guideline is provided.

1 Strongly disagree	2	3	4	5	6	7 Strongly agree

Comments :

DOMAIN 4 : CLARITY OF PRESENTATION

15. The recommendations are specific and unambiguous.

1 Strongly disagree	2	3	4	5	6	7 Strongly agree

Comments :

16. The different options for management of the condition or health issue are clearly presented.

1 Strongly disagree	2	3	4	5	6	7 Strongly agree

Comments :

17. Key recommendations are easily identifiable.

1 Strongly disagree	2	3	4	5	6	7 Strongly agree

Comments :

DOMAIN 5 : APPLICABILITY

18. The guideline describes facilitators and barriers to its application.

1 Strongly disagree	2	3	4	5	6	7 Strongly agree

Comments :

19. The guideline provides advice and/or tools on how the recommendations can be put into practice.

1 Strongly disagree	2	3	4	5	6	7 Strongly agree

Comments :

20. The potential resource implications of applying the recommendations have been considered.

1 Strongly disagree	2	3	4	5	6	7 Strongly agree

Comments :

21. The guideline presents monitoring and/or auditing criteria.

1 Strongly disagree	2	3	4	5	6	7 Strongly agree

Comments :

DOMAIN 6 : EDITORIAL INDEPENDENCE

22. The views of the funding body have not influenced the content of the guideline.

1 Strongly disagree	2	3	4	5	6	7 Strongly agree

Comments :

23. Competing interests of guideline development group members have been recorded and addressed.

1 Strongly disagree	2	3	4	5	6	7 Strongly agree

Comments :

OVERALL GUIDELINE ASSESSMENT

For each question, please choose the response which best characterises the guideline assessed :

1. Rate the overall quality of this guideline

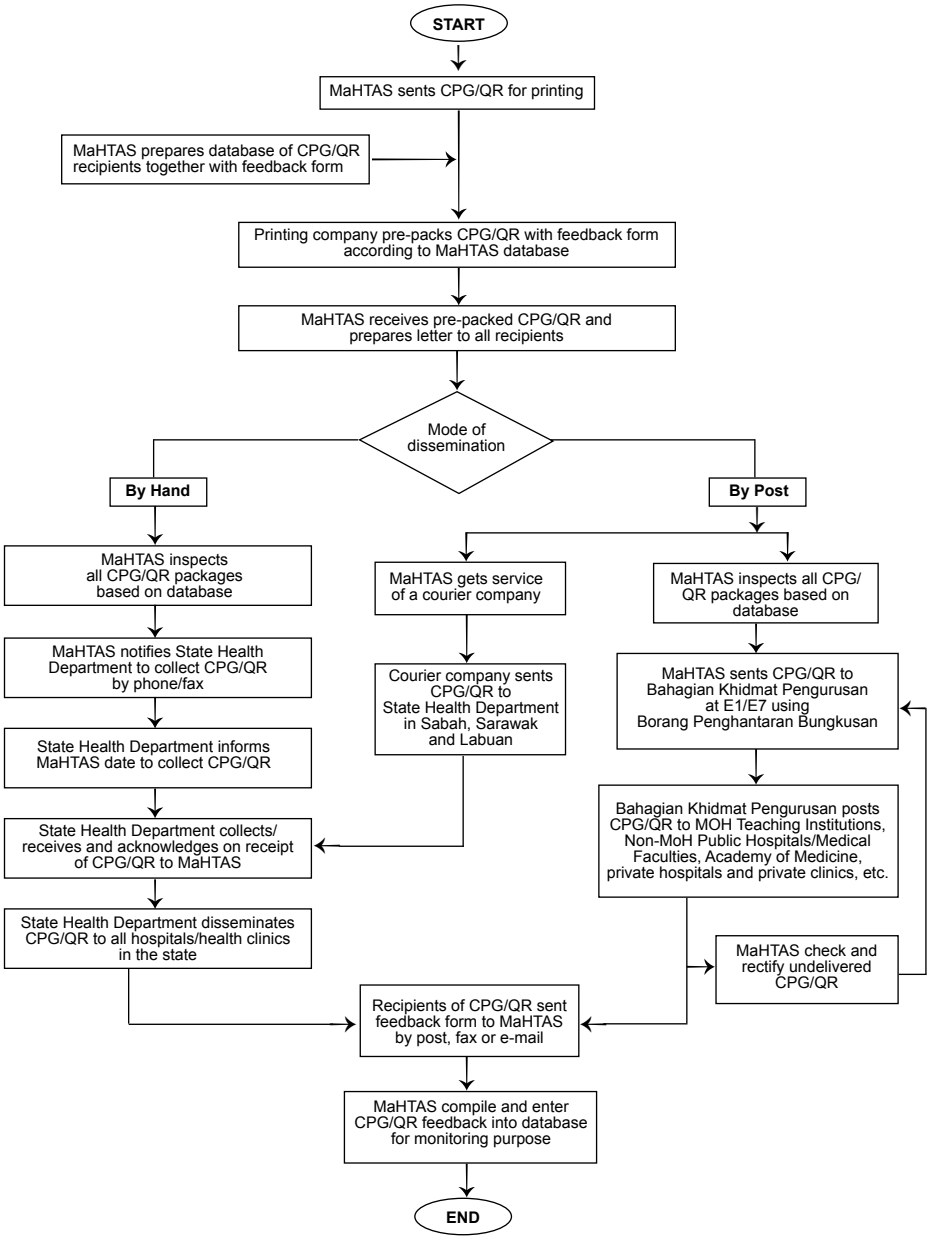
1 Lowest possible quality	**2**	**3**	**4**	**5**	**6**	**7** Highest possible quality

2. I would recommend this guideline for use. (Tick √ in the box)

Yes	
Yes, with modifications	
No	

NOTES

DISSEMINATION OF CPG & QR



List of abbreviations

AGREE	Appraisal of Guidelines for Research and Evaluation
BRMS	bibliographic reference management software
CASP	Critical Appraisal Skilled Programme
CPG	clinical practice guidelines
DG(s)	development group(s)
ET	evidence table
G-I-N	Guidelines International Network
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HTA	health technology assessment
MaHTAS	Malaysian Health Technology Assessment Section
MeSH	Medical SubHeading
MoH	Ministry of Health
PICO	population, intervention, comparator and outcome
QR	quick reference
RC	review committee
RCT(s)	randomised controlled trial(s)
TAC	Technical Advisory Committee
TOR	terms of reference
US/CPTF	US/Canadian Preventive Task Force
WHO	World Health Organization

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