The ecosystem of health decision making: from fragmentation to synergy

Holger J Schünemann, Marge Reinap, Thomas Piggott, Erki Laidmäe, Kristina Köhler, Mariliis Põld, Brendalynn Ens, Alar Irs, Elie A Akl, Carlos A Cuello, Maicon Falavigna, Michelle Gibbens, Luciana Neamtiu, Elena Parmelli, Mouna Jameleddine, Lisa Pyke, Ilse Verstijnen, Pablo Alonso-Coello, Peter Tugwell, Yuan Zhang, Zuleika Saz-Parkinson, Tanja Kuchenmüller, Lorenzo Moja

Clinicians, patients, policy makers, funders, programme managers, regulators, and science communities invest considerable amounts of time and energy in influencing or making decisions at various levels, using systematic reviews, health technology assessments, guideline recommendations, coverage decisions, selection of essential medicines and diagnostics, quality assurance and improvement schemes, and policy and evidence briefs. The criteria and methods that these actors use in their work differ (eg, the role economic analysis has in decision making), but these methods frequently overlap and exist together. Under the aegis of WHO, we have brought together representatives of different areas to reconcile how the evidence that influences decisions is used across multiple health system decision levels. We describe the overlap and differences in decision-making criteria between different actors in the health sector to provide bridging opportunities through a unifying broad framework that we call theory of everything. Although decision-making activities respond to system needs, processes are often poorly coordinated, both globally and on a country level. A decision made in isolation from other decisions on the same topic could cause misleading, unnecessary, or conflicted inputs to the health system and, therefore, confusion and resource waste.

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Department of Health Product Policy and Standards (L Moja MD) **and Department of Research for Health** (T Kuchenmüller MA), **WHO, Geneva, Switzerland; Michael G. DeGroote Cochrane Canada Centre and McMaster GRADE Centres, Department of Health Research Methods, Evidence, and Impact, Department of Medicine, and WHO Collaborating Center for Infectious Diseases, Research Methods and Recommendations** (Prof H J Schünemann MD, T Piggott MD, C A Cuello MD, Y Zhang PhD), **McMaster University, Hamilton, ON, Canada; Dipartimento di Scienze Biomediche, Humanitas University, Milan, Italy** (Prof H J Schünemann); **Division of Country Health Policies and Systems, WHO Regional Office for Europe, Copenhagen, Denmark** (M Reinap MA); **Department of Medicines and Medical Devices, Estonian Health Insurance Fund, Tallinn, Estonia** (E Laidmäe MSc); **WHO Country Office in Estonia, World Health Organization, Tallinn, Estonia** (K Köhler MSc); **Institute of Family Medicine and Public Health, Health Technology Assessment Unit, University of Tartu, Tartu, Estonia** (M Põld PhD); **Canadian Agency for Drugs and Technology in Health, Ottawa, ON, Canada** (B Ens MN, C A Cuello, M Gibbens MSW, L Pyke MA); **State Agency of Medicines of Estonia, Tartu, Estonia** (A Irs MD); **Heart Clinic, Tartu University Hospital, Tartu, Estonia** (A Irs); **Department of Internal Medicine, American University of Beirut, Beirut, Lebanon** (Prof E A Akl MD); **National Institute for Health Technology Assessment, Federal University of Rio Grande do Sul, Porto Alegre, Brazil** (M Falavigna MD); **Joint Research Centre, European**

Introduction

Many actors influence or make decisions at various levels using systematic reviews, health technology assessments (HTAs), guideline recommendations, coverage decisions, selection of essential medicines or diagnostics, quality improvement, and policy or evidence briefs.[1–7] We provide a brief overview of the different actors who influence or make health decisions (panel 1; appendix p 2).

The extent to which these different actors use structured processes and transparent criteria differs, and these processes and criteria are often poorly coordinated, despite a general increased interest in the intersectionality of using key evidence and how closely processes relate to each other.[6–9] Thus, the absence of broad coordination can result in duplication of efforts, inadequate use of scarce time and resources and, if decisions are not well aligned, confusion and conflicts.[10] For example, differences in recommendations between international HTA agencies for drug listing seem to occur often, due to inconsistencies in how the supporting evidence informs decisions and how domestic priorities affect approvals.[7]

In response to these gaps in coordination and recognition of mutual interests, we launched an international project aimed at improving how the evidence that influences decision making, and the actual decisions that are made, relate to each other in a coherent framework, borrowing the term theory of everything, which is the hypothetical, singular, all-encompassing, cohesive theoretical framework in physics.[11] Our goal was to lay out all-encompassing concepts of health decision making using a theoretical framework across disciplines. Through that conceptual description we aimed to analyse what bridges can exist between disciplines that go beyond already well established partnerships, such as the partnership of systematic review authors and guideline developers.

Under the aegis of WHO (Regional Office for Europe, the Country Office in Estonia, and the headquarter WHO Department of Health Product Policy and Standards), and in collaboration with the Estonian Health Insurance Fund, we brought together representatives of different areas to discuss similarities in the criteria and processes encompassing evidence evaluation across different health system decision levels. This process, beginning in 2019, was inclusive, involving key stakeholders, such as systematic reviewers, guideline developers and panelists, regulators, policy makers, and payers, whose roles were not mutually exclusive. Participants served in their personal capacity as usually requested by WHO. However, several members had recognised experience in organisations that are active in informing or making health decisions, such as the Guidelines International Network, the International Network of Agencies for Health Technology Assessment, the Professional Society for Health Economics and Outcomes Research, or the Cochrane Collaboration (appendix p 10).

