Decision criteria for selecting essential medicines and their connection to guidelines

Piggott, Thomas; Moja, Lorenzo; Akl, Elie A.; Lavis, John N.; Cooke, Graham; Kredo, Tamara; Hogerzeil, Hans V.; Huttner, Benedikt; Alonso-Coello, Pablo; Schünemann, Holger

Published in:
Journal of Clinical Epidemiology

DOI:
10.1016/j.jclinepi.2022.12.007

Journal of Clinical Epidemiology 154 (2023) 146−155

Journal of Clinical Epidemiology

OTHER GRADE PAPERS

Decision criteria for selecting essential medicines and their connection to guidelines: an interpretive descriptive qualitative interview study

Thomas Piggott[a], Lorenzo Moja[b], Elie A. Akl[a,c], John N. Lavis[a,d,e], Graham Cooke[f], Tamara Kredo[g,h], Hans V. Hogerzeil[i], Benedikt Huttner[b], Pablo Alonso-Coello[j,k], Holger Schünemann[a,l,m,n,*]

[a]*Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, Canada*
[b]*Department of Essential Medicines and Health Products, World Health Organization, Geneva, Switzerland*
[c]*Department of Internal Medicine, American University of Beirut Medical Centre, Beirut, Lebanon*
[d]*McMaster Health Forum, McMaster University, Hamilton, Canada*
[e]*Africa Centre for Evidence, University of Johannesburg, Johannesburg, South Africa*
[f]*Department of Infectious Disease, Faculty of Medicine, Imperial College London, London, UK*
[g]*Cochrane South Africa, South African Medical Research Council, Cape Town, South Africa*
[h]*Clinical Pharmacology, Department of Medicine, Stellenbosch University, Cape Town, South Africa*
[i]*University Medical Centre, Groningen, Netherlands*
[j]*Iberoamerican Cochrane Center-Servicio de Epidemiología Clínica y Salud Pública, Biomedical Research Institute (IIB-Sant Pau), Barcelona, Spain*
[k]*CIBER of Epidemiology and Public Health (CIBERESP), Barcelona, Spain*
[l]*Institut für Evidence in Medicine, Medical Center & Faculty of Medicine, University of Freiburg, Freiburg, Germany*
[m]*Department of Biomedical Sciences, Humanitas University, Milan, Italy*
[n]*Department of Medicine, McMaster University, Hamilton, Canada*

Accepted 8 December 2022; Published online 27 December 2022

Abstract

Background and Objectives: The World Health Organization Model List of Essential Medicines has led to at least 137 national lists. Essential medicines should be grounded in evidence-based guideline recommendations and explicit decision criteria. Essential medicines should be available, accessible, affordable, and the supporting evidence should be accompanied by a rating of the certainty one can place in it. Our objectives were to identify criteria and considerations that should be addressed in moving from a guideline recommendation regarding a medicine to the decision of whether to add, maintain, or remove a medicine from an essential medicines list. We also seek to explore opportunities to improve organizational processes to support evidence-based health decision-making more broadly.

Declaration of interest: Thomas Piggott: Member of the GRADE Working Group. Lorenzo Moja: Staff member of the Secretariat of the Expert Committee on the Selection and Use of Essential Medicines and an employee of the WHO, Geneva, Switzerland. Elie A. Akl: Member of the GRADE Working Group. John Lavis: Declared none. Graham Cooke: was the chair of the 2019 and 2021 EML Expert Committee. He is supported in part by the Imperial NIHR Biomedical Research Centre. Tamara Kredo: Member of the GRADE Working Group, Co-director of South African GRADE Network and member South African Essential Medicines List Committee. Hans Hogerzeil: Was secretary of the WHO Expert Committee from 1999 to 2007 and Director of WHO's Essential Medicines Department from 2003 to 2011. He declares unrelated consultancy work for WHO, the Access to Medicine Index, Health Action International, and Management Sciences for Health. Benedikt Huttner: Staff member of the Secretariat of the Expert Committee on the Selection and Use of Essential Medicines and an employee of the WHO, Geneva, Switzerland. Pablo Alonso-Coello: Member of the GRADE Working Group, Director Barcelona GRADE Center. Holger Schünemann: Member and co-chair of the GRADE Working Group, Director Cochrane Canada and McGRADE Centre.

Author Contributions: Thomas Piggott: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Software; Validation; Visualization; Roles/Writing−original draft; Writing−review & editing. Lorenzo Moja: Conceptualization; Formal analysis; Investigation; Methodology; Validation; Roles/Writing−original draft; Writing−review & editing. Elie Akl: Formal analysis; Investigation; Methodology; Validation; Writing−review & editing. John Lavis: Formal analysis; Investigation; Methodology; Validation; Writing−review & editing. Graham Cooke: Investigation; Methodology; Validation; Writing−review & editing. Tamara Kredo: Investigation; Validation; Writing−review & editing. Hans Hogerzeil: Investigation; Validation; Writing−review & editing. Benedikt Huttner: Investigation; Validation; Writing−review & editing. Pablo Alonso-Coello: Investigation; Validation; Writing−review & editing. Holger J. Schünemann: Conceptualization; Formal analysis; Investigation; Methodology; Project administration; Resources; Supervision; Validation; Visualization; Roles/Writing−original draft; Writing−review & editing.

