World Health Organization

WHO guidance on the ethics of health research priority setting

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Contents

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Abbreviations

CAM	combined approach matrix
CHNRI	Child Health and Nutrition Research Initiative
COVID-19	coronavirus disease
ENHR	Essential National Health Research
JLA	James Lind Alliance
LMIC	low- and middle-income country
PSP	priority-setting partnership
REPRISE	Reporting guideline for priority setting of health research

Glossary

Accountability	"A relationship between an actor and a forum, in which the actor has an obligation to explain and to justify his or her conduct, the forum can pose questions and pass judgement, and the actor may face consequences" [1]
Benefit	Improvement along any dimension of well-being
Distributive justice	Fairness in how resources, opportunities or other sources of advantage are allocated
Dual-use research	Research whose results or products might be misused and thereby cause harm
Epistemic injustice	Wrongs to an individual or group in terms of their treatment as knowers – this can occur when someone is treated as less credible (testimonial injustice) or because their experiences are not recognized in the dominant conceptual schemes used by science (hermeneutical injustice)
Equity	Absence of unfair, avoidable or remediable differences among groups of people, whether those groups are defined socially, economically, demographically or geographically, or by other dimensions of inequality (e.g. sex, gender, ethnicity, disability or sexual orientation)
Fair procedure	A process that is justifiable to others, including the potential producers, users and beneficiaries of health research – this typically requires a process that is accountable, transparent and inclusive
General obligations	Ethical obligations that are not dependent on one's role, history or relationships to specific others, which include, for example, the duty of non-maleficence – contrasts with special obligations
Health research	Research aimed at better understanding or improving human health broadly construed – this includes research on the social determinants of health, basic science, clinical research, epidemiology, translational research, public health, and health policy and systems research, among others
Health research priority setting	The process through which decisions or recommendations are made about what health research should be prioritized

1 Bovens M. Analysing and assessing accountability: a conceptual framework. Eur Law J. 2007;13(4):447–68 (https://doi.org/10.1111/j.1468-0386.2007.00378.x), accessed 10 March 2025.

Interested parties	The parties who have an interest in the results of the research priority setting (also called "stakeholders"), which typically fall into three categories: research producers (e.g. scientists, funders), research users (e.g. health workers, policy-makers) and research beneficiaries (e.g. patients, carers)
Project-based priority setting	A priority-setting exercise that aims to identify particular research questions or hone the design of research studies – contrasts with thematic priority setting
Proportionality	Balance between the time and resources allocated to a priority-setting exercise and the significance of the decisions being made
Qualitative equality	The elimination of power disparities among participants in an activity or process
Reciprocity	Obligations based in reciprocity that entail one party providing benefits to another who previously benefited them
Research	Any systematic investigation that is expected to generate knowledge using recognized scientific methods
Research ecosystem	The system comprising the actors who affect what research is conducted, the decision points at which allocation decisions are made, and the scarce resources that limit what health research can be conducted
Special obligations	Ethical duties that one party owes to another in virtue of their role, relationship or history – for example, physicians' and nurses' special obligations to their patients, or polluters' special obligations to those they have harmed – contrasts with general obligations
Social value	The importance of the information generated by health research (for example, due to the expected benefits to patients from the use of new knowledge about a disease) – a function of: • the likelihood that benefits result from conducting the research • the magnitude of the benefits if they were to result • the extent to which providing those benefits would reduce inequity
Thematic priority setting	Priority-setting exercises that identify broad areas of research that should be prioritized without specifying particular questions or studies to carry out – contrasts with project-based priority setting
Wasteful research	Research that has no social value – for example, because its results are not expected to lead to any benefits
Value judgement	Any judgement about what is good or bad, better or worse, or what should or should not be done

Executive summary

Health research has brought humanity tremendous benefits, but those benefits have not been evenly distributed. Enormous disparities remain built into the global research agenda. Control over what research is done remains in a small number of hands, often in high-income countries, with for-profit, non-profit and government-supported research all still disproportionately focused on conditions that affect populations that are better off. Meanwhile, the coronavirus disease (COVID-19) pandemic revealed ongoing challenges with coordinating research, avoiding duplication and ensuring that the science that is conducted is socially valuable. In the face of these concerns, there is an urgent need for those involved in health research to set priorities for that research in an ethical way.

This guidance responds to continuing calls for greater equity in health research globally. It is widely accepted that decisions about the allocation of health care are matters of ethical concern. Consequently, policies and methodologies for health-care priority setting are critiqued and revised on the basis of considerations of social justice. Likewise, it is accepted that ethics applies to the conduct of health research when it involves human participants or non-human animals. It is time for similar attention to be applied to priority setting for health research. Justice in research should begin before the research starts.

Health research priority setting is a process through which decisions or recommendations are made about what health research questions or areas should be prioritized. This broad definition encompasses activities that organizations currently call not only "priority-setting exercises" but also "strategic planning", "agenda setting" and the like. Priority setting is necessary in order to allocate limited resources effectively and efficiently – whether they be time, funding, staff or infrastructure.

This guidance aims to synthesize current good practice for incorporating ethics into health research priority setting. It is expected to be refined over time in the light of experience with implementation.

> **Decisions about what research to conduct, promote or support should be made explicitly, in a systematic way, and guided by ethical principles**

The most important message of this guidance is that **decisions about what research to conduct, promote or support should be made explicitly, in a systematic way, and guided by ethical principles**. In other words, **there is an ethical obligation to engage in ethically informed health research priority setting**, grounded in considerations of justice.

This ethical obligation falls on all those who make decisions about what research is done. These decision-makers include:

- **funders**, whether public or private, non-profit or for-profit, who set priorities not only during strategic planning but also when making policies on eligibility criteria for funding, deciding review criteria for grants, and designing new programmes;
- **policy-makers**, including national bodies that may publish priority topics for a country

or region, and transnational bodies that may set disease- or topic-specific global priorities;
- **research institutions**, such as universities, who can set priorities to inform their strategic planning, allocation of internal resources and so forth;
- **researchers and research units**, who make decisions about their own research priorities, as well as participating in and using the results of larger priority-setting exercises; and
- **community organizations, professional associations and advocacy groups**, who may set priorities for their members or advocate for research conducted by others.

Although all these actors should engage in some form of priority setting, it is important to recognize that the resources available to set priorities are themselves limited. The time and resources devoted to priority setting should be proportionate to the resources available and to what is at stake in the priority-setting exercise.

Ethical considerations are relevant to the goals of health research priority setting, and to designing and implementing the process. This means that it is not possible to separate the ethical from the technical aspects of an exercise. Ethical questions can and should be asked during each stage of priority setting:

- in the **preparation** stage, in deciding on governance, methodology, participants and the criteria used for comparing research options;
- in the **prioritization** stage, in administering surveys and running the meetings during which the criteria are applied and priorities are set; and
- in the **follow-up** stage, in reporting results, acting on priorities and evaluating the priority-setting exercise.

There is no single correct approach to health research priority setting. The appropriate process should reflect the nature of the priority setter, their situation, available resources and other contextual factors. Ethical priority setting can be based on the use of an existing method, or can use a process that is designed from scratch. Either way, **four key ethical principles** should guide the priority-setting process (Fig. 1). These principles are not hierarchically ordered; they should be considered as a whole; and they cannot be read in contradiction to each other.

Fig. 1. The four key ethical principles

How the ethical principles apply in practice should be specified by those setting priorities in the light of their particular context. This guidance includes detailed recommendations for applying the principles though each stage of priority setting. It also provides a flowchart and a set of guiding questions to assist with implementing the guidance. The companion casebook illustrates the principles through real cases and constructed scenarios.

The ethical principles in depth

1 Optimize social value

Every priority-setting exercise involves comparing research options using some set of criteria. These criteria should be chosen in the light of the ethical principles and specified to fit the context. In particular, the criteria used should include indicators corresponding to each component of social value:

- the likelihood that the research will produce knowledge that will lead to benefits for patients and populations;
- the magnitude of the benefits if they were to result; and
- the extent to which providing those benefits would reduce inequity.

For almost all research, whether it will lead to any benefits and what those benefits will be is inherently uncertain. Comparisons of social value will generally be imprecise approximations using proxy measures. Nonetheless, a good-faith effort to make such comparisons is an essential part of ethical priority setting.

Where scarce resources are being allocated – such as a limited pool of funds – research options should also be compared on their relative **cost** (the amount of the scarce resource they would use) in order to optimize the social value of the overall research portfolio.

How the social value of research should be conceptualized and estimated depends on the type of research. Basic biomedical science is not less important than clinical or public health research. However, by virtue of being more distant from practice or policy translation, there may be greater uncertainty about its eventual application. While the social value of both can be assessed, different kinds of research will generally require different criteria to evaluate them.

2 Respect special obligations

Priority setters should aim to optimize social value while respecting the special obligations of those involved. These may restrict the scope of the research options considered. Special ethical obligations depend on the individual or entity's role, as well as actions they have taken to incur obligations, as in the following examples.