We evaluated selected examples of how health-care questions about interventions are created, the factors (ie, criteria) that influence a decision, the type of evidence required, where this evidence is used, who is making recommendations and decisions, and in what context these recommendations and decisions are being made. We used case studies from Estonia on the use of direct oral anticoagulants (DOACs) and a Canadian Agency for Drugs and Technology in Health (CADTH) case study on dialysis (appendix pp 11–19), during large and small group sessions in a 2-day workshop to identify what elements substantially apply to all types of decision making, regardless of intervention, population, or topic.

Commission, Ispra, Italy (L Neamtiu PhD, E Parmelli PhD); **Health Technology Assessment Department, National Authority for Assessment and Accreditation in Healthcare, Tunis, Tunisia** (M Jameleddine PharmD); **Research and Development, International Affairs, National Health Care Institute, Diemen, Netherlands** (I Verstijnen PhD); **Iberoamerican Cochrane Center, Biomedical Research Institute Sant Pau-CIBERESP, Barcelona, Spain** (P Alonso-Coello MD); **Centro GRADE Barcelona, Barcelona, Spain** (P Alonso-Coello); **Department of Medicine, University of Ottawa, ON, Canada** (Prof P Tugwell MD); **Health Technology Assessment Agency, Instituto de Salud Carlos III, Madrid, Spain** (Z Saz-Parkinson PhD)

Correspondence to: Prof Holger J Schünemann, Michael G DeGroote Cochrane Canada Centre, McMaster University Health Sciences Centre, Hamilton, ON L8S 4K1, Canada
schuneh@mcmaster.ca

See Online for appendix

Panel 1: The different actors who influence or make health decisions

Regulators

Regulators for medicines and medical devices play an important role in the review of evidence in advance of approval for a medical treatment. Regulatory agencies include, for example, the US Food and Drug Administration and the European Medicines Agency. Regulatory agencies require drug or device manufacturers to submit evidence from investigational treatments, pre-clinical review, clinical review, and drug approval for manufacturing and use in the jurisdiction they are responsible for.[12–14] Regulators also play a role in assessing risk (eg, from environmental exposures or food).

Systematic review authors and organisations coordinating these activities

Systematic reviews have increased since their origins in the 1970s. Systematic reviews are now prevalent and influential publications to support health decision making.[15] Organisations like the Cochrane Collaboration have supported the coordination and methodological rigour of systematic reviews worldwide. A systematic review begins with a predefined protocol, includes a systematic literature search, screening, and study selection, and then qualitative or quantitative synthesis of findings. Systematic review methodology is used in health technology assessment (HTA) and systematic reviews informing decision criteria such as benefits and harms of an intervention, values associated with outcomes, and other factors inform decisions in guidelines, quality improvement, listing of essential medicines, and policy making.

HTA agencies

HTA "uses explicit methods to determine the value of a health technology at different points in its lifecycle. The purpose is to inform decision-making in order to promote an equitable, efficient, and high-quality health system".[1] HTA supports coverage, reimbursement decisions and other types of decisions (eg, technology management, optimisation, health system organisation, service delivery).[2] Many organisations including CADTH, UK NICE, HITAP (Thailand), CONITEC (Brazil), INEAS (Tunisia,) and networks like EUNetHTA, among others, support the assessment of health technologies using varied criteria considering effects, costs, and other factors.[10] There is emerging evidence that HTA agencies use similar criteria to guidelines in addressing uncertainty in effectiveness assessment.[16]

Guideline developers

Guidelines can be defined as systematically developed evidence-based statements that assist providers, patients, policy-makers and other stakeholders to make informed decisions on health care and public health policy.[3–5] A variety of respected institutions have developed standards for trustworthy guideline development.[3–5,17–20] The GRADE working group developed evidence-to-decision frameworks, an approach to structured reflection that can help stakeholders making decisions for different types of health interventions be more systematic and explicit.[17,21–25]

Coverage decisions makers

Coverage decisions are decisions by competent authorities or third-party payers (public or private health insurers) about whether to reimburse, and how much to pay, for medicines, tests, devices, or services, and under what conditions. Decisions are made at national, regional, or local levels, depending on the type of interventions and the way health services are paid for in a country. Reimbursement decisions are based on several criteria, such as eligibility for priority diseases, effectiveness, safety, or special status of some medicines (eg, generic substitution).

Essential medicines and diagnostics decision makers

Essential medicines are defined as medicines that "satisfy the priority health care needs of the population".[26] The Model List of Essential Medicines, produced by WHO since 1977, prioritises medicines, identifying the most effective therapeutic options in each disease area. This list represents the bare bones of what a health system should provide access to and is intended to serve as the country's basis for selection, procurement, supply of medicines, reimbursement schemes, medicinal donations, and in the development of their own national lists of essential medicines.[27] Essential diagnostics follow a similar trajectory.[28]

Quality improvement actors

The development of measurable targets, quality assurance, or performance measure targets is crucial to assessing progress in the implementation of health decisions. The development of effective quality indicators that are appropriately linked to health recommendations and accredited to ensure adherence is crucial for the improvement of health-care outcomes. Quality indicators are measurable items referring to structures, processes, and outcomes of care.[29] Ideally, the development of quality indicators should be grounded in evidence-based health-care recommendations, derived from trustworthy guidelines.[30]

Evidence-informed policy makers

Evidence-informed policy making is an approach aiming to ensure that policy decision making is informed by the best available research evidence. Evidence-informed policy making includes systematic and transparent processes for articulating global and local evidence as a valuable input to local decision making.[31] WHO established the Evidence-informed Policy Network as a global network that develops and fosters country capacity in knowledge translation. Other networks are focused on specific evidence areas, such as the Rx for Change, which covers behaviour change in health care,[32] or are collaborative efforts by specific groups, such as the Science Advice for Policy by European Academies.[33]

CADTH=Canadian Agency for Drugs and Technologies in Health. NICE=National Institute for Health and Care Excellence. HITAP=Health Intervention and Technology Assessment Program. CONITEC=National Commission for the Incorporation of Technologies. INEAS=National Authority for Assessment and Accreditation In Healthcare. GRADE=Grading of Recommendations Assessment, Development and Evaluation.

This workshop was followed by review and input from additional targeted individuals with expertise in the areas of interest. Our aim was to describe the health decision-making disciplines, the criteria used, the commonalities, the differences, and the implications for practice and research, and suggestions for how to move forward.

Health decision-making background

A commonality across the different disciplines is the formulation of questions using the population, intervention, comparison, and outcomes (PICO) approach.[34] Although derivations of the PICO approach exist, almost all questions dealing with interventions or management decisions can be brought back to this basic framework. The PICO pillars should be described in detail and could differ slightly from actor area to another (eg, the population might be broader or narrower) when referring to similar bodies of evidence. The PICO approach has gained acceptance because it provides a clear structure and definition of what the question of interest is. For example, in our case example from Estonia (appendix p 11), the population is defined as people with atrial fibrillation, the intervention is the use of DOACs, the comparison was the use of DOACs following a trial of the less expensive warfarin, and the outcomes were stroke, bleeding, and other people-important outcomes (eg, arterial thrombotic events). The clear definition of the PICO elements not only facilitates understanding the question and searching for and including evidence, but also allows for understanding reasons for heterogeneity in study findings and the generalisability or applicability of studies.[35–37]

Primary research and systematic reviews

To be evidence-based, all disciplines should have primary research as a basis for influencing recommendations or decisions. As we will describe, for decision making beyond regulation, which is often based on single studies and focused on avoiding harmful interventions or exposures, primary research should be synthesised through transparent and impartial methods reflected in the tenet of systematic reviews.

Systematic reviews synthesise what is known about any of the criteria in a decision process, the actual processes used to make decisions, improvement in methodology, and so forth. We view the approach to systematic reviews as a method to systematically identify research and other evidence, and as the main way to provide the least biased evidence to support all of the disciplines that we discuss here, as a source to support the processes applied to making decisions. For example, a systematic review is necessary to obtain the best evidence on how people value health outcomes (eg, through a review of evidence on values or utilities).

Panel 2: **GRADE questions to consider when deciding to recommend or reject an option[38]**

- Are the expected health benefits greater than the harms or vice versa (including considerations about the priority and severity of the problem, the effects of the intervention, and the values people place on the outcomes)?
- What is the magnitude of the resource requirements (and associated cost) related to the intervention or strategy, and is it cost-effective?
- What is the effect of the intervention or strategy on equity, including societal implications and environmental impact?
- Is the intervention or strategy acceptable to different stakeholders, in particular patients or people affected by a condition, their caregivers, and their health-care providers (including ethical and other considerations)?
- Is the intervention or strategy feasible (including health-system, social, legal, political, and other considerations)?
- Are you certain about the estimates of effects, associations and other evidence informing the decision criteria (including considerations about the certainty of the evidence for all of the criteria)?

GRADE=Grading of Recommendations Assessment, Development and Evaluation.

Ideally, all available research evidence that is used when applying the criteria that influence a decision should be the result of a systematic review, including data about the problem that is being addressed (eg, baseline risk or prognosis, benefits and harms of an intervention, values, cost). Systematic reviews are also useful to evaluate equity, feasibility, and acceptability of interventions.

Factors influencing a recommendation or decision

To identify model examples of factors influencing decisions, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) evidence-to-decision (EtD) frameworks served as a starting point for different types of recommendations and decisions in clinical practice, public health, coverage decision, and health policies. The questions proposed by GRADE to guide decision makers are simple and can be tailored to the type of decision (panel 2).[21,22,39] This approach has been used in thousands of recommendations; for example, in the context of recommendations of drugs for the prevention and treatment of venous thromboembolism, recommendations for breast cancer screening, recommendations about the global COVID-19 pandemic, and WHO recommendations for the management of tuberculosis.[17,21,40–45]

EtD criteria across disciplines

We outline a unifying overview of the bridging of decision-making approaches across disciplines of health

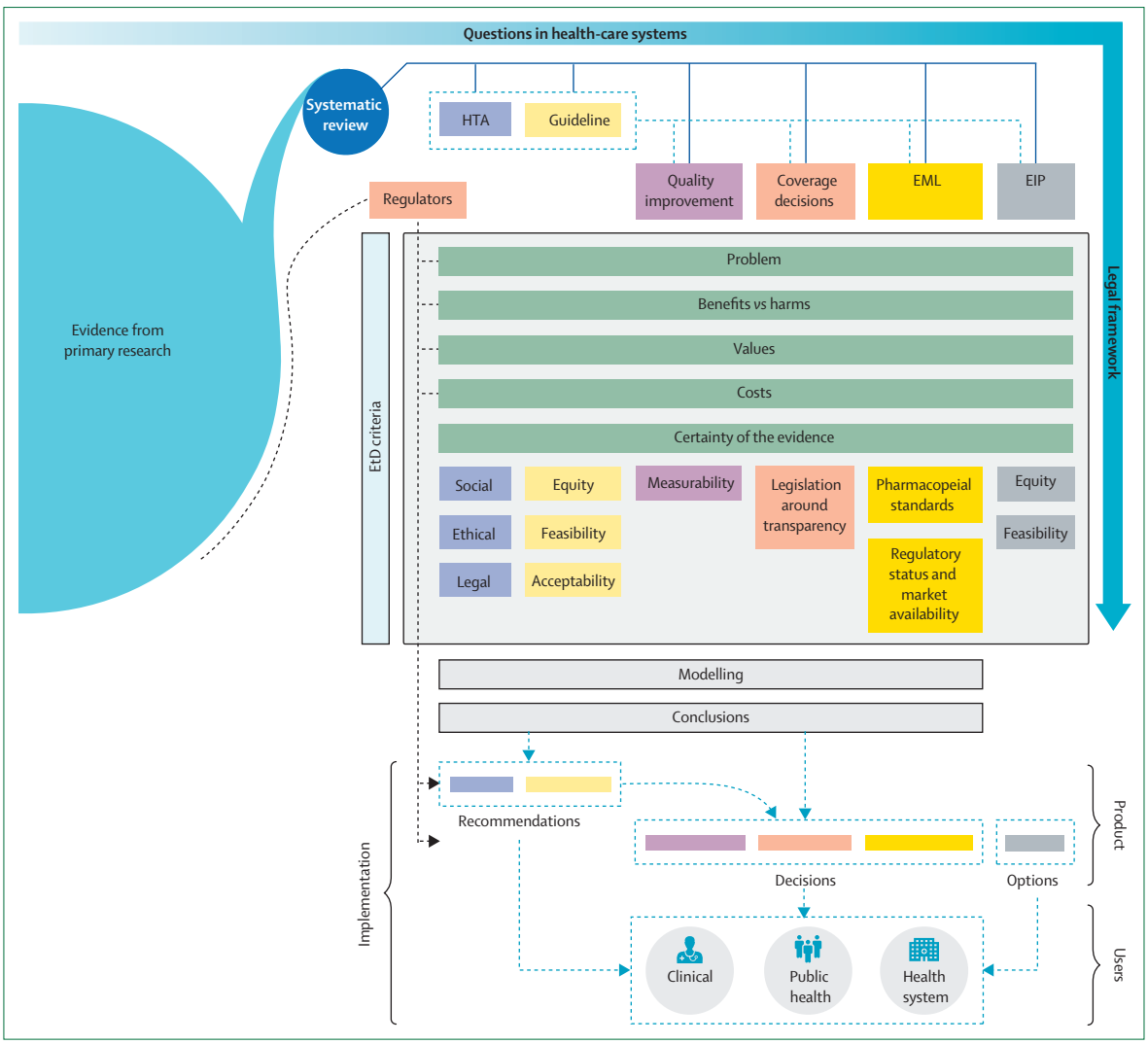

Figure: **The interconnectedness of health decisions across disciplines**
Actors in the health decision-making ecosystem formulate questions following the PICO approach. Evidence from primary research is synthesised in systematic reviews, a methodology that is applied in any of the disciplines that are involved in decision making: HTAs, guidelines, quality assurance and improvement, coverage decisions, EML decisions, and EIP making. Regulators, including those in the field of environmental health and risk assessment, often use one or a few studies (in early phases of evidence assessment), but might rely on systematic reviews depending on the regulatory context and the available evidence. All of the disciplines have the EtD criteria in common, focusing on the problem, health benefits and harms, values (or utilities in the health economy context), costs, and the certainty in the evidence on those criteria. Criteria that are more strongly linked to context are often overlapping within disciplines (eg, cost, feasibility), and across disciplines (eg, equity, ethics, acceptability), and could require emphasis depending on the decision-making actor and perspective. Criteria are broadly summarised under social, ethical, legal, feasibility, acceptability, standards, and equity headings. Legal frameworks could prescribe which criteria are relevant for decisions, or which criteria must be considered in jurisdictions. All disciplines use some degree of modelling, from very simple to complex models, to understand the consequences. For example, a simple model is applying relative effect estimates to baseline risks to derive absolute effects or calculating confidence intervals. Other disciplines use complex approaches and include modelled cost–benefit analyses and Bayesian statistics. Groups or organisations then make recommendations (in guidelines and in some HTA efforts). Products include the recommendations, decisions, or options described by the various actors. Recommendations from HTAs and guidelines are either directly used by decision makers in the clinical, public health, or health system (the users') context. Other disciplines (eg, coverage decisions or a national EML) make decisions either directly or based on the recommendations of HTA and guidelines. These decisions are implemented by health professionals and at the system level. Evidence-informed policy tools lay out contextualised options (rather than making specific recommendations). Implementation can take place in the context of research which, together with new evidence, completes the evidence generation and synthesis cycle in the updates of decisions. EML=essential medicines list. EIP=evidence-informed policy making. EtD=evidence-to-decision. HTA=health technology assessment.

decision making (figure). We refer to a discipline as a specific branch of knowledge and practice of actors that make health decisions. In the following sections we will summarise decision criteria and processes that the included actors use.

Regulation

The regulatory approval process is highly monitored and stringent to protect the public against unsafe treatments. The evidence review process might vary on the basis of priority, including, for example, regulatory

review during the COVID-19 pandemic when fast tracking and emergency use authorisation enabled quicker regulatory review.[46] Regulatory review is usually the first form of evidence review for medicines, but might not be cumulative, as it is often based on one or two clinical trials funded by pharmaceutical companies. Often, regulatory agencies have an active role in trial design, for instance, in defining outcomes of interests and relevant comparators, to ensure a trial will answer relevant questions for regulatory approval. The decision criteria primarily focus on harms, health benefits, and systems in place for pharmacovigilance for post-marketing surveillance of drugs. Cost might be considered for regulation regarding market authorisation. Over the past two decades, a number of initiatives have been established to bring HTA and regulatory approval processes in closer alignment both nationally and internationally.[47] For example, a systematic review suggested improvement in the interaction between regulatory bodies and HTA bodies over time (eg, through early dialogue and parallel submission for review).[9] In Australia, Europe, the UK, and the USA, pharmaceutical companies, regulators, and HTA agencies participate in information exchange platforms that are aimed at reducing duplications, determining assessment requirements, and discussing potential divergences.[9,48–50] The European Medicine Agency (EMA) released guidance for EMA–HTA parallel scientific advice procedures in an effort to harmonise processes.[51]

Health technology assessment

HTAs use not only systematic review methods, but also modelling; for example, to explore whether interventions are cost-effective, which emphasises the role of health economists. HTAs might use modelling to draw conclusions and make recommendations to stakeholders, typically stemming from a process involving multidisciplinary expert panels. The model inputs, however, should preferably result from a systematic review. Cost-effectiveness analysis, based on these models, is used to compare the costs and outcomes of alternative policy options and as an informative tool in assessing value for money. Cost-effectiveness ratios and thresholds could be used alongside affordability, budget impact, feasibility, and other important contextual criteria.[52,53] However, using thresholds as isolated decision rules can lead to wrong decisions being made.[52] Indeed, depending on the decision-making context, HTAs often consider societal, ethical, or legal contexts.[54] However, HTAs differ from guideline development.

Guidelines

The input from systematic reviews or HTA reports is used in multidisciplinary group processes to find agreement through formal or informal consensus processes, including voting, about the interpretation of evidence according to criteria that could influence a decision. Criteria that are related to HTAs and other disciplines include equity, feasibility, and acceptability, which include multiple facets as described in the guidance to the use of EtD frameworks by the GRADE working group and others.[21–23,55] Considerations about ethics (under values, equity, and acceptability) and legal aspects (under feasibility and acceptability) are included in these EtD frameworks. A difference between guidelines and HTAs is how the decision makers consider the precise balance and weight of the different criteria. HTAs often lead to coverage decisions with a focus on the results of economic evaluations, whereas guidelines make recommendations with a focus on health benefits and harms, relying on formalised consensus judgments and contextual factors.[56] We define contextualisation of guidelines as the need for dialogue and formal consideration of the local best available evidence and criteria for adoption, adaption, or de novo creation of recommendations from an existing trustworthy guideline to a national, local, or other level. Considerations should be made to decide whether these recommendations are right for that setting and modifying or adding to the recommendations to optimise their implementation using structured and transparent processes. HTAs and guidelines can involve a broad group of stakeholders but often differ in who initiates them (eg, industry for HTAs and professional societies for guidelines).[57] The case study (appendix p 11) from the Estonian Health Insurance Fund describes the interplay between systematic reviews, HTAs, guidelines, and coverage decision making. Another example comes from the alignment of HTAs and guideline development in Brazil, a middle-income country where the Ministry of Health now promotes synergy between HTAs and guideline production after a period of independent development within the same ministry.[58]

Coverage decisions

Processes and criteria used for coverage decisions vary across and within countries.[59] Processes and criteria are often the result of an HTA or a guideline process by considering similar factors and, thus, have become more systematic. However, the type of conclusion drawn from a coverage decision process differs from HTAs and guidelines; the conclusions are typically decisions and not recommendations. These decisions often include the following alternatives: do not cover; cover with evidence development; cover with price reduction; restricted coverage (with conditions); or cover for all indications and populations.[23]

Other alternatives have been proposed for coverage, including risk sharing agreements between industry and the payers and policy makers covering the intervention (volume-based or performance-based, or both), usually alongside prospective data collection of use, effectiveness,

and safety of the intervention in the health-care system, outside the context of clinical trials.[60] Some regulatory agencies blend approval, HTAs, and coverage decisions (eg, the Italian Medicines Agency). The Italian Medicines Agency agency conducts its own HTAs and uses these assessments in decisions about coverage and reimbursement of medicines.

Essential medicines and diagnostics

Regardless of the level at which essential medicine lists operate (eg, national or international), there are common principles that should be applied in the evidence-based selection of medicines and diagnostics to prioritise the most effective and most important medicines. Dimensions that should inform addition or rejections of medicines are: assessing benefits and harms; defining the therapeutic role through best available guidelines; considering resource implications, comparative costs, and cost-effectiveness; addressing potential conflicts of interest; and ensuring transparency in decision making. Evidence synthesis and its critical appraisal have a central role in recognising the value of a medicine.

At WHO, a multidisciplinary committee with evidence appraisal skills serves to reflect the overall health-care process and a rigorous scientific approach. The criteria used to make decisions on whether or not to list a medicine on the WHO Essential Medicines List (WHO EML) include: public health relevance, review of benefits, review of harms and toxicity, summary of available data on comparative cost and cost-effectiveness of the medicine, summary of regulatory status and market availability of the medicine, and availability of pharmacopoeial standards.[27] WHO has reinforced the links between guideline development groups' recommendations and the evaluation of medicines that lead to listing in the WHO EML, and medicine procurement agencies, such as UNICEF, or vertical programmes such as the Stop TB Partnership (eg, in the treatment of tuberculosis). Decisions about which medicines are essential are made in a broad context that encompasses the intellectual property status of patented medicines already included on the list, and new candidates for the WHO EML for low-income and middle-income countries (LMICs), as well as procurement conditions. For example, essential medicines can be prioritised for voluntary license negotiations with patent holders.[61] These public-health oriented agreements are aimed at increasing access to these medicines in LMICs, generating generic competition, and thereby reducing medicine prices.[61] Based on the WHO EML and other strategic advice, WHO prequalification prioritises medicines and diagnostics that are produced following rigorous standards of quality, safety, and efficacy to optimise the procurement of these health resources. At a country level, the uptake of a medicine in an essential medicines list could be the strict result of a coverage decision-making process that might follow or precede an HTA or guideline process.

Quality assurance and improvement

Quality improvement is a broad field. To manage and improve health, guidelines usually form the basis for the development of quality indicators, performance measures, and performance indicators.

The Agency for Healthcare Research Quality suggests considering the following factors in quality improvement: making comparisons; databases and benchmarks; trends over time; service delivery systems; unit of analysis; staff experience and user support; and costs.[62]

Selection and identification of quality indicators should be based on a systematic and transparent approach,[63] and if quality indicators are not directly derived from specific guideline recommendations, these indicators require special consideration and transparent reporting on the rationale for selection. For instance, National Institute for Health and Care Excellence (NICE) indicators generally measure outcomes that reflect the quality of care or processes linked by evidence to improved outcomes;[64] similarly, the EML is closely linked to simple metrics to improve the quality of prescribing and use of medicines at the country level.[65] Work on the linkage between guideline development and quality indicators revealed a relation between the criteria that are used to make recommendations in guidelines and the criteria that can serve to develop quality indicators, and connects the PICO and guideline development process to the identification and selection of quality indicators, performance measures, and performance indicators.[66–68]

Evidence-informed policy making

Policy debate and decision making are inherently political and are therefore anchored in political values, persuasion, and negotiation.[69] The aim of evidence-informed policy (EIP) is to apply explicit, systematic methods, and to increase transparency of the decision-making process. Thus, as for the other disciplines, evidence that is summarised using systematic review methodology should be obtained to support the use of values and resources to overcome subjectivity. Also, evidence syntheses for policy commonly assess questions related to complex interventions, focusing not only on the interventions' intrinsic benefits and harms, but also how to ensure better results through adequate contextualisation with intervention adaptations (if needed) and effective implementation.[70] According to the European Evidence-Informed Policy Network manual for developing EIP, the criteria and considerations related to choosing among options are feasibility, the possible effects (eg, benefits and harms), equity, cost, cost-effectiveness, and implementation considerations, which describe the strategies to overcome barriers and assist facilitators in implementing the options.[71] This evidence also can be summarised using systematic review methodology.

Approaches to integrating evidence and judgments

Multicriteria decision analysis and modelling to arrive at answers

Most decision-making processes involve the consideration of multiple criteria and modelling of options to derive the greatest net desirable consequences, which include the results of considering multiple criteria relevant for a given decision-making process (figure).[72] Models can be defined as a mathematical framework representing variables and their inter-relationships to describe observed phenomena or predict future events in health-related disciplines and are typically used in multicriteria decision analysis (MCDA).[73,74] MCDA is a varied methodology for assessing complex issues across disciplines with greater application in economics. The application of MCDA has been broad in health care, with wide variability in the criteria and steps used. MCDA primarily addresses the costs and benefits of options available to decision makers and could include stakeholder input. A systematic review of the use of MCDA suggested that between three and 15 criteria are used in benefit–cost evaluations with health outcomes and cost-effectiveness is commonly used.[75] For instance, WHO published a catalogue of 12 families of bacteria that pose the greatest threat to human health.[76] The list was developed using a MCDA technique in which criteria for selecting pathogens were judged by experts. However, the processes of how MDCA is used (eg, in HTA) to arrive at decisions currently differs between organisations, to varying degrees.[72,77]

Consideration of the results of theoretical modelling leads to conclusions that are made in the form of recommendations or decisions (eg, the use of models to derive WHO recommendations for cervical cancer screening).[78,79] In addition, public-health decisions are made on the basis of resources available following a process of multicriteria optimisation. If a recommendation cannot be implemented in some regions or countries due to scarcity of resources, even if an HTA appears favourable, an adapted solution could be proposed. For example, a recommendation might suggest a screening test every *x* years; however, due to scarcity of resources, a country might decide to implement a pragmatic recommendation to test every *x*+2 years.

Laying out options without modelling

For some decision makers, modelling is beyond scope or not (politically) desirable or feasible. Laying out the alternative options, including their potential effectson desirable and undesirable consequences is an approach that is used particularly in EIP making, but also in guidelines.[80] For instance, the WHO antimicrobial stewardship toolkit for implementation in LMICs is a stepwise approach on doing and measuring antimicrobial stewardship resource-stratified activities.[81] The problem with this approach, being quantitative or qualitative, is that it might not be transparent or clear—if not described in an EtD or other multi-decision criteria analysis frameworks—which factors were used or weighted to arrive at a decision.

Drawing conclusions: making recommendations and decisions

Recommendations

A recommendation in the health context is broadly defined as an actionable statement for the best course of action, put forward by an authoritative body.[82] A guideline development group or HTA body, draws conclusions about the strength of recommendation or type of decision assessing the extent to which one can be confident that the desirable consequences of an intervention outweigh the undesirable ones. The assessment might be based on the criteria of the GRADE EtD framework in which the recommendation can be strong or conditional (sometimes called weak, discretionary, or qualified) and be issued for or against interventions or options.[21] The overlap between recommendations and decisions by various bodies is vast. For example, CADTH makes recommendations at the end of the HTA process and considers the implementation of these recommendations. The CADTH case study on home-based dialysis for the treatment of end-stage kidney disease (appendix p 14) described that the integration of recommendations in HTA and guidelines facilitated implementation and policy development of the intervention.

Decisions

Decisions differ from recommendations because decisions are binding in some form. For example, a coverage decision or policy decision will be binding for a jurisdiction, as opposed to a recommendation by a guideline panel that will be implemented depending on the individual or public-health circumstances (although they can sometimes be used in the court of law).[83,84] HTAs can be binding depending on the jurisdictional legal context. A regulator decision could provide market authorisation but this authorisation does not mean a guideline process will recommend the product strongly or even conditionally (eg, if the desirable consequences do not outweigh the undesirable consequences). In our case example from Estonia (appendix p 11), DOACs in atrial fibrillation had a favourable risk–benefit ratio, acceptable cost-effectiveness compared with warfarin, but excessive effect on budget, and the resulting recommendation was conditional rather than strong for DOACs, and was conditioned upon a trial of warfarin, a less expensive alternative. Price negotiations then allowed for a reduction in the effect on budget, and subsequent implementation of the recommendation (ie, use of DOACs without a trial of warfarin).

Influence of legal frameworks

National or regional legislation will inform how decisions are made. Systematic reviews, HTAs, and guidelines

Panel 3: **Solutions to overcome fragmentation among health decision makers**

- Recognise that the criteria for decision making are similar across all disciplines, not only within clusters (such as health technology assessment [HTA], regulators and drug developers, or HTA and guideline developers)
- Agree on the importance of declaring and managing conflict of interest
- Agree on conceptual underpinnings including problem or populations, interventions, comparisons, and outcomes (PICO) questions; primary research evaluation; and methods of systematic reviews to provide the common ground and foundation for decision making
- Conduct collaborative priority setting for PICO questions across actors in the health decision ecosystem
- Agree on health outcome definitions and measurement
- Agree on essential criteria for decision making: the problem (including burden of disease), health benefits and harms (including burden to recipients) of an intervention or exposure, values and utilities, costs, and the certainty of evidence
- Agree on standardised approaches to presenting information (eg, how benefits and harms of interventions are described and reported in living and other evidence synthesis)
- Describe evidence used that informs judgments on essential and other criteria in transparent ways and make this information available for other actors in the ecosystem
- Agree on criteria that are linked to context and recognise that they are overlapping and could require emphasis depending on the decision-making actor and perspective (eg, summarised under social, ethical, legal, feasibility, acceptability, standards, and equity headings)
- Agree on key domains for rating the certainty of evidence for intervention effects and other criteria that determine decision making
- Agree on assessing the trustworthiness of a model and how conclusions are drawn to arrive at recommendations or decisions

could, or could not, be influenced by legal considerations whereas other types of decisions will be made considering the legal framework that prescribes decision making, but in theory the criteria could be independent of legal frameworks. Guideline recommendations and HTAs could be used to change or alter legal constraints. For example, laws might provide the right to access (eg, to an intervention) or regulate the details of health service provision.

Perspective taken

Decision makers should specify the perspective they are taking. For example, a clinical practice guideline development group might take a patient perspective or a population perspective. Coverage decisions and other policy level decisions usually take a population perspective or systems perspective. The type of perspective taken will influence the approach to decision making, and type of decisions being made. For example, less emphasis is placed on economic consequences or the effects on equity that an intervention has when a patient perspective is taken in a guideline, and these are two factors that must be considered when a population or public health perspective is taken, as described in detail in articles about EtD frameworks and elsewhere.[17,21,85] Many national guideline developers (eg, NICE) consider cost-effectiveness in guidelines from a population perspective, but increasingly, professional societies, a major contributor to clinical guidelines, are taking a population perspective by considering cost-effectiveness.[86] For example, despite the absence of important harms and suggestion for small population benefits, the American Society of Hematology conditionally recommended against the use of graduated compression stockings for long distance travellers without risk factors because it was not cost-effective, and there were concerns about inequity because of out-of-pocket expenses.[42] However, the guideline group remarked that individual patients could opt to use compression stockings depending on the value they placed on the outcomes, and whether they could pay for the device. In our case study from Estonia, the system perspective taken by the guideline committee led to a conditional rather than a strong recommendation for DOACs. DOACs were judged to be cost-effective but had unfavorable budget impact (appendix p 11).

Implementation

Implementation of the recommendation or decision will differ on the basis of the context and type of stakeholder. For example, a systematic review might be used by a clinician to directly inform a decision based on net health benefits (eg, the use of aspirin in acute myocardial infarction). An HTA agency could have direct influence on coverage decisions, sometimes made by the same entity. A guideline recommendation might be used to inform a therapeutic decision with a single patient or a public-health decision on a population level. A decision regarding an essential medicines list at a country level will be made by a national body, often using suggestions from the WHO EML. Implementation considerations should specify key concerns about the feasibility and acceptability of the intervention, strategies to address those concerns, and any important information about how to implement the intervention, particularly for complex interventions.[21] Thus, depending on the criteria used for making a decision, discrepancies, both warranted and unwarranted, could exist between the WHO EML and national essential medicines lists. In most settings, decisions are made after recommendations are reviewed by national agencies, including ministries

of health or committees that include broad representation of stakeholders, including the government and insurances. For example, in France, the Haute Agence de la Santé provides recommendations that are considered for pricing and reimbursement decisions. Decisions are made at the national insurance fund level and the pricing decision is made at the ministry of health level. These entities collaborate and work together in a fluid and systematic way but ultimately, HAS makes scientific decisions, and the other stakeholders make policy decisions. In our two case examples, the recommendation of DOACs for atrial fibrillation, the reduction in prices from the Estonian Health Insurance Fund, and implementation strategies for haemodialysis in Canada resulted from a multidisciplinary approach and use of decision criteria that were aligned between the different actors. These decision makers followed transparent decision-making processes that built on the scientific evaluations preceding those decisions and included similar criteria.

Conclusion

This Health Policy paper presents a first attempt at bridging criteria for decision-making processes across disciplines, that have not all been sufficiently interacting with each other, by reviewing the different processes each discipline uses and trying to find a common ground. These different disciplines have commonalities, but there is also the use of different terminology which requires clarification across disciplines to bridge the gap and create collaboration, allow for evidence sharing, and allow for better mutual recognition (figure).[87] We summarise some solutions to overcoming fragmentation, to create bridges between actors in the health decision ecosystem (panel 3).

PICO questions, primary research evaluation, and methods of systematic reviews provide the common ground preceding frameworks for decision making. Given the similarity of the criteria used for decision-making, despite alternative use of terms, it is evident that the disciplines relate to each other and should build on each other. For example, all disciplines aim to build decisions on the best available evidence regarding the considered options. We suggest agreeing on the concepts of the role of evidence from primary research, and systematic review methods to synthesise this evidence across criteria used by the disciplines (figure). Setting priorities together for evidence synthesis could foster collaboration.[42] In addition to transparent methods for priority setting,[88] we also suggest that there should be agreement on core criteria. Core criteria include the problem (including burden of disease), health benefits and harms (including burden to recipients) of an intervention or exposure, values, costs, and the certainty of evidence. Criteria that are linked to context are often overlapping and could be prioritised depending on the decision-making actor and perspective. These criteria are broadly summarised under social, ethical, legal, feasibility, acceptability, standards, and equity headings.[54] Agreement on assessing the trustworthiness of a model and how conclusions are drawn to arrive at recommendations or decisions have been described by the GRADE working group and others, and are transferable.[17,21–23,73]

Beyond terminology, conceptual ideas such as the Standardized Outcomes Linking Across Stakeholders system and hub-and-spoke model for direct core outcome measures in health care, provide individual components for creating the bridges.[89] The concept describes how the different actors could agree on outcomes that matter to people affected by interventions to bridge research, evidence synthesis, and decision making.

Operationalising the bridge between different actors must include contributions that clarify other concepts, such as methods of systematic reviews, including rapid systematic reviews, or approaches to rating the certainty of evidence. Standardisation of the way in which the benefits and harms of interventions are described and presented in evidence synthesis will allow for use across actors. Similarly, process issues, such as conflict of interest declarations and management, is relevant for all disciplines but not considered appropriately by all. Nevertheless, there will be similarities that have merits and should be identified. For example, recognition of both financial and intellectual interests that can create conflicts and standardised declaration by all actors will create synergies.[90,91] Moreover, approaches to the joint or collaborative prioritisation of topics across actors through collaborative platforms that go beyond regulators, HTA, and drug manufactures should be addressed as an overarching topic. To accomplish these goals, sharing and a culture of openness and collaboration are required.[87] There are few, if any, reasons for not being open about how decisions are made. Transparency, therefore, in all of these processes, is a requirement—eg, by explicitly and publicly listing the criteria used for a decision, the evidence considered, and the deliberations and judgments made by a decision maker. This transparency will facilitate contextualisation of decisions across jurisdictions. Furthermore, considering the perspectives of patients or people living with a condition, and their active participation, is crucial for the processes we describe here, although this field requires much more effort by the various actors.

This Health Policy paper builds on the work done by groups on the articulation of decision criteria in different disciplines and on the practical experience of the stakeholders involved. Building on these selected experiences poses a potential limitation of our work as it probably does not represent all decision makers. We used two structured country case studies that were purposively selected to anchor the discussion to real decision-making ecosystems, but both case studies

were from high-income countries. We supplemented these case studies with the accomplished work in a middle-income country, Brazil, where alignment of HTA and guideline development was achieved by bringing actors together and highlighting the similarities of the processes.[58] We believe that the theory we present about how various actors use similar elements and criteria to arrive at health decisions should not differ globally, but the context that dictates how they are implemented will differ. For example, processes for aligning HTA with the national essential medicines list exist in South Africa,[92] and they could be further aligned with our theory, but the availability of resources and legal frameworks can determine a decision about a specific intervention, which will be context specific. However, harmonisation of efforts across decision makers, including regulators and international guidelines, could lead to unwanted consequences if bias or errors occur upstream. For example, omission of important research evidence or failure to mitigate conflicts of interest in an upstream HTA that is used in global guidelines, for the essential medicines list or by regulators, would have effects on all users of that HTA. Setting priorities based on cost-effectiveness also bears challenges as it might not address societal or population priorities.[52]

Our work is meant to create a stepping stone for additional efforts that aim to build bridges across these disciplines, and we encourage considerations of how the principles laid out here apply in low-income countries. Following dissemination and feedback on our work, we aim to convene a larger group of representatives of the key actors to create specific recommendations and further operationalise the theory and identifying, in more depth, the different agendas, values, goals, and legal contexts that influence the actors and create barriers.

Decision makers should be aware of the need for transparent criteria and processes for moving from evidence to implementation in different contexts. Our work focuses on the first steps to enhance the possibility for common approaches by laying out the overlap and differences. Isolated decision making without a broader view of the other decision-making actors could miss key elements—akin to missing one of the known physical phenomena in the theory of everything—about an intervention and its wider implications.

Research into joining these areas of decision making is required. This research could focus on how this framework can connect data over time to ensure claims of benefits and value are realised, and how the system should implement new interventions, in particular when considering living evidence synthesis and recommendations beyond the narrow clinical context. For example, given that all costs of implementing a technology are rarely captured in modelling, it is not clear what the best method is to retrieve the true system costs when they are not (yet) known. Could legal frameworks further support transparent data sharing, both of primary studies and synthesised evidence, or metrics and benchmarking by creating or cultivating feedback loops and approaches? Such legal frameworks could trigger reviews and modified recommendations including disinvestments and fair pricing.[93]

In conclusion, in appraising the evidence for health-care interventions, actors involved in decision-making should be aware that they do not exist with their responsibilities as single entities but as part of a complex system that has many commonalities. This Health Policy paper presents an attempt at creating bridges across disciplines that can help policy makers, integrating the wider agenda to avoid narrow, misleading decisions, that could waste resources and time by understanding these commonalities and starting to identify strategies to overcome silos.

Contributors

HJS, MR, and EL initiated the project. HJS, TP, MR, and LM contributed to the conceptualisation, writing, and revisions. All other authors contributed to conceptualising, writing, reviewing, and editing the manuscript.

Declaration of interests

HJS is cochair of the GRADE Working Group and reports honoraria from WHO. MF reports support from HTAnalyze Consultoria e Treinamento outside the submitted work. EP and LN are employed by the European Commission. All other authors declared no competing interests.

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