* Corresponding author. McMaster University, 1280 Main Street, Hamilton, L8S 4K1 Ontario, Canada. Tel.: +1-905-525-9140x26771.

E-mail address: holger.schunemann@mcmaster.ca (H. Schünemann).

https://doi.org/10.1016/j.jclinepi.2022.12.007

Methods: We conducted a qualitative study with semistructured interviews of key informant stakeholders in the development and use of guidelines and essential medicine lists (EMLs). We used an interpretive descriptive analysis approach and thematic analysis of interview transcripts in NVIVO v12.

Results: We interviewed 16 key informants working at national and global levels across all WHO regions. We identified five themes: three descriptive/explanatory themes 1) EMLs and guidelines, the same, but different; 2) EMLs can drive price reductions and improve affordability and access; 3) Time lag and disconnect between guidelines and EMLs; and two prescriptive themes 4) An ''evidence pipeline'' could improve coordination between guidelines and EMLs; 5) Facilitating the link between the WHO Model List of Essential Medicines (WHO EML) and national EMLs could increase alignment.

Conclusion: We found significant overlap and opportunities for alignment between guideline and essential medicine decision processes. This finding presents opportunities for guideline and EML developers to enhance strategies for collaboration. Future research should assess and evaluate these strategies in practice to support the shared goal of guidelines and EMLs: improvements in health.

Keywords: Essential medicines; Drug coverage; Evidence-to-Decision framework; GRADE; Pharmaceutic policy; Universal health coverage

1. Background

Recommendations about medicines by health guideline developers and decisions about essential medicine lists (EMLs) are both important instruments to support health decision-making. EMLs use a medicine-focused approach, while guidelines use a disease/problem focused approach. They both strive to improve individual and population health outcomes through better policy decisions and more appropriate prescribing [1]. On the one hand, if a medicine is considered ''essential,'' trustworthy practice guideline recommendations to guide its most appropriate use should also be available. On the other hand, medicines recommended by practice guidelines should be available, accessible, affordable, and of good quality, and at least be evaluated for ''essential medicine'' status.

Essential medicines are defined by WHO (2001 criteria) as medicines that 1) meet the priority healthcare needs of the population, 2) are selected based on public health/disease prevalence, evidence of efficacy and safety, and comparative cost-effectiveness, and 3) are intended to be available at all times within functioning health systems in adequate amounts, dosage forms, and quality assurance at an affordable price [2]. Listing the medicine on the EML can improve access to medicines through prioritization for procurement, quality assurance, distribution, reimbursement, and use. While essential medicines are more widely available globally than nonessential medicines, access to them is still inequitable [3].

The Model List of Essential Medicines, produced by the World Health Organization (WHO) since 1977, prioritizes medicines, identifying the most effective therapeutic options in each disease area. It serves as a global reference list and as a model list for national EMLs and reimbursement. The WHO EML is important because it supports Universal Health Coverage (UHC) for all, and the UN Sustainable Development Goal #3, which strives to develop ''access to safe, effective, quality, and affordable essential medicines and vaccines for all'' [4].

The Expert Committee on Selection and Use of Essential Medicines updates the WHO EML every 2 years. This multidisciplinary panel is composed of about 10−20 experts, which act in their own capacity, with expertise and experience in medicine assessment and policy. At least 137 countries produce and use national EMLs [2]. The implication of a national listing of a medicine is that governments should ensure that the included essential medicines are available, accessible, affordable, and of good quality at all times [2]. National lists are developed for context-specific application of the EML, which every country should ideally produce to support UHC. The WHO has recently produced an implementation guide to facilitate the evidence-based development of national EMLs [2].

Any individual or organization can apply to make an addition, deletions, or changes to the WHO EML. Decisions are made based on applications submitted and all submitted data and reviews made publicly available by WHO with opportunities for interested parties to comment. Each application describes the request for change and provides evidence and other elements supporting the request. Considerations that have traditionally gone into EML applications, presented in the WHO EML application are informed by the 2001 WHO Executive Board resolution. Not all criteria that the EML application requests are comprehensively presented in applications to the EML. Review of applications may identify important information, but EML committees may be missing important information for decision-making. For example, Moucheraud and colleagues found that only 6% of applications to the WHO EML expert committee between 2002 and 2013 contained complete pricing information [5]. There are criteria and evidence that have been omitted from applications, but there may also be medicines where that information is simply not available.

Growing, but longstanding interest in linking EML decisions to health guideline recommendations exist [1]. This involves strengthening the synergies between selection of therapeutic options, a phase associated with procurement and purchasing, and the actual use of medicines at clinical

What is new?

Key findings

- Overlap and opportunities for alignment exist between health guidelines and essential medicine decision processes. These opportunities could improve coordination and decrease duplication of work, accelerating access to essential medicines.

What this adds to what is known?

- Recommendations for listing essential medicines and in guidelines follow similar processes, but unique considerations. Notably essential medicine lists have an important role in improving access and affordability of medicines.
- Time lags exist between the development of guideline recommendations and EML decisions. Improving alignment, using a shared underlying evidence 'pipeline' and aligning the WHO MLEM with national EMLs could improve processes.

What is the implication, what should change now?

- Similar processes, including shared decision criteria frameworks should be utilized to align decisions between health guidelines and essential medicine list committees.

level. Gray and colleagues highlight the question ''should the list automatically include any medicine mentioned in a WHO treatment guideline?'' [6].

Evidence-to-decision (EtD) frameworks facilitate guideline committees to support effective guidance that considers a wide range of important considerations [7−9]. They are currently being used by a wide-range of WHO and other guideline development groups. The use of EtD frameworks, or closer linking, in supporting EML applications could make criteria clearer and explicitly included. EtD frameworks support guideline groups to provide judgements on a series of criteria to bridge the evaluation of evidence to making a recommendation regarding an intervention. The GRADE system may be used to estimate and indicate the certainty of the supporting evidence. The typical questions considered in the standard EtD process are included in Box 1; however, GRADE EtD frameworks, when appropriate, allow tailoring of criteria and judgements.

Although the WHO EML selection criteria and EtD framework were conceived at different times, and in different contexts, the parallels are clear [1]. For example, both approaches consider desirable and undesirable health effects, comparative cost-effectiveness, and availability of appropriate medicines. Differences between EML considerations and EtD frameworks may have important implications. There are considerations discussed by EMLs that are only implicitly incorporated into the EtD framework, for example, under acceptability and feasibility; these include, therapeutic equivalence (that is, square box listing, which groups medicines with therapeutic equivalency [11]), patents, on/off label uses, procurement, purchasing and availability. There might be also differences in the nature of the evaluation process: guideline panels often start with the disease and often assess several clinical questions in relation to a single disease area, while the EML expert committee starts with the medicine and assesses a single question (is the medicine essential for a given indication?) across several diseases.

In addition to selection criteria considered, a robust process is also important for the development of trustworthy EMLs. One such process consideration is the selection of experts for the Expert Committee, which are chosen every 2 years by WHO from a standing list of technical experts proposed by WHO and approved by WHO member states; and the careful management of their potential conflict of interest. The lack of management of potential conflict of interests in EMLs has previously been subject to criticism [12].

Improving EMLs and their synergy with guidelines requires a greater understanding of the current state of these decision paradigms and their interplay. Our objectives were to identify considerations that should be addressed in moving from a guideline recommendation regarding a medicine to the decision of whether to add, maintain, or remove a medicine from an EML. The opposite trajectory is also possible, with a medicine first listed as essential and then considered by guideline recommendation. To achieve these objectives, our research question was: what are the perspectives and experiences of experts from both EML and guideline contexts with decision-making criteria for essential medicines? In this article we specifically seek to describe the current processes and opportunities. We also seek to explore opportunities to improve organizational processes to support evidence-based health decision-making more broadly.

2. Methods

2.1. Research protocol, ethics review and consent

We developed a research protocol and report this work in accordance with the COnsolidated criteria for REporting Qualitative research (COREQ) checklist (available in Appendix 1) [13]. The protocol was developed in coordination with the WHO Secretariat of the Expert Committee on the Selection and Use of Essential Medicines, to ensure strong integration of research results into global and national EML processes. The Hamilton Integrated Research Ethics Board (HIREB) approved this research (approval # 7534). We obtained written consent from all participants in accordance with institutional protocol.

Box 1 Questions/Decision-Criteria for WHO EML Applications and Guideline EtDs

Product	WHO EML application criteria [10]	Guideline EtD criteria [7–9]
Decision criteria	• Public health relevance (item 8 of the standard application form).	• Is the problem a priority?
	• Review of benefits: clinical evidence, summary of available data and summary of available estimates of comparative effectiveness (item 9).	• How substantial are the desirable and undesirable anticipated effects?
	• Review of harms and toxicity: estimates of total patient exposures, description of adverse events and estimates of their frequency, summary of available data, summary of comparative safety against comparators, identification of variation in safety that may relate to health systems and patient factors (item 10).	• What is the overall certainty (quality) of the evidence of effects (following GRADE criteria)?
	• Summary of available data on comparative cost and cost-effectiveness of the medicine (item 11).	• Is there important uncertainty about or variability in how much people value the main outcomes?
	• Summary of regulatory status and market availability of the medicine (item 12).	• Does the balance between the desirable and undesirable effects favour the intervention or the comparison?
	• Availability of pharmacopoeial standards (item 13) (also referred to as prequalification and manufacturing standards).	• How large are the resource requirements (costs)?
		• What is the certainty (quality) of the evidence of resource requirements (costs)?
		• Does the cost-effectiveness of the intervention favour the intervention or the comparison?
		• What would be the impact on health equities?
		• Is the intervention acceptable to key stakeholders?
		• Is the intervention feasible to implement?

2.2. Participant recruitment

We began by identifying two preliminary lists of key informants drawing from two paradigmatic expertise groups: EML experts and guideline experts. The list was developed through expert input of study authors familiar with global EML and guideline experts and online searches (google search and google scholar search: ''essential medicine list''). From this long list we categorized respondents as technical experts, methodologists, clinicians, patient advocates, and policy-makers. Additionally, we categorized by organization type, professional background, geography, gender, and racial backgrounds. Participants were recruited with attention to diversity across all of these domains to provide equitable and representative input. We used a respondent-driven sampling approach seeking additional participant referrals from all participants interviewed expanding the original list of possible experts, and continued recruitment until theoretical saturation was reached. We invited all preliminary key informants to participate using a defined e-mail script and consent form that was approved by HIREB. We followed up with key informants on at least two additional occasions, at least 2 weeks apart if they did not respond to our initial invitation. We balanced participant recruitment in the two expertise groups.

2.3. Development of interview guide and background briefing documents for participants

We reviewed key WHO documents, national EML technical documents and GRADE EtD publications to compile

Box 2 Final Themes

1. EMLs and Guidelines, the same, but different;
2. EMLs can decrease price and improve affordability and access;
3. Time lag and disconnect between guidelines and EMLs;
4. An evidence pipeline could improve coordination between guidelines and EMLs;
5. Facilitating the link between the WHO EML and national EMLs could increase alignment;

information on decision criteria and processes in EMLs and guidelines. We assessed EMLs and guideline EtD frameworks and developed an interview guide to inform key informant interviews. We generated two different background briefs for participants, tailored to their expertise and planned focus of the interview: EML or guideline oriented decision-making (available Appendix 2) [2]. We sent this background brief to participants for their reading 1 week or greater before the interview. The guideline background brief described guideline development processes, and decision-criteria across a range of guideline recommendation types (health system & public health, clinical, coverage decisions etc.) (available Appendix 3) [7−9,14,15]. Both background briefs shared the same sample EML applications to inform the discussion.

2.4. Semistructured qualitative interviews

The semistructured interview guide is available in Appendix 4. An interviewer trained at the graduate level in qualitative interview (TP) conducted semistructured open-ended qualitative interviews. Participants were asked to read the background brief shared with them in advance of the interview. The first interview was conducted to pilot the interview guide with a coauthor (LM). We debriefed and refined the interview approach, keeping the semistructured guide constant through the course of the interviews. We conducted debriefing sessions throughout the interview process with key collaborators (TP, HJS, LM, EAA, JL). All interviews were conducted via Zoom (Zoom Video Communications, California, USA) or Webex (Cisco Webex, California, USA) and video-recorded with written participant consent. Video recordings were transcribed by one investigator (TP) immediately following their completion and video recordings were retained for reference on respondent tone and context during the analysis period.

2.5. Reflexivity, interpretive descriptive coding and thematic analysis

This research was led by researchers at the MacGRADE centre (TP, HJS) in collaboration with staff from WHO Access to Medicines and Health Products Division (LM, BH). The authors have methodological involvement in guidelines, including as members of the GRADE working group, or as members of essential medicine list committees. The authorship group is primarily, but not entirely, from the global north. In keeping with reflexivity on personal privilege that may inform research perspectives, the lead researcher TP is a cisgender male, white, settler in Canada. We strive to be reflexive on position and perspective in the analysis presented.

Interviewer journaling to support reflexive analysis was conducted through each interview and reviewed with the authorship group at several stages through the interview recruitment process. One investigator (TP) uploaded the transcribed interviews into NVIVO v12 (QSR International, Melbourne, Australia). We kept an interviewing journal for reflective discussion through the progress of interviews. After the completion of three interviews from each expertise group, we began preliminary coding, using a coding methodology within NVIVO v12 [16]. We reviewed preliminary codes and preliminary themes as a research team at interim reviews, and team review was conducted to verify theoretical saturation and completion of participant enrolment (TP, HJS, LM, EA, JL). We used an interpretive descriptive inquiry methodology to explore our research question and develop our final thematic analysis for presentation [17].

3. Results

We identified 42 potential experts, invited 25 key informants and ultimately conducted 16 interviews (response rate 64%). Of the nine individuals not participating, three declined due to time limitations and 6 did not respond after three attempts to contact. Characteristics of each participant are available in Appendix 5 and summarized in Table 1. The majority of participants were male (11, 69%) and working in the WHO European region (9, 56%). However, all WHO regions were represented among participants. Interviews were a median of 41:15 minutes in duration (range 26:20 to 61:22 minutes).

We coded the 16 interviews using 64 preliminary codes at 252 locations. Codes were then classified into seven labelled categories and an ‘‘other’’ category. The table of coding frequency is available in Appendix 5. Most frequently the labelled codes related to cost-effectiveness, connection of guideline to EML, duplication of work, transparency of EML decisions, and WHO coordination.

Thematic analysis of coded quotes yielded five themes, themes 1−3 were descriptive and explained the current processes and challenges with guidelines and EMLs, while themes 4−5 were prescriptive in nature with recommendations to improve processes around EML and guidelines, and their connection. Box 2 shows the final themes identified through thematic analysis. Key quotes are presented by theme in Appendix 6.

3.1. Theme 1: EMLs and guidelines, the same, but different

The first theme includes the similarities between the objectives and processes of guidelines and EMLs. In discussing the application process and questions for the WHO EML, respondents felt there was important overlap between the EML and guideline decision criteria and multiple respondents felt the two processes needed to be more effectively interlinked. While conceived for different purposes, guidelines to inform clinical practice and decision-making, and EMLs to support procurement, purchasing, and access to medicines, their decision criteria have many

Table 1. Participant characteristics

Characteristic	Characteristic	Number	Percentage
Gender	Female	5	31%
	Male	11	69%
	Other/Not Reported	0	0%
Primary Expertise	EML	9	56%
	Guideline	7	44%
Perspective[a]	Academia	7	44%
	National EML Staff	5	31%
	National Guideline Staff	1	6%
	WHO Department	1	6%
	WHO Model List of Essential Medicine	5	31%
WHO Region of Work	AFRO	2	13%
	EMRO	1	6%
	EURO	9	56%
	PAHO	2	13%
	SEARO	1	6%
	WPRO	1	6%

[a] More than one response possible.

shared elements. Decision criteria that are shared between both guidelines and EMLs were problem priority/public health relevance, benefits, harms, and comparative cost-effectiveness.

Participants described that equity is considered as a key criterion in EtDs in guidelines, but not explicitly considered on an EML application. Medicine production and availability were considered by EMLs, but not often explicitly by guidelines. Availability of pharmacopeial standards is considered by EMLs, but not often by guidelines.

Criteria we found distinct to guideline decisions included values & preferences, equity, acceptability, and feasibility (which is implicitly considered in market availability) although decision makers integrate values implicitly when weighing desirable and undesirable effects. Criteria unique to EMLs included regulatory status and market availability, and pharmacopeial standards. Feasibility is intended to incorporate approved indications and access to the medicine in the original GRADE EtD [8]. Figure 1 visualizes the use of guideline EtD and EML

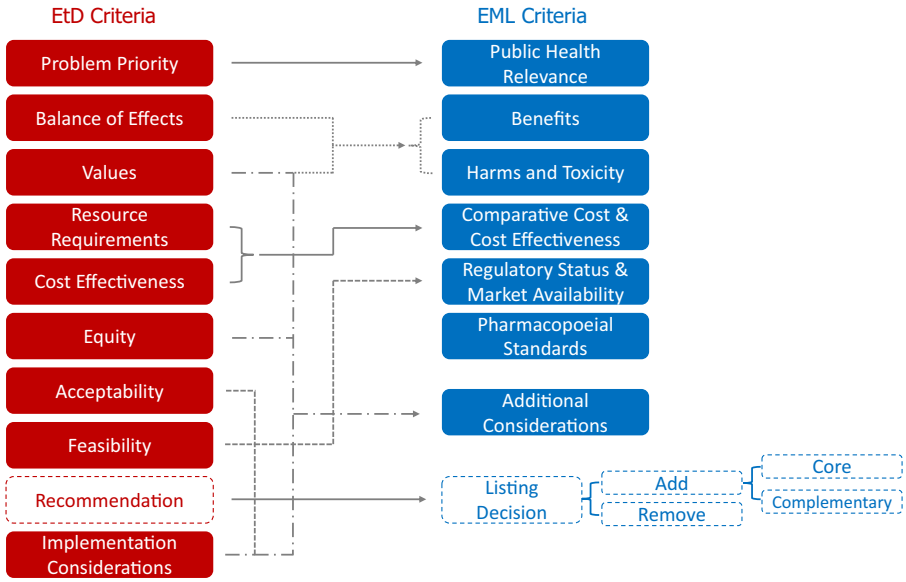

Fig. 1. Shared and distinct decision criteria for guideline EtDs and EML applications (from the WHO EML application criteria).
Figure description: this figure visualizes the decision criteria for guideline evidence-to-decision processes andEML applications. Solid lines draw connections between EtD criteria and EML criteria. Dashed lines highlight decision criteria, for a guideline this is a recommendation (strong or conditional), for an EML this is a listing decision. Listing decisions can be to add or remove a medicine from the core or complementary EML.

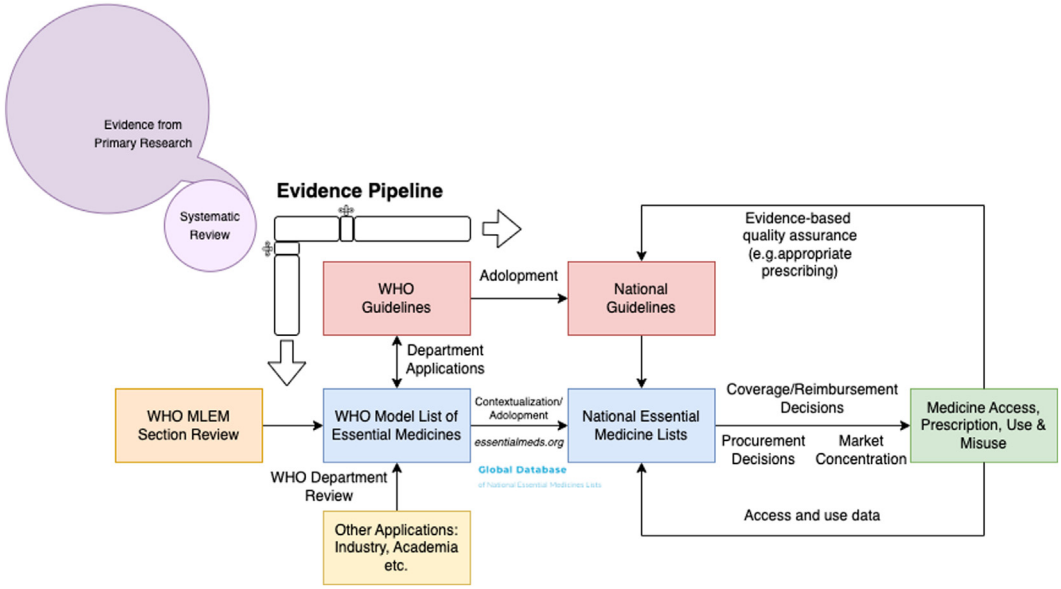

Fig. 2. A possible evidence pipeline for guidelines and EMLs.
Figure legend: Evidence from primary research is synthesized by systematic reviews. This common evidence base from systematic reviews feeds the evidence pipeline that could be applied to different purposes including guidelines at WHO or national level, and applications to the WHO EML or national EMLs. Listing at a national level ultimately impacts access, prescription, use and misuse of medicines. Adolopmentea GRADE term conceived as a contraction of adapt/adopt/de novo development refers to the EtD-based standardized process to contextualize guidance from one setting to another.

application criteria. Some respondents reflected that while explicit mention of other considerations are not listed in the application (for example health equity) they play an important role in the WHO's EML Expert Committee review assessment and are therefore important criteria. Additionally, while feasibility, which is an EtD criterion is not an explicit EML criterion, regulatory status, market availability and pharmacopoeial standards are factors impacting the feasibility of listing a medicine on an EML. Finally, the output differs, with the output of a guideline being the formulation of a recommendation (for example, clinical or public health) and an EML committee ultimately making decisions around inclusion or removal of a medicine on the list.

3.2. Theme 2: EMLs can decrease price and improve affordability and access

The second theme we identified was the unique impact that EMLs can have in improving access and affordability of medicines through focusing the market on the purchasing of a select number of essential medicines. Respondents shared that this can decrease cost by increasing demand for select priority medicines, increasing purchasing volumes, and improving negotiation opportunities for bulk purchasing. This could have significant benefits decreasing price and improving health equity in access to medicines for important health conditions. One prominent example discussed was HIV. The efforts to focus on selecting priority antiretrovirals (ARVs) for HIV led to increased quality of prescribing and focused the market on the most essential medicines, which contributed to improved access and greatly decreased cost [18].

3.3. Theme 3: time lag and disconnect between guidelines and EMLs

The third theme reflects a time lag and disconnect between the creation of guidelines and EMLs. This creates delays in the listing of medicines onto EMLs and may decrease access to essential medicines that guideline groups are recommending. Experts voiced that the 2-year time cycle for review for the WHO EML can delay the listing of new medicines recommended by guidelines. This may also be true at a country-level depending on the frequency of national EML updates. For guideline groups who may review the evidence and issue recommendations, some participants suggested that they could be given authority to add medicines to an EML directly, or after verification by a separate EML review committee. There are instances we identified, including in South Africa, where guideline groups issue recommendations directly adding/removing medicines from the national Essential Medicine List improving coordination, decreasing duplication of work, and decreasing time lag to listing medicines.

One respondent shared the 2002 WHO EML experience where the HIV guideline development group and the WHO Expert Committee on the Selection of Essential Medicines were intentionally collaborating and meeting in the same week in the same building. By the end of the week WHO's evidence-based clinical guidelines for HIV developed by the first group were fully reflected in the first list of ARVs

included in the WHO EML by the Expert Committee. Both documents were published around the same time. This example was provided as an example of thoughtful coordination to decrease the time lag to listing of essential medicines.

3.4. Theme 4: an evidence pipeline could improve coordination between guidelines and EMLs

In the fourth theme, respondents articulated specific challenges in coordinating between guidelines and EMLs. This applied to effective listing of medicines by the WHO EML, because of variable quality and frequency of applications by WHO departments and other guideline-producing bodies. Where no WHO department exists for a health condition (for example, dermatology), respondents also reflected on gaps in WHO EML listings. One specific suggestion for improved coordination within WHO and national EMLs, included overlapping representation of individuals involved in guidelines and the EML.

Respondents also suggested that an ''evidence pipeline'' for evidence synthesis could improve efficiency and coordination of guidelines and EMLs. This concept would coordinate research synthesis efforts from primary research across multiple types of health decision efforts (for example, systematic reviews, EMLs, guidelines, health technology assessments) [1]. This work to coordinate has been broadly presented previously, however, we have developed a more specific visual conceptualization of a possible global evidence pipeline for coordination of guidelines and EMLs in Figure 2.

In discussing an evidence pipeline, respondents highlighted the significant redundancy in research synthesis, including systematic reviews for practice, a multitude of guidelines, essential medicine lists, health technology assessments and other purposes. If an evidence pipeline coordinated research synthesis, the same high-quality evidence should be used across a range of areas. One respondent reflected that an improved connection between the WHO EML and national EMLs could also support the linkage of an evidence pipeline globally because international and national evidence synthesis efforts are often duplicative and not aligned.

3.5. Theme 5: facilitating the link between the WHO EML and national EMLs could increase alignment

A fifth and final theme related to linking the WHO EML listings and process with national EMLs. Research has found wide variability in national EMLs including lists that are more restrictive and not nearly restrictive enough to be ''essential'' [19,20]. One challenge repeatedly identified as driving the disconnect is capacity at the national EML level. However, even where there is capacity, sometimes there is still no comprehensive connection to the WHO EML and the evidence produced for those initial applications. This may result in duplication of work and represents an opportunity to better share evidence and decision-criteria to improve alignment and efficiency. Respondents suggested improving the quality and alignment between WHO EML and national EMLs through support for capacity in national EMLs and aligning application processes. Respondents suggested possibly creating a software solution for EML application and decisions that might support an online portal for information to be shared between stakeholders at global and national levels.

4. Discussion

In this qualitative research, we explored the processes and decision criteria informing both guidelines and selection of essential medicines. We identified important overlap in processes and the opportunity to better coordinate, both within WHO, and between other levels of health decision-making. We also identified shared and distinct decision-criteria, and an important role for both guidelines and EMLs, particularly at the WHO global level, in driving improvements in health outcomes and equitable access to essential medicines. In the current context, significant duplication of work and challenges with capacity may mean there are conditions and countries that may not be as well served by evidence-based EMLs. Our interpretive descriptive qualitative methodology offers important new areas of study for the present practice and future development of guidelines, EMLs and their interface.

4.1. Strength and limitations

Strengths of our study include the exploratory qualitative methodology in a nascent field of health evidence decision-making with an emphasis on guidelines and EMLs, which has so far been minimally explored. Another strength is the positioning of this exploratory research in the context of both guideline and EML decision paradigms. Starting from both guideline and EML decision orientations, we prepared background briefs that were tailored to each paradigm, and purposefully selected participants to inform this work from both paradigms.

Limitations of our study include reduced emphasis on national EMLs among our respondents and findings, as compared to the WHO EML. Our work was primarily driven by an examination of the WHO EML, and further work should explore differences at national levels by country and context. Additionally, the study is limited to qualitative interpretation of the case studies and historical example from interview respondents. Independent triangulation and validation of these examples is required in future research. Finally, additional work of specific applications and assessment of strategies is needed to bring alignment in decision processes between guidelines and EMLs.

4.2. Implications for practice and policy

We have identified opportunities to align decision-criteria and processes more closely between health guidelines and EMLs in practice. This includes improving coordination between WHO treatment guidelines and the WHO EML, creating an evidence pipeline to improve EML and guideline coordination and decrease duplication, and finally facilitating the link between the WHO EML and national EMLs. This ''evidence pipeline'', using similar EtD criteria to support EML applications, and contextualization tools for EMLs, warrants exploration to improve both the utility of guidelines and the impact of EMLs.

One opportunity for improving coordination between the WHO EML and national EMLs is the work that has been done for guideline adoption, adaptation and de novo development, for example, GRADE adolopment [15,21,22]. This method, where EtD frameworks produced by one guideline group are considered and contextualized by another, could decrease duplication of work, while still supporting an important contextualization process for countries that are producing their own EML and strengthen WHO EML to national EML linkages.

This work is linked to recent work we have led on the broader ecosystem for health decision-making, demonstrating synergy in the criteria between various health decision-making paradigms including guidelines and Essential Medicine Lists [1]. Future work will assess the use of EtDs to support EML applications and describe applications of this approach to real guideline and EML scenarios.

4.3. Implications for research

Further research including evaluation of strategies identified here is needed to improve coordination of guidelines and EMLs. This research should focus on evaluation at different levels of health decision-making from local/national guidelines and EMLs to a global context; the WHO should play a key role in these next steps. Methods for how to facilitate an evidence pipeline, and strategies to develop this concept are also needed. Finally, research to trace health guideline development in relation to the connection to EMLs and to bring their recommendations more closely aligned is needed for the practical application of the concepts explored here. This should include the identification of gaps where strong guidelines do not exist for important essential medicines or groups of medicines to inform guideline development and prioritization.

5. Conclusions

Despite different origins, guidelines and EMLs share many commonalities, including decision criteria and processes. We have identified opportunities to better align guidelines and EMLs. Universal and equitable access to medicines that have been classified as ''essential'', is a critical component of universal health coverage and improvements in health equity. Alignment of processes and evidence synthesis that inform guidelines and EMLs is important to improve transparency, efficiency, and evidence-based decision-making to unite towards their shared objective: improvements in health through universal access to evidence-based treatments.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jclinepi.2022.12.007.

References

[1] Schunemann HJ, Reinap M, Piggott T, Laidmäe E, Köhler K, Põld M, et al. The ecosystem of health decision making: from fragmentation to synergy. Lancet Public Health 2022;7(4):e378−90.
[2] Selection of essential medicines at country level: Using the WHO model list of essential medicines to update a national essential medicines list, ed. World Health Organization.. Geneva, Switzerland: Medicines Selection, IP and Affordability Team, WHO Headquarters; 2020.
[3] Bazargani YT, Ewen M, de Boer A, Leufkens HG, Mantel-Teeuwisse AK. Essential medicines are more available than other medicines around the Globe. PLoS One 2014;9:e87576.
[4] Wirtz VJ, Hogerzeil HV, Gray AL. Essential medicines for universal health coverage. Lancet 2017;389:403−76.
[5] Moucheraud C, Wirtz VJ, Reich MR. Evaluating the quality and use of economic data in decisions about essential medicines. Bull World Health Organ 2015;93(10):693−9.
[6] Gray AL, Wirtz VJ, t Hoen EF, Reich MR, Hogerzeil HV. Essential medicines are still essential. Lancet 2015;386:1601−3.
[7] Alonso-Coello P, Oxman AD, Moberg J, Brignardello-Petersen R, Akl EA, Davoli M, et al. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 2: clinical practice guidelines. BMJ 2016;353:i2089.
[8] Alonso-Coello P, Schünemann HJ, Moberg J, Brignardello-Petersen R, Akl EA, Davoli M, et al. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 1: Introduction. BMJ 2016;353:i2016.
[9] Parmelli E, Amato L, Oxman AD, Alonso-Coello P, Brunetti M, Moberg J, et al. GRADE evidence to decision (EtD) framework for coverage decisions. Int J Technol Assess Health Care 2017;33(2):176−82.
[10] WHO medicines strategy: Revised procedure for updating WHO's Model List of Essential Drug. Geneva, Switzerland: World Health Organization; 2001.
[11] Cappello B, Moja L, Figueras A, Magrini N. The ''square box'': therapeutic Equivalence as a Foundation of the WHO model List of essential medicines. Front Pharmacol 2020;11:578000.
[12] Welch C. The composition of WHO's expert committee on essential medicines needs more scrutiny. BMJ 2014;349:g5211.
[13] Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int J Qual Health Care 2007;19:349−57.
[14] Moberg J, Oxman AD, Rosenbaum S, Schünemann HJ, Guyatt G, Flottorp S, et al. The GRADE Evidence to Decision (EtD) framework for health system and public health decisions. Health Res Policy Syst 2018;16(1):45.
[15] Schünemann HJ, Wiercioch W, Brozek J, Etxeandia-Ikobaltzeta I, Mustafa RA, Manja V, et al. GRADE Evidence to Decision (EtD) frameworks for adoption, adaptation, and de novo development of

trustworthy recommendations: GRADE-ADOLOPMENT. J Clin Epidemiol 2017;81:101−10.
[16] Zhang Y, Wildemuth BM. Qualitative analysis of content. Appl Soc Res Methods Quest Inf Libr Sci 2009;308:319.
[17] Thorne S. Interpretive description: Qualitative research for applied practice. Routledge; 2016.
[18] Waning B, Kyle M, Diedrichsen E, Soucy L, Hochstadt J, Bärnighausen T, et al. Intervening in global markets to improve access to HIV/AIDS treatment: an analysis of international policies and the dynamics of global antiretroviral medicines markets. Global Health 2010;6(1):9.
[19] Persaud N, Jiang M, Shaikh R, Bali A, Oronsaye E, Woods H, et al. Comparison of essential medicines lists in 137 countries. Bull World Health Organ 2019;97(6):394−404C.
[20] Piggott T, Nowak A, Brignardello-Petersen R, Cooke GS, Huttner B, Schünemann HJ, et al. Global status of essential medicine selection: a systematic comparison of national essential medicine lists with recommendations by WHO. BMJ Open 2022;12(2):e053349.
[21] Darzi A, Harfouche M, Arayssi T, Alemadi S, Alnaqbi KA, Badsha H, et al. Adaptation of the 2015 American College of Rheumatology treatment guideline for rheumatoid arthritis for the Eastern Mediterranean Region: an exemplar of the GRADE Adolopment. Health Qual Life Outcomes 2017;15:183.
[22] Schunemann HJ, Wiercioch W, Brozek J, Etxeandia-Ikobaltzeta I, Mustafa RA, Manja V, et al. GRADE Evidence to Decision Frameworks for adoption, adaptation and de novo development of trustworthy recommendations: GRADE-ADOLOPMENT. J Clin Epidemiol 2016;81:101−10.