- **Governments** have obligations to their national populations, and the governments of wealthy countries have further obligations to the global population.
- **Non-profit funders** frequently have special obligations set out in their founding instruments, such as research into a particular disease area. Mission statements often spell out special obligations, but could be revised.
- **For-profit entities** have obligations to pursue socially valuable research, and to refrain from practices that make the overall research ecosystem less effective at benefiting patients and populations.
- **Researchers** and **research units** may have special obligations to the patient populations and communities they work with. They should otherwise aim to conduct the most socially valuable research they can.

3 Assess risks

Sometimes research poses risks of harm to parties who are not expected to benefit from the knowledge the research generates. These fall into the following categories.

- Research options that cannot be investigated ethically should not be supported. However, it

is usually best to assess the ethics of possible research studies with **human research participants** at the protocol development stage, not while setting research priorities.
- Where predictable during priority setting, consideration should be given to the harms that would be inflicted on **non-human animals** by different research options. These harms should be minimized and justified by the social value of the research. In some cases, programmes of research with non-human animals should not be supported because there are comparably valuable alternatives that do not involve animals, or because the research will cause excessive suffering.
- Research options should be assessed for whether the results might pose risks to **third parties or bystanders** who are not themselves likely to benefit (for example, dual-use research). Any additional risks of harm should be minimized and justified by the social value of the research. Sometimes, such research should not be pursued because the third-party risks are too high.

4 Follow fair procedures

Health research priority setting should be conducted through a process that is efficient and procedurally fair. This requires designing a process consistent with the values of **accountability**, **transparency** and **inclusivity**.

- Lines of accountability depend on the nature of the entity concerned. For example, government bodies should be accountable to their publics. This entails obligations to:
    - communicate about priorities and priority setting
    - give opportunities for feedback
    - put mechanisms in place to ensure that priority setting is conducted fairly.
- Most priority setters have an ethical obligation to be transparent about the process and the results of priority setting. Clear communication of results also increases the likelihood that research priorities are followed.
- Most priority-setting exercises should involve multiple parties. This helps to ensure that they are responsive to the cultures, values, and health and health-care experiences of the diverse groups affected by their decisions. In deciding whom to include, priority setters should consider the following categories of potential participants:
    - research producers (for example, funders and researchers)
    - research users (such as health-care workers, health administrators and policy-makers)
    - research beneficiaries (including patients and carers).

In each category, consideration should be given to whether there is sufficient diversity of participants. Meaningful inclusion also requires engaging participants under conditions designed so that power disparities are mitigated, and everyone is able to speak up and be heard. Special attention should be paid to ensuring the meaningful inclusion of members of relevant disadvantaged and marginalized groups.

Conclusion

The actors involved in setting research agendas around the world all have ethical obligations to set priorities explicitly, in a systematic way, and guided by ethical principles. This guidance is intended to assist them in doing so. On its own, ethical priority setting will not correct the enormous disparities in power and resources that characterize the global health landscape and reflect the harrowing legacies of colonial and post-colonial exploitation. Nor can any individual actor be expected to do so by themselves. Nevertheless, each can still play a part in achieving justice for all by improving justice in health research.

1. Introduction

This guidance can be used by anyone involved in priority setting, agenda setting or strategic planning for health research. Potential users include ministries of health, international organizations, research funders, universities and researchers. Ethical reflection on research priorities is valuable even for very small organizations or individuals who cannot devote substantial resources to formal priority setting. No matter who is undertaking it, decisions about what research to conduct, promote or support should be made explicitly, in a systematic way, and guided by ethical principles.

Ethics and health research priority setting

The benefits that health research can generate are vital to human flourishing. Thanks to medical research, vaccines can protect children from infectious diseases that once killed millions every year. Public health research has improved knowledge about how diseases spread and how sanitation can stop them. Health research means that it is possible to ameliorate pain, replace organs, treat many cancers, correct vision and much more. But the benefits of research are not received equally by all. Who is ultimately likely

to benefit from future research depends on which populations, conditions and modalities are prioritized *(1)*.

The resources available for health research at any given time – including money but also time, infrastructure and personnel – are scarce.[2] Not every valuable research project can be carried out. Investing resources in one project takes resources away from others. This means that decisions must be made about which among the many possible valuable research projects should be conducted first. **Health research priority** setting is the process through which decisions or recommendations are made about what health research should be prioritized.

Since decisions about what health research is carried out are decisions about how to distribute scarce and very important potential benefits among different populations, such decisions are not merely technical. They cannot be made solely on the basis of data and modelling. These decisions also incorporate **value judgement**s, such as what counts as a benefit, how benefits ought to be distributed, and which populations should get benefits when not all can. This means that **ethics** is a fundamental element of research priority setting: to identifying the goals at which it aims, the way it is conducted and who it involves. Almost everyone involved in health research makes decisions that affect what research gets done. Government ministries make far-reaching decisions about national strategies for health, education and research. International organizations develop research agendas that guide the funding decisions of others. Private corporations decide which disease areas to invest in and which drug candidates to take into clinical testing. Funding bodies decide how to design grant schemes and which research programmes to support within the remit of their missions.

Ethics is a fundamental element of research priority setting: to identifying the goals at which it aims, the way it is conducted and who it involves

University officials decide on faculty hires, which research centres to establish, and how to apportion university research funds. Patient advocacy groups support research and lobby on behalf of their constituents. Even individual researchers exercise discretion in deciding which research opportunities to pursue, which grants to apply for, and which projects to propose within the scope of those grants' criteria.

This guidance is designed to support all these actors: governmental decision-makers, international organizations, private companies, funders, universities, researchers and more. All of them have ethical obligations with respect to the research they decide to conduct or support, and should be able to justify their own allocation decisions *(2)*.

The principles, tools and case studies described in this publication and the companion casebook can guide ethical research prioritization. But the most important message of this guidance is that **decisions about what research to conduct, promote or support should be made explicitly, in a systematic way, and guided by ethical principles**.

Aims and scope

This guidance aims to describe the ethical considerations relating to setting priorities for health research, and to guide key decision-makers

2 The question of whether more resources should be dedicated to health research overall is beyond the scope of this guidance.

in incorporating these ethical considerations into their work. The terms used in this statement of aims should be understood expansively.

- "Research" refers to any systematic investigation that is expected to generate knowledge using recognized scientific methods. "Health research" includes any research aimed at better understanding or improving human health broadly construed, which could be research on the social determinants of health, as well as basic biomedical science, clinical research, epidemiology, translational research, public health, and health policy and systems research.
- "Ethical considerations" encompasses any value judgements relevant to how others are treated and to what benefits they are entitled.

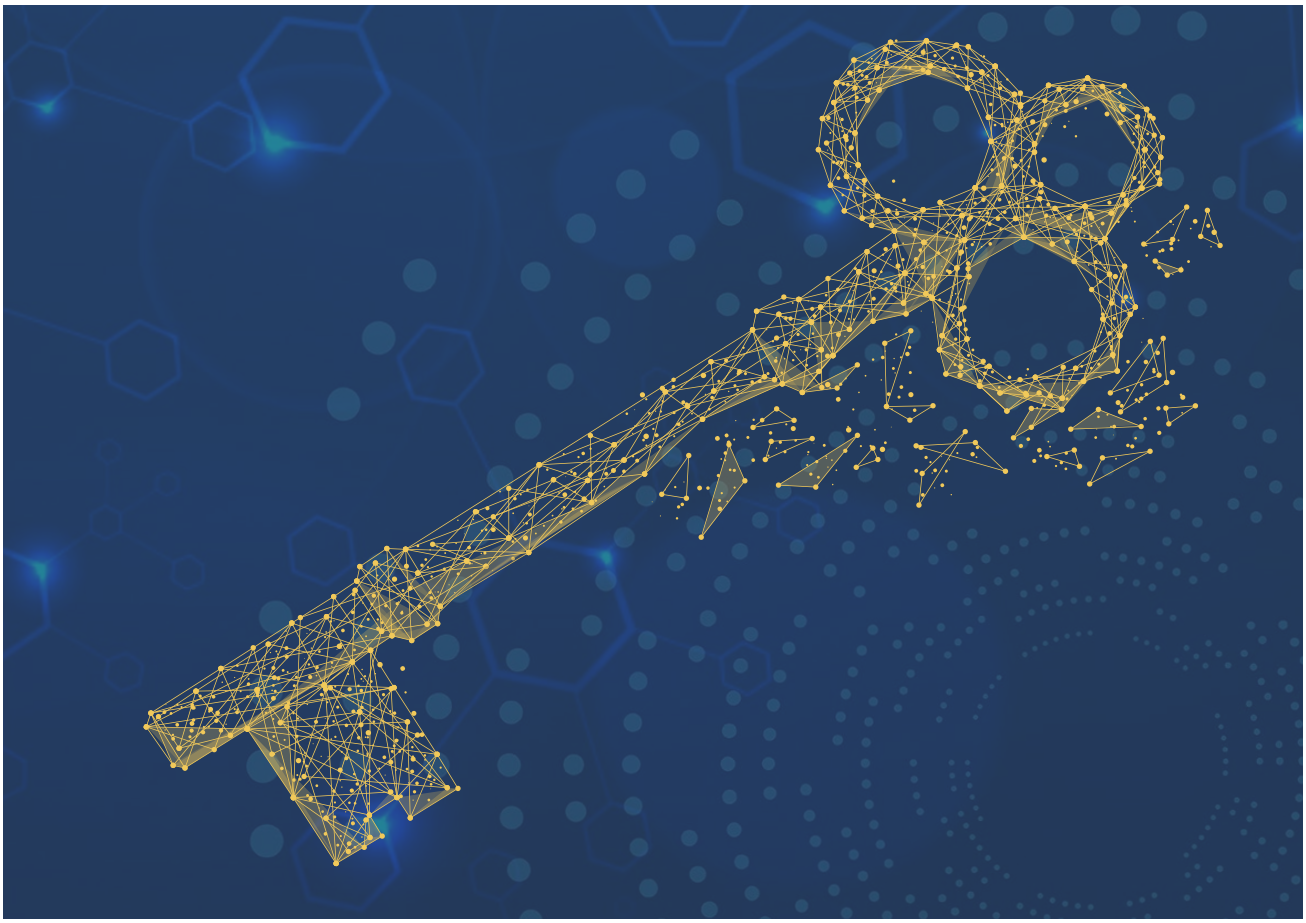
Research priority setting may take place at different levels with implications for the scope of specific decisions or exercises. The scope may be geographical (global, regional, national or subnational), topical (for example, encompassing a disease area or scientific discipline) or role-based (such as for a specific funder or institution). It may be project-level, so that specific research questions are identified, or it may simply recommend broad themes (such as antimicrobial resistance or mental health). The priority setting may be direct (for example, a funder deciding the scope of a new grants programme) or indirect (for example, an advocacy group drafting a research agenda for others). The ethical principles described in this publication apply to all shapes and sizes of priority setting. Any decisions that affect what research gets conducted are open to ethical analysis.

How to use this guidance

This guidance is intended for use with all sorts of health research priority-setting processes – whether large or small, thematic or project-level. Different parts of the guidance will be more or less relevant depending on the specific situation. It can be used to supplement use of an existing research priority-setting method (see Chapter 4) or as the basis for designing a bespoke process. The case studies and scenarios in the casebook accompanying this guidance *(3)* illustrate how the principles apply to different types of priority setting and different actors – they can be dipped into to understand an ethical principle better or to find a similar situation to the current exercise.

Chapter 2 sets out the ethical principles that should inform the design of any priority-setting process. Chapter 3 goes into detail about how the principles apply to activities at each stage of a priority-setting exercise. Depending on the available resources and needs, some or all of the activities may be part of the priority-setting exercise. Chapter 4 relates this guidance to the most commonly used existing methods for research priority setting. This will be relevant when considering using or adapting an existing method. Chapter 5 includes a number of frequently asked questions under thematic headings. Annex 1 describes the process by which this guidance was developed. Annex 2 describes the research ecosystem in which priority setting takes place. For more extensive priority-setting exercises that involve many participants, consult Annex 3. For concrete recommendations on how to compare the social value of alternative research options, see Annex 4. For further resources and recommendations for literature related to but beyond the scope of this guidance, see Annex 5. Annex 6 may prove useful throughout the process. It provides a flowchart and a set of guiding questions to help ensure that your exercise addresses each ethical consideration at each stage.

2. The ethical principles



Anyone who allocates resources for health research or makes recommendations on how they should be allocated engages in health research priority setting. All health research priority setting should be done explicitly, in a systematic way, and guided by ethical principles.

The ethical principles: in brief

Any process for setting health research priorities should be designed in the light of the following four broad ethical principles. These are synthesized from best practices and consensus values described in the literature on health research priority setting, health-care priority setting and research ethics *(4–7)*. Of note, they specify both **substantive** and **procedural** elements, since both are essential: ethical health research priority setting is a matter not only of having a fair process but also of reaching just outcomes. The principles are not hierarchically ordered, should be considered as a whole, and cannot be read in contradiction to each other.

Principle 1 is **optimize social value**. There is widespread agreement that health research priority setting should aim at two broad goals: maximizing the benefits of health research to patients and populations, and reducing

population inequity *(5,8)*. These goals are encapsulated by the principle that health research priority setting should optimize the social value of research. Aiming to optimize social value aligns health research priority setting with justice, since the greater the social value of research, the more its results promote just outcomes.

Principle 2 is **respect special obligations**. Some actors allocating scarce resources for health research have special ethical obligations based on their roles, relationships or history. Examples include the ethical duties a charity has to those it seeks to serve, and those clinicians have to their patients. Research priorities should be set consistent with these special obligations.

Principle 3 is **assess risks**. Some research projects impose a predictable risk of significant harm to individuals who are not expected to benefit from the research. Such risks should be minimized and, where unavoidable, should be justified in terms of social benefits that could not otherwise be obtained. This principle applies both to conduct towards research participants, including non-human animals, and to potential harms from the use of the results of research.

Principle 4 is **follow fair procedures**. Any explicit decision about what research to prioritize (to support or conduct) results from a process. The principle of following fair procedures entails that the process should be one that is justifiable to interested parties, including the potential producers, users and beneficiaries of health research. This typically requires a process that is **accountable**, **transparent** and **inclusive**.

Proportionality and relevance

The process for health research priority setting developed in the light of the ethical principles outlined above should be proportionate, and should guard against the use of irrelevant considerations as far as possible.

> **Ethical health research priority setting is a matter not only of having a fair process but also of reaching just outcomes**

Proportionality

Everyone involved in making decisions about what research gets done should engage in some sort of priority setting. That priority setting should be based on evidence and guided by the ethical principles described in this guidance. But the resources available for priority setting are themselves limited, and so it may take away from other valuable activities. The time and resources allocated to a priority-setting exercise should therefore be **proportionate** to what is at stake. This depends on:

- the amount of data, analysis and input from others needed to make good prioritization decisions;
- the extent of the allocation decisions the priority setting will affect; and
- the resources available for the priority-setting exercise.

Compare, for example, a national funding body engaged in five-yearly strategic planning with an individual research unit deciding on the grant applications it will make in the coming year. Both can benefit from ethically informed, evidence-based priority setting, but the former should invest substantially more resources, gather more data and seek much more outside input than the latter.

Proportionality also applies to the frequency with which priorities should be revisited. Research priority setting should be done with an explicit time frame, and periodic follow-up is important so that adjustments can be made in response to

research advances, epidemiological changes, new funding opportunities and the like. Priorities may also need to be revisited in the light of events, such as an emerging health crisis. Generally, however, priorities should not be revised too often. That can undermine efforts to follow the priorities that have been set, and risks wasting previous research investments.

Irrelevant considerations

The individuals and organizations involved in health research experience various constraints, pressures and incentives that affect what research they conduct or support. In the process of priority setting, it can be valuable to articulate the likely motivations of individuals and organizations so that they can be examined critically for their influence on what priorities are chosen. These motivations may include the following.

- Everyone involved in health research faces **practical constraints** on what they can do, which may limit the scope of their own priority setting. For example, research teams may need outside funding in order to continue carrying out research – or simply to make a living – and so they may have to adjust their priorities to fit with those of funders.
- Some powerful incentives for carrying out specific research projects are **irrelevant considerations** in terms of what should be prioritized *(9)*. These include status within one's field, the views of authority figures (for example, what a CEO, dean, thought-leader or other powerful individual currently cares about), career progression, good publicity and making money. Any of these could be instrumental to generating social value in some circumstances. For example, career progression might lead to more opportunities to pursue socially valuable research in the future. Nevertheless, these are not goals that matter in themselves in the context of ethical priority setting. For that reason, unlike the ethical principles above, they should not guide priority setting.

These common motivations are frequently not aligned with what research priorities should be. This itself generates ethical obligations for more powerful actors within the research ecosystem. They may have obligations to remove practical constraints on others, where the constraints impede high-priority research. They also ought to engage in collective efforts to change research culture so that what is needed to survive and thrive in health research coincides with carrying out socially valuable research.

The ethical principles: in depth

Principle 1. Optimize social value

Defining social value

According to the Council for International Organizations of Medical Sciences, "social value refers to the importance of the information that a study is likely to produce" *(4)*. The information generated by health research can be important because it is **directly** relevant to policy or practice – for example, a clinical trial that demonstrates safety and effectiveness of a new treatment. It can also be important **indirectly** – for example, by improving understanding of a biological mechanism, mapping disease transmission, validating a measurement tool and so on – and thereby ultimately contributing to research that is directly relevant. Either way, social value is grounded in the potential benefits to patients or populations that may result. These potential benefits are what justifies spending scarce societal resources on health research.

This guidance defines social value more precisely as a function of *(10)*:

- the **likelihood** that research will produce knowledge that will ultimately benefit patients and populations;
- the **magnitude** of the benefits if they were to result; and
- the extent to which providing those benefits would reduce **inequity**.

> **Equity is the absence of unfair, avoidable or remediable differences among groups of people, whether those groups are defined socially, economically, demographically, or geographically**

Social value thereby includes both the moral importance of how much benefit research is expected to generate and how far it will alleviate inequity in outcomes. To illustrate, research will be more socially valuable if it focuses on a condition that greatly reduces patients' quality of life, cuts their lives very short, or predominantly affects people who are poor or marginalized.

Limited resources should be distributed among research projects in the way that will generate the greatest overall social value. This means that by aiming to optimize social value, research priority setting promotes distributive justice *(11)*.

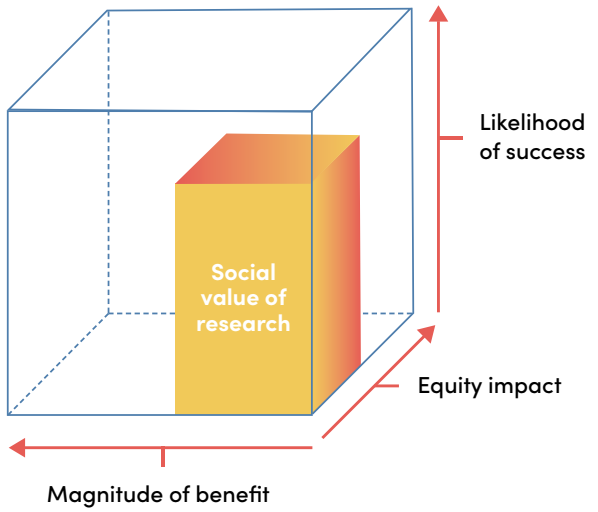
The definition of social value should be specified further by those engaged in priority setting in a way that reflects their context. That entails the following.

- **What counts as a benefit** needs to be defined. Consistent with WHO's expansive definition of health as "a state of complete physical, mental and social well-being" *(12)*, there are dimensions of well-being that are not always thought of as components of health but may be affected by health research. Examples might include freedom from stigma, improved autonomy or personal security. All dimensions of well-being are potentially relevant to social value, depending on the research options being compared.
- **Potential beneficiaries** should be identified. Clinical and public health interventions can have effects beyond their direct recipients – such as through herd immunity, by relieving caregiver needs or via their impact on the environment. Where there are predictable and substantial indirect effects from successful research projects, they should be included in estimates of social value. Researcher training and other forms of capacity-building can also eventually lead to significant benefits (via the results of future research). These could also be added into assessments of social value.
- Attention should be paid to **what equity means**. According to WHO, "Equity is the absence of unfair, avoidable or remediable differences among groups of people, whether those groups are defined socially, economically, demographically, or geographically or by other dimensions of inequality (e.g. sex, gender, ethnicity, disability or sexual orientation)" *(13)*. This encompasses not only differences in health status among groups but also differences in other factors relevant to well-being. How equity is best specified will depend on the scope – geographical, topical and so on – of the priority-setting exercise.

Estimating social value

Research is an inherently uncertain enterprise. The results of research cannot be known ahead of time; nor can the use to which those results will be put. Sometimes the utility of a scientific discovery is not known until many years later. Nevertheless, in order to set priorities, alternative research options need to be compared. Depending on the nature of the exercise, these options might comprise broad themes (such as which health conditions within a population to prioritize) or specific projects (such as which studies to conduct). Priority-setting exercises typically use several criteria to score or rank research options to make these comparisons. These criteria should be selected with the aim that applying them will generate the greatest overall social value (consistent with following the other ethical principles). In so far as the context allows, each component of social value – likelihood of success, magnitude of benefit and impact on equity – should map onto one or more criteria (Fig. 2).

Fig. 2. Three dimensions of social value



The context and the type of research being prioritized affect what criteria are appropriate. Roughly speaking, the majority of health research can be divided into three broad categories: basic biomedical research, clinical research and public health research. Basic biomedical research projects often focus on understanding mechanisms, may be exploratory in nature, and may not have a specific disease target *(14)*. Their translational value might also not be apparent; even if it is, it will be tenuous when the projects are conceptualized. Nevertheless, basic biomedical research is vitally important for medical breakthroughs *(15)*. Rather than the probability of defined benefits to population health and well-being, criteria used for evaluating the likelihood of success of basic biomedical research will typically focus on:

- factors that improve the probability that the research leads to knowledge (such as experimentalist skills, statistical soundness of study designs, recruitment plans, institutional support and so on); and
- factors that improve the probability of uptake (such as external validity, plans for publication and dissemination, coordination with other research groups and so on).

Likewise, where the use case for the results is not known, the magnitude of expected benefits might be evaluated with criteria that assess whether a topic is neglected, whether the results are potentially transformative, or the significance of knowledge gained for other scientific questions.

The translational value of clinical and public health research is generally more direct and more apparent. Research projects may be directed at specific patient populations, and the potential interventions may be well characterized. For example, for a particular intervention being investigated, it might be possible to get numerical estimates of how many additional lives could be saved if the intervention proved to have a particular level of effectiveness. As such, priority setting in these categories can be more driven by quantitative estimates of the potential benefits of the research.

Note that estimates of social value should consider both possible benefits and possible losses or harms from research. Where the potential benefits and harms are to the same population, they should both be considered as components of social value. However, predictable harms to populations who are not potential beneficiaries of the research, including harms to non-human animals, fall under Principle 3.

Efficient allocation

When allocating scarce resources for research, what matters is not only the social value of each research project under consideration but also the amount of the scarce resource each would need. For example, if a scientific question can be answered using existing data sources, rather than collecting new data, that might free up money and time for other valuable research. The scarce resources available should be allocated among possible research projects in the way estimated to generate the greatest overall social value. For priority-setting exercises that aim only to identify broad priority themes, this point may not apply. But for any exercise that aims

to recommend which specific projects should be carried out, **efficiency** should be taken into account explicitly.

In addition to thinking about how to allocate their own resources efficiently, decision-makers have an ethical obligation to take into account what others are doing or planning *(16)*. At a minimum, this will involve carrying out scoping reviews and – where relevant – checking clinical trials databases or other sources of up-to-date evidence. For some priority setters, such as funders and governments, it may require active coordination. Coordination among the actors involved in health research globally is necessary to avoid waste and duplication *(17)*. The overall social value of research can thereby be increased, and it will be possible for individual actors to adjust what they are doing to increase fairness in how research resources are distributed.

Further guidance

Detailed recommendations for how to operationalize social value judgements, including several examples, can be found in Annex 4. Some resources and examples of good practice for coordinating research efforts to ensure efficiency are listed in Annex 5. In addition, the case studies and scenarios in the companion casebook *(3)* illustrate how the principle of optimizing social value can be applied by different actors in various priority-setting situations.

Principle 2. Respect special obligations

Special obligations are ethical duties that one party owes to another in virtue of their role, relationship or history – for example, physicians' and nurses' special obligations to their patients *(18)*, or polluters' special obligations to those they have harmed *(19)*. They contrast with **general obligations**, which apply to everyone. Everyone involved in health research has a general obligation to support socially valuable research. Many also have special obligations that will shape how they fulfil this general obligation.

Some special obligations are non-negotiable, and will rule out particular research options from the outset. For example, a government agency might be legally mandated to support only a specific type of research (see, for example, Case 2 in the companion casebook *(3)*. Other special obligations just mean that greater weight should be put on some research projects versus others. For example, a research group that is working within a particular community has ethical obligations to carry out research that is responsive to the health needs of that community *(4,20)*. That does not rule out taking into account potential benefits for benefit patient populations outside the community too.

Note that not everyone who believes themselves to have special obligations is correct: they require justification in the same way as any other ethical obligations. For example, there are compelling arguments against forms of nationalism that entirely disregard the interests of non-nationals. Moreover, unlike general obligations, some special obligations can be acquired or changed. A charity that raises funds on the promise to spend them on heart disease research acquires a duty to do so; it could also change its duties in the future by changing what it promises to new donors.

Examples of actors whose priority setting might be affected by special obligations include government bodies, non-profit funders, for-profit entities and researchers (Table 1).

Table 1. Key actors and their ethical obligations	
Entity	**Obligations**
Government body	• Support socially valuable research relevant to citizens and residents • Support international research with global social value (if a wealthier country)
Non-profit funder	• Prioritize socially valuable research consistent with mission • Consider whether mission can be changed to better align with optimizing social value
For-profit entity	• Pursue profit only when consistent with socially valuable research • Refrain from practices that make the overall research ecosystem less effective
Researcher and research institution	• If already committed to working with specific populations or communities, give higher priority to their needs • Otherwise, optimize social value of research

Government bodies, such as national funding agencies and ministries of health, are usually accountable to other parts of the government. In addition, individual government bodies share the obligations of the government as a whole. Governments have obligations to treat their citizens and residents – present and future – justly. Within a country, this entails supporting socially valuable research to improve population well-being and equity.

Governments also have some obligations beyond their borders. These international obligations are greater for more wealthy and powerful countries (although there may be solidarity-based reasons for less wealthy countries to support mutually beneficial research too) *(21)*. Supporting socially valuable research can be an important part of fulfilling these international obligations (as well as being in a country's long-term self-interest *(22)*. There are multiple justifications for thinking that governments' obligations extend beyond their borders *(23)*. These include the following.

- **Beneficence:** obligations of beneficence to help those in desperate need apply regardless of national boundaries *(24)*.
- **Distributive justice**: no one chooses their country of birth. Just like with other unchosen characteristics – like race, gender and sexuality – it is **unfair** if someone is worse off than another simply because of where they are born *(25)*.
- **Reparative justice:** the inequalities in wealth among countries are no accident. They partly result from a long history of colonialism, exploitation and violence *(26,27)*. The current global economic system was shaped by the wealthy and the powerful to benefit themselves *(28)*.

Many **non-profit funders** have mission statements or similar statements of the goals and values of the organization. These set out the organization's remit, and can be a source of special obligations *(2)*. For example, if a non-profit has developed relationships with a patient community that supports its mission, it has obligations to them. Likewise, if it raises funds on the basis of its mission, it is implicitly promising to spend the money in a particular way. These special obligations may narrow the scope of the research that the non-profit supports. For example, it is reasonable for an HIV/AIDS charity

to support only health research relevant to people with or at risk for HIV/AIDS. It should then aim to optimize social value within that scope.

For many non-profits, mission statements are not fixed. Those with the power to do so should consider whether to change a mission statement in order to allow the organization to support more socially valuable research (for example, by expanding its remit from national to global, or by increasing flexibility in the types of health research supported).

For-profit entities are permitted to pursue profits only within the constraints of law and ethics. Businesses that are engaged in research may have special obligations to their owners and shareholders, but they are still bound by the same ethical principles as other research entities.

One important ethical constraint on for-profit entities is that they should not undermine governments carrying out their obligations of justice *(2)*. At a minimum, this means that business practices that make the research sector as a whole less effective at creating health technologies that improve health cannot be justified. In addition, businesses exist and are able to pursue their commercial interests only in virtue of an economic system that is set up and enforced by governments. States subsidize research and development directly and indirectly through tax breaks, by adjudicating whether new technologies can be legally marketed, by enacting the laws that allow the creation of intellectual property, and by purchasing health care that is developed through health research. For-profit actors therefore also have reciprocal ethical obligations to society to carry out socially valuable research.

Many **researchers, research units and research institutions** are unconstrained by special obligations concerning which research projects they pursue. Those researchers should aim to optimize the social value of their research.

For some, however, there may also be special obligations. For example, researchers who are already committed to working with specific populations or communities should give some priority to research that is relevant to those groups. The same points apply to groups of researchers and research institutions.

> **Special obligations are ethical duties that one party owes to another in virtue of their role, relationship or history**

Principle 3. Assess risks

The conduct of research and the application of its results can cause harms as well as provide benefits. Where there is some risk of harm to the same population that the research aims to benefit, both expected harms and expected benefits should be included in estimates of social value. For example, the social value of a new medicine would depend on both how well it treated the target disease and the frequency and severity of its side-effects. Sometimes, however, the populations who might be harmed are not the same as the ones that might be benefited. Putting one individual at risk of harm in order to benefit someone else has a higher threshold of ethical justification. The principle of **assessing risks** says that such harms to third parties should be minimized, necessary and justified by the social value of the research.

In the context of health research priority setting, this principle applies in two types of case: first, regarding the treatment of research participants, including non-human animals (**research ethics**); second, regarding potential harms from the use of the results of research (**harms from research results**).

Note that the prospects of estimating harms may vary depending on the type of priority-setting exercise. In thematic exercises that prioritize broad research areas, estimating harms may be more difficult or speculative than in exercises that compare specific research projects. For the former, this principle might not be applicable, or concerns raised about potential harms should be addressed later when designing more specific research projects.

Research ethics

The conditions under which health research can be unethical because it violates ethical prohibitions on the treatment of **human participants** have been analysed extensively elsewhere *(4)*. Among others, these include obligations to ensure that the risk:benefit ratio for participants is acceptable, to select participants fairly, and to obtain the informed consent of competent prospective participants (Annex 5). These principles of research ethics are taken as given by this guidance and so are not repeated here. During priority setting, if it is clear that a research project could not be carried out without the unethical treatment of human participants, then it can be eliminated from consideration. However, it is rare that enough information is available to make such judgements during priority setting. Such ethics review should normally be left to research ethics committees, as part of the standard path to having individual research studies approved.

The use of sentient **non-human animals** in health research deserves special mention. While the scientific merits of non-human animal models are debated *(29)*, and alternatives to their use are gaining traction *(30)*, many millions of animals are still used in medical research every year *(31)*. The vast majority of experiments using non-human animals are carried out for the benefit of humans, involve killing the subjects after the experiments, and impose suffering or discomfort.

There is much more disagreement over the ethics of research using non-human animals than about the ethics of research with human participants. Nonetheless, there is widespread agreement that the welfare of sentient non-human animals matters morally to some extent *(32)*. This is relevant when setting research priorities, since there are frequently choices to be made about research programmes that would be very different in terms of their use of animal subjects. Whole lines of research may involve or not involve animals, may use very different numbers and species, and may entail enormous or minimal suffering. For example, one proposed research programme might aim to develop a rodent model of a disease, while another works with human cells in vitro on the same disease. This means that questions about the justifiability of harms to non-human animals cannot all be postponed until the point when individual studies are reviewed.

> **There is widespread agreement that the welfare of sentient non-human animals matters morally to some extent**

When choosing among research projects that might involve non-human animals, priority setters should, at a minimum:

- consider whether equally valuable knowledge could be gained using alternatives to animals;
- choose projects involving animals so as to minimize harms given the scientific aims of the research; and
- choose only research projects where the harms to animals are likely to be justified by the social value of the knowledge gained through the research.

Depending on one's views on the ethics of animal use, more demanding criteria might also

be justified *(33)*. These points, of course, apply only to integrating consideration of non-human animals into health research priority setting: the ethical standards for animal research still need to be applied to individual proposed studies through relevant research oversight processes in each jurisdiction.

Harms from research results

The results of research can also lead to harms. To illustrate, reports of a study looking at the genetic correlates of mental health conditions in an Indigenous population might pose some potential risks to that population (for example, if reporting were to reinforce prejudices in the wider population) *(34)*. They might also present a prospect of benefit (for example, if the research guided the development of treatments). When the risks and expected benefits are to the same population, they can be aggregated as part of a social value evaluation. However, sometimes the benefits of research are likely to be received by one population while harms are predicted to fall on a different population. Suppose that the genetic research just described was conducted because this relatively isolated population allowed a specific scientific question about gene-environment interactions to be answered – one whose benefits, if any, would probably be received by different, less marginalized patient groups. Then the risk to the Indigenous population would not be balanced by benefits to them from the knowledge gained. Such research would be very hard to justify.

Other examples of research that poses uncompensated risks of harm in this way may include research that will predictably lead to serious environmental harms and "dual-use research". Dual-use research leads to results or products that might be misused and thereby cause harm *(35)*. For example, scientists might experimentally manipulate a pathogen to see what would make it more transmissible. This might help them learn about how to combat the pathogen, but it also opens up the possibility of accidental or malign release of a more dangerous infectious disease *(36)*. Potential environmental harms and harms from dual-use research should be assessed during priority setting. Where research poses a plausible risk of serious harm to those who are unlikely to be beneficiaries, those harms should be minimized, they should be necessary in order to achieve the scientific aims, and they should be justified through weighty social benefits.

Principle 4. Follow fair procedures

Who makes decisions about research and how they make them is critical to the legitimacy of allocation decisions and to the likelihood that the resulting research will actually benefit those in greatest need. The principle of **following fair procedures** entails that the decision-making process that implements the previous three ethical principles should be one that is justifiable to others, especially those who are affected by the conduct or results of the research. This requires that the processes by which priority-setting decisions are made should be consistent with the values of **accountability** and **transparency**. It also frequently requires the **inclusion** of other parties in decision-making.

Accountability

Accountability involves "a relationship between an actor and a forum, in which the actor has an obligation to explain and to justify his or her conduct, the forum can pose questions and pass judgement, and the actor may face consequences" *(37; see also 38)*. Thus, for example, a minister may be accountable to parliament, and individual parliamentarians may be accountable to the public.

In the context of priority setting, accountability has three main elements: communication; opportunities for feedback; and the enforcement of procedural fairness. To whom a priority setter should be accountable varies. For example, government bodies should typically be accountable to their publics when setting

research priorities. They should communicate to the public how they have set research priorities, on what basis, and who participated. Members of the public should have the opportunity to weigh in on those priorities and how they were set – not just when included as participants in a priority-setting exercise but before and after the exercise. There should be some mechanism through which procedural fairness is enforced (such as an opportunity to appeal or a complaints procedure) *(39)*. Other priority setters should consider to whom they might have an obligation to be accountable, and what that looks like *(40)*. A good starting-point is to look at the special obligations identified under Principle 2.

Transparency

Transparency is important for thorough accountability, promoting adherence to ethical standards, preventing conflicts of interest and bias, countering corruption, and building trust *(41)*. All priority-setting exercises should be transparent with participants regarding their scope and methods. Participants, in turn, should be transparent regarding potential conflicts of interests. In addition, information on both the process and the results of priority setting should normally be made available to those who are directly affected by it. Priority setters should pay particular attention to ensuring access for individuals or groups to whom they are accountable.

For the larger priority-setting exercises carried out by funders and national or international bodies, at a minimum, reports of the process and its outcomes should be made available on a publicly accessible website. There is also normally an ethical obligation to disseminate the products of priority setting to participants in the priority-setting exercise, potential users of the results and other interested parties (see Chapter 3). Care should be taken to match both the method and content of communications to the intended audiences. For example, if priorities are being set for research with a specific patient population, the process and outcomes should be communicated in a way that is understandable and accessible to members of that population.

Transparency is important for thorough accountability, promoting adherence to ethical standards, preventing conflicts of interest and bias, countering corruption, and building trust

Inclusion

The question of who should be included and how should be asked for each stage of priority setting – preparation, prioritization and follow-up. It is especially critical to do so for the preparation stage because it determines who leads the priority-setting process.

Although levels of inclusion lie on a spectrum, more is not always better. Decisions about how many participants will be involved and how extensively should be sensitive to the need for **proportionality** in priority setting. They should reflect:

- how much input is needed from others in order to make justifiable decisions;
- the extent of the allocation decisions the exercise will affect (for example, the quantity of resources being allocated);
- the time and resources available for priority setting; and
- the special obligations of the priority setter.

For example, a doctoral student deciding on their project is allocating few resources, and probably does not have a budget for priority setting. It would be excessive to expect them to engage in an intensive and inclusive priority-setting process. At the other extreme, a government

ministry setting national research priorities is allocating much more, has more time and resources, and has special obligations requiring accountability to its population. It should aim for a deeply inclusive process.

Given the wide variety of actors who allocate resources for research and the contexts in which they act, it is essential to critically reflect on the **reasons for inclusion**. Asking why other parties should be included will guide principled decisions about who should be included and how. Tokenism should always be avoided. The reasons it may be valuable to include individuals or representatives of a group fall into three categories: epistemic, pragmatic and intrinsic.

- **Epistemic** reasons apply when including members of a group may increase the accuracy of priority setting and reduce bias. For example, patient perspectives may be needed to find out which aspects of a disease most affect quality of life, scientific experts may be best placed to judge the solvability of specific problems given the state of scientific knowledge, community members' input may be essential to understand the cultural context and values of different groups, and so forth.
- **Pragmatic** reasons apply when including members of a group may increase the impact of priority setting. For example, involving community members in priority setting may increase trust in subsequent research; including policy-makers may make it more likely that a set of priorities gets uptake; and building capacity within an organization may lead to priority setting being sustained over time *(42–44)*.
- **Intrinsic** reasons apply when members of a group have the right to be included in decisions that affect them. This may apply if a priority setter is accountable to a particular group (for instance, national priority-setting exercises should involve public participation) or is working within a specific community (for instance, research groups in defined communities should involve community members in priority setting). It also applies to research collaborations, where each of the research groups or institutions involved should be represented in decision-making.

As well as identifying the individuals and groups to be included it is important to pay attention to the **diversity of participants**. Ensuring sufficient breadth entails *(45)*:

- sufficient **range** of participants from each category (such as research producer, research user and research beneficiary), so that participants span the spectrum of actors in each category and a wide spectrum of demographics, meaning that they can collectively represent the diversity of interested parties; and
- sufficient **mass** of participants from each category and across demographics, so that there are enough individuals representing each group for their voices to be effective.

Meaningful inclusion occurs when participants are able both to raise their voice and to be heard

Inclusion is not as simple as just asking people what they think. Meaningful inclusion occurs when participants are able both to raise their voice and to be heard *(46)*. The amount of influence participants have depends on when they enter the priority-setting process and their level of participation. They have greater say when included earlier and at a higher level *(47,48)*. Participants should be included under conditions of **qualitative equality**, which requires mitigating power disparities, structuring the

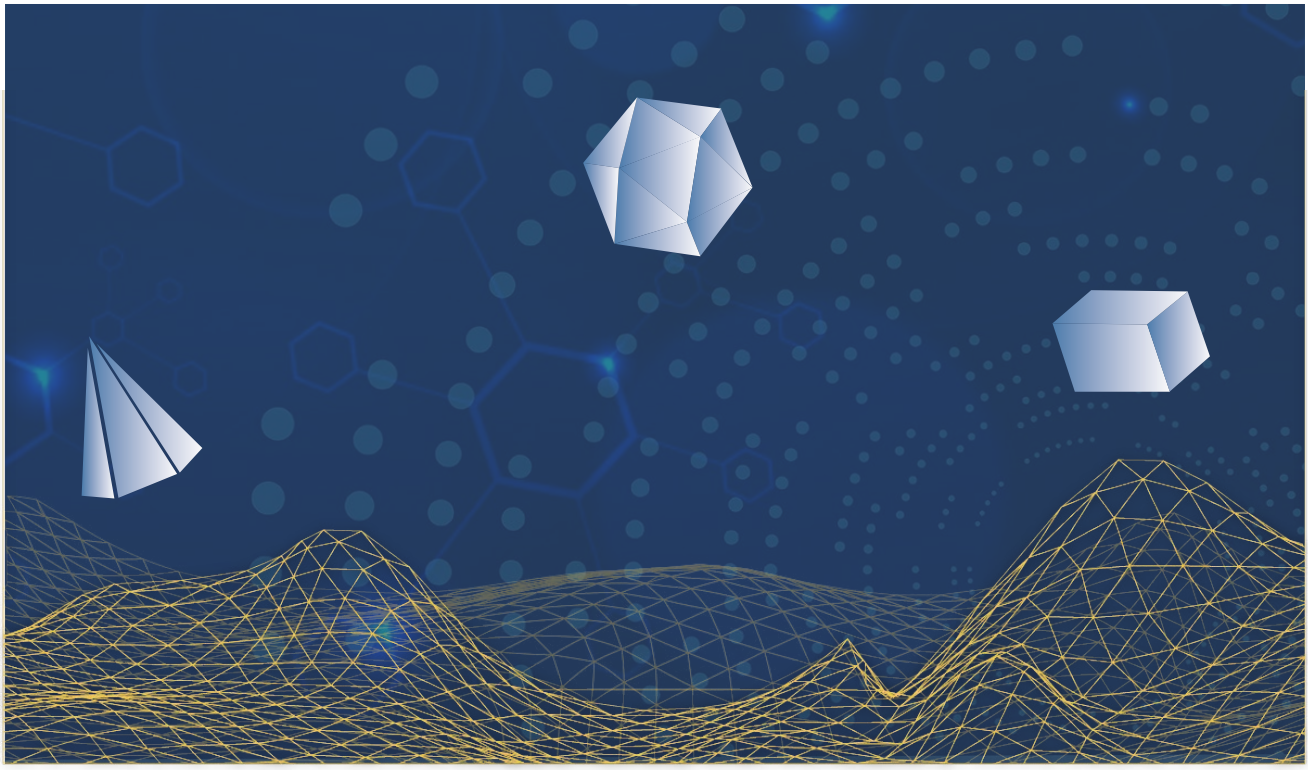
process to empower everyone to be involved, and ensuring that differences in social status do not lead to the contributions of some participants being valued over those of others *(45)*. Particular care should be taken with respect to the inclusion of more disadvantaged and marginalized groups. If their valuable perspectives are to have an effect on what priorities are set, they must be included in ways that give them genuine representation, and give their representatives genuine voice (see Annex 3).

Collaborative partnerships among researchers and research groups frequently generate concerns about power disparities and power sharing. Such concerns have been raised, in particular, in the context of collaborations between research groups in high-income countries and low- and middle-income countries (LMICs). Researchers in high-income countries may have greater access to funds, institutional support or other resources. In some cases, researchers in LMICs find themselves excluded from decision-making, or treated more as data collectors or field workers, rather than partners *(49,50)*. As with other interested parties, it is important that partners in LMICs take part in decisions under conditions of qualitative equality *(51)*. In addition to this guidance, more specific assistance with fair research partnerships can be found through the Research Fairness Initiative *(52)* and in the relevant academic literature *(53–56)*.

Further guidance

Chapter 3 provides detailed recommendations on applying the principle of following fair procedures at each stage of priority setting. Annex 3 outlines some good practices for the meaningful inclusion of members of more disadvantaged and marginalized groups in health research priority setting.

3. Putting the principles into practice



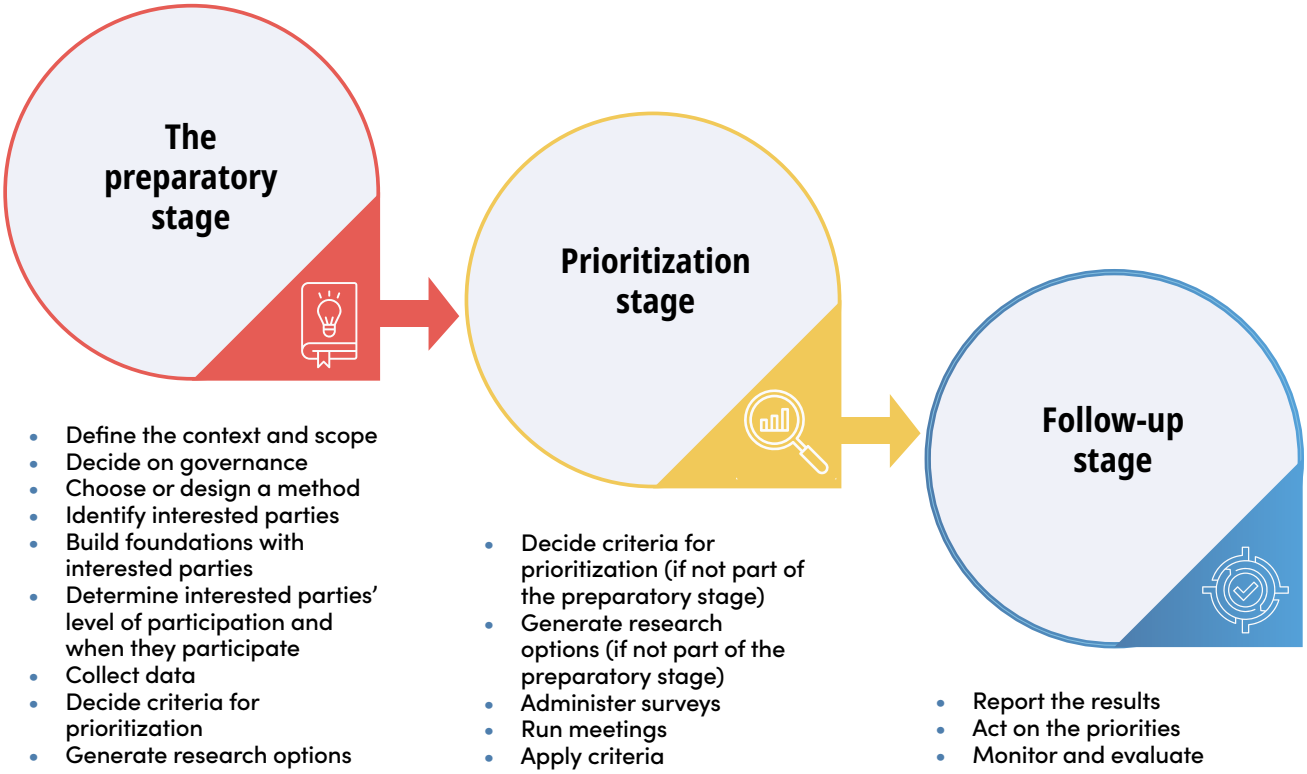
The three stages of priority setting

Most priority-setting exercises can be divided into three stages: the preparation stage, the prioritization stage and the follow-up stage *(57,58)*. This chapter describes typical activities for each stage (Fig. 3), synthesized from the various methods that have been used in priority-setting exercises (see Chapter 4 and the references therein). It illustrates how the ethical principles should be considered for each.

Not every priority-setting exercise needs to include every activity. Exactly which activities the exercise should involve will depend on the particular situation, needs and resources. The time and resources invested in priority setting should always be proportionate to what is at stake (see Chapter 2). In all cases, the ethical principles apply and should guide decision-making about how to design, carry out and follow up on the priority-setting exercise.

Annex 6 includes a flowchart summarizing these activities and the key ethical considerations that relate to each. In addition, it includes guiding questions to help priority setters incorporate the ethical principles into the design of their priority-setting exercise. The guiding questions can be answered during the preparation stage activities and then consulted throughout.

Fig. 3. Typical research priority-setting activities by stage



Stage 1. Preparation

The preparation stage covers all the activities up to actually setting priorities. Typical activities for this stage include the following *(57–64)*.

a. Defining the context and scope

Following the Reporting guideline for priority setting of health research (REPRISE) framework *(65)*, defining the context and scope of the priority-setting exercise may cover:

- defining the geographical scope (for example, global or national);
- defining the health area, field or focus (for example diabetes, tobacco use or health-care delivery);
- defining the intended beneficiaries (for example, patient groups);
- defining the target audience for the priorities (for example, policy-makers, funders or researchers);
- identifying the research area or level (for example, public health, clinical research or basic science);
- identifying the types and granularity of research questions (for example, etiology, implementation science or drug and vaccine development); and
- defining the time frame (for example, five-year plan, one-off or periodic priority setting).

In addition, it will be helpful at this point to identify the resources available for priority setting and the timeline of the exercise, and to check whether the scope of the proposed exercise is covered by any existing published set of research priorities.

If using the guiding questions for ethical research priority setting (Annex 6), the questions in parts

1–5 should be answered now. The answers to those will be a valuable resource when incorporating the ethical considerations into this and the following activities.

Ethical considerations for this activity include the following.

- In deciding the scope, the **special obligations** of the priority setters or any other parties to whom the priorities are directed should be taken into account (Chapter 2). The priority-setting team might consider, for example:
  - if setting national priorities for a government, what obligations are owed inside and outside of the country's borders – in particular, high-income countries may have substantial ethical obligations to other populations;
  - if setting priorities for a funder, the funder's mission, commitments to donors and/or relevant legislation – for example, a cancer research charity will have its scope restricted to cancer, a government funder may be legally required to focus on some conditions, types of research or potential beneficiaries; and
  - if setting priorities for clinician-researchers, whether there are patient populations whose needs should be prioritized – for example, a researcher whose clinical work is with a particular community may have obligations to conduct research that benefits that community.
- Pragmatic considerations may also limit the scope. For example, researchers setting priorities must consider their expertise and the available sources of funding.
- Within what is allowed by special obligations and pragmatic considerations, making the scope as wide as possible should be considered. Having a more open scope gives participants a better opportunity to choose priorities that will optimize the **social value** of the research.
- There should be **transparency** about the scope of priority setting and why. This can help prevent participants and potential beneficiaries having unrealistic expectations *(40)*.
- The resources used for research priority setting should be **proportionate** to what is at stake. This means that, in deciding what resources to allocate, the priority-setting team should consider what will be necessary for a systematic, evidence-based and ethical priority-setting exercise. While conducting priority setting is an ethical obligation, and so some resources should be allocated to it (see Chapter 1), the appropriate investment will vary. For example, a large global health funder developing its five-year strategic plan should assign more resources to priority setting than a small funder deciding how to spend a one-off pot of additional funds.

Having a more open scope gives participants a better opportunity to choose priorities that will optimize the social value of the research

b. Deciding on governance

Decisions must be made about the governance structure and leadership of the priority-setting exercise. Those who lead the exercise should have the relevant technical and interpersonal skills *(57)*. Depending on the nature and extent of the exercise, it may be necessary to put together a team, which could include a steering committee, expert advisory group, project manager, workshop facilitators and so forth.

Ethical considerations for this activity include the following.

- The leadership team should be constituted so that its members are **accountable** to their constituents, if any. For example, if this is a

governmental priority-setting exercise, it should be clear how citizens and residents can have input, and which governmental officials take responsibility for the process and its outputs.

- Governance structures should be **transparent**, so that they are communicated to participants before and during priority setting and reported afterwards.
- **Inclusion** should be considered when deciding who should lead priority setting and who should be involved in its governance. For larger priority-setting exercises, the team should ideally include members of groups who are expected to be producers, users and beneficiaries of research, including members of disadvantaged and marginalized groups. Including individuals who are independent of any organizations for whom priorities are being set can improve transparency, reduce bias and aid with accountability.
- In research priority-setting exercises involving actors in both high-income countries and LMICs, it is particularly important that those involved recognize their moral responsibility to address power imbalances within global health. Reflexivity and consideration of context, including the legacies of colonialism, should inform the nature and methods of involvement during the preparation stage.
- Power sharing is more effective when it is incorporated into priority setting from the preparation stage. This means that interested parties may need identifying (see Stage 1d) before finalizing the governance structure.
- In multinational research collaborations, particular care should be taken that leadership represents all the countries involved, and that researchers from less well-resourced institutions are included as equal partners.
- A system for identifying and managing conflicts of interest should be established at the outset. Those with serious conflicts of interest should not normally have decision-making power.
- In contexts where governance structures are already in place, they should be evaluated in the light of the ethical principles to ensure that they are fit for purpose.

Governance structures should be transparent, so that they are communicated to participants before and during priority setting and reported afterwards

c. Choosing or designing a method

The method lays out the exact steps the priority-setting process will take: what activities, in what order – from preparation through the prioritization and follow-up stages. A number of different methods for research priority setting have been published. In addition, useful guides are available that provide overviews of how to set up and manage a priority-setting exercise *(43,61,64)*. Many priority-setting exercises adapt existing methods or design their own to suit their needs and context. Recommendations on how to use this guidance alongside some common methods are given in Chapter 4.

Ethical considerations for this activity include the following.

- Whether they follow a published method or devise one themselves, priority setters should use some systematic process that allows alternative research options to be compared in a structured way. Because decisions about health research priorities are decisions about how to allocate scarce and valuable resources, there is an ethical obligation to make those decisions systematically, on the basis of evidence, and consistent with ethical principles.
- The method chosen should be **proportionate**

to the resources available for priority setting and what is at stake.

- The method should be chosen or designed with the four ethical principles in mind. That means ensuring that each of its component activities are consistent with the ethical considerations listed in this chapter. It also means ensuring that priority setters are confident that, when viewed as a whole, the method:
  - is likely to **optimize the social value** of the research options selected (within the scope of the priority-setting exercise);
  - takes any **special obligations** into account;
  - if relevant, includes points in the decision-making process where research options will be examined for whether the research would involve **unjustified harms**; and
  - is procedurally fair, so that, given available time and resources, all relevant interested parties are included in a way that ensures the desired level of participation; and follow-up activities meet obligations of transparency and accountability.

d. Identifying interested parties

The parties who have an interest in the results of the research priority setting typically fall into three categories: research producers (for example, researchers or funders), research users (for example, clinicians or policy-makers) and research beneficiaries (for example, patients or carers). Where it is not obvious who these parties are, it may be valuable to undertake a "stakeholder analysis" *(64)*. The preparation stage will include making decisions about who among the interested parties to include, and so also about outreach to members of those groups (see Stage 1e).

If using the guiding questions for ethical research priority setting (Annex 6), the questions in part 6 should be answered now to inform this and the following activities.

Ethical considerations for this activity include the following.

- Who is included and how they are included is the core of **inclusion**. Consideration should be given to:
  - the epistemic, pragmatic and intrinsic reasons for including members of different groups (Box 1);
  - whether identified groups span all three categories – research producers, research users and research beneficiaries – and relevant demographics, so that the diversity of participants can match the diversity of interested parties;
  - whether enough individuals will be representing each category and demographic for their voices to be effective; and
  - what special efforts should be made to ensure participation from members or representatives of disadvantaged and marginalized groups (see Annex 3).
- In addition to thinking about who should be included in the priority-setting exercise, the team should consider to whom the priority setters are **accountable**. This may be relevant to how the results of an exercise are reported, and to monitoring and evaluation (see Stage 3a and Stage 3c).
- The **special obligations** of priority setters or those to whom priorities are addressed may be relevant to the stakeholder analysis. For example, government bodies may have special obligations to citizens and residents, with implications for who should be included and to whom they are accountable.
- The level of engagement should be **proportionate** to the resources available for priority setting and what is at stake. For smaller priority-setting exercises, it may be neither practical nor a good use of resources to try to include all parties who might have an interest in the results of priority setting. Nonetheless, it can be valuable to identify them so that a principled decision can be made about inclusion and for follow-up (particularly reporting – see Stage 3a).

Box 1. Whom to include and how

Step 1. Epistemic reasons for inclusion

1. Decide what information will be needed in order to make principled, informed decisions.
2. Work out how to obtain that information. Some information may come from consulting people; other information may be available elsewhere (for example, literature reviews or existing priority-setting exercises).
3. For information that will be gathered from people, undertake the following tasks.
    a. Map the different types of information needed to the individuals and groups who will be included.
    b. For each, consider how they should be included – at what level of participation, when in the process and so on. Groups might – or might not – be included separately and using different methods. For example, data from patients about their health-care experiences might be gathered through surveys and focus groups; estimates from scientists about the probability of success for research options might be gathered through the Delphi method (see Chapter 4).
4. Special care should be taken to include disadvantaged or marginalized groups in ways that allow them to participate in a meaningful way (Annex 3).

Step 2. Pragmatic reasons for inclusion

1. If including additional individuals or groups in order to gain trust or buy-in, ensure that the priority-setting process is in fact trustworthy and merits their buy-in.
2. Consider the following questions:
    a. Whose buy-in is necessary for the priority setting to be effective? How can those groups be included?
    b. How might strategies for gaining trust or buy-in conflict with other aspects of the priority-setting process?
    c. Are there interested parties who should be included but who pose a risk to ethical decision-making (for example, powerful funders or politicians who may have disproportionate influence on the outcome, or participants with conflicts of interests)? How could those risks be mitigated?
3. Given the answers to questions 2a–2c, consider how any additional individuals or groups should be included – at what level of participation, when in the process and so on.

Step 3. Intrinsic reasons for inclusion

1. Consider the following questions. Affirmative answers support intrinsic reasons to include members of particular groups in decision-making around priority setting.
    a. Is the priority setter accountable to a defined population (for example, government agencies to their public)?
    b. Does the priority setter have existing obligations to a defined population (for example, a relationship with a patient population or a specific community; a long-standing collaborative research partnership)?
    c. Are there identifiable groups that these decisions will have a big effect upon?
    d. Are the groups that these decisions will have a big effect upon particularly disadvantaged, at risk, disempowered or unheard (for example, in setting priorities for HIV research this could apply to injecting drug users, sex workers or adolescents)?
2. For each, consider how they should be included – at what level of participation, when in the process and so on.
3. Special care should be taken to include disadvantaged or marginalized groups in ways that allow them to participate in a meaningful way (Annex 3).

Step 4. Ensuring breadth

1. Consider the individuals and groups identified in steps 1–3 as a whole and answer the following questions.
    a. Is there a sufficient range of participants, such that they represent the diversity of interested parties?
    b. Is there a sufficient mass of participants, so that there are enough individuals representing each group for their voices to be effective?

e. Building foundations with interested parties

Once the interested parties are identified and plans made for whether and how to include them, some sort of outreach and relationship-building will usually be necessary. Building foundations with interested parties may inform the design of the priority-setting method; it can build knowledge and comfort with prospective participants, and it is an opportunity to inform potential audiences about the exercise and get buy-in.

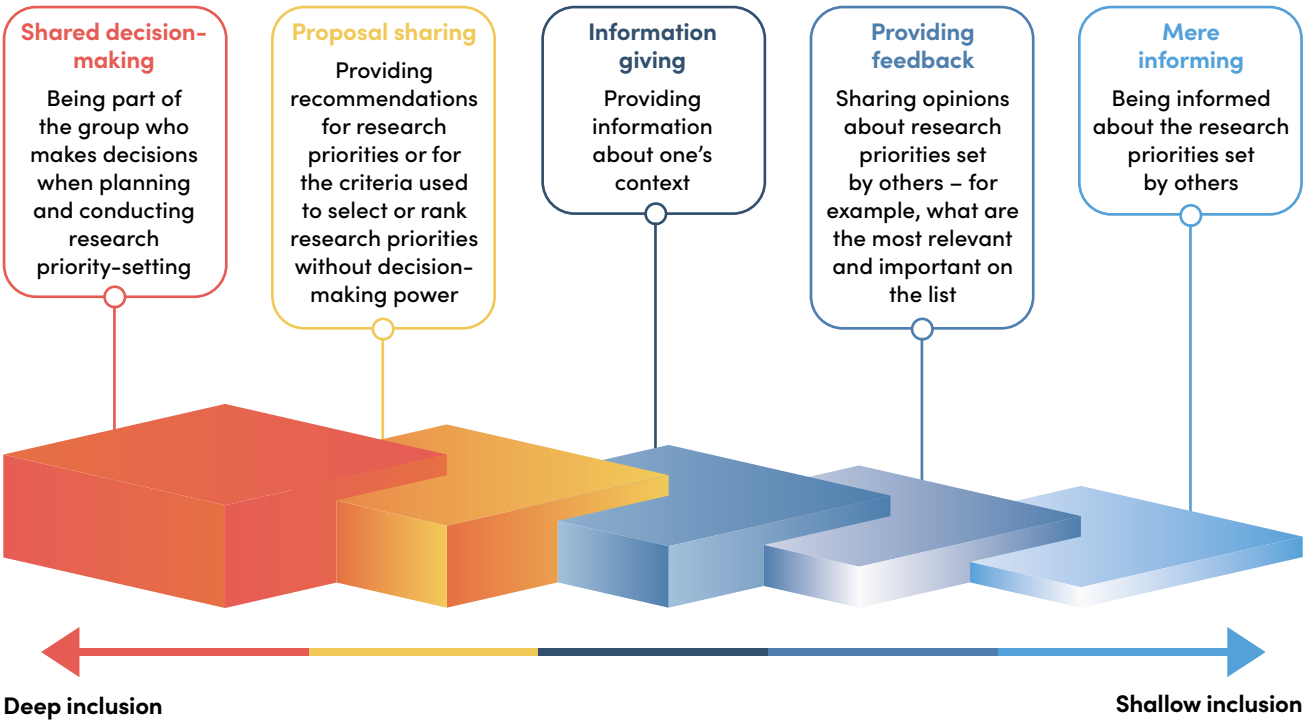
Ethical considerations for this activity include the following.

- For any priority-setting process, the goals of **inclusion** will be best served by forming connections and building trust with participants *(66)*. Consideration should be given to how relationships and trust can be built or made stronger before priority setting starts.
- The environmental supports that may help people to participate as equals and to the best of their ability should be considered. These might include training for those who need it, creating a pairing or mentoring system, accommodation of varying needs and other strategies. Such considerations are particularly important for members of disadvantaged or marginalized groups *(66)*.
- Consideration should be given to how capacity can be built among participants so that they are equipped with the skills and knowledge to be involved in future research priority-setting processes.

f. Determining interested parties' level of participation and when they participate

For interested parties who will be included in the priority-setting process, a decision should be made about their appropriate level of participation (Fig. 4).

Fig. 4. A spectrum of modes of inclusion



Source: Pratt, Merritt & Hyder *(45)*, adapted from Arnstein *(68)*.

Levels of participation range from pure collaboration (for example, representatives of all interested parties take part in workshops to solicit research options, decide on criteria for prioritizing among them, and jointly make decisions about the final list) to pure consultation (for example, members of a group are surveyed and the information they provide feeds into the priority-setting exercise) to simply being informed of the results of priority setting *(67)*. Some priority-setting processes involve a mix of consultation and collaboration (for example, a group is surveyed about their health problems, criteria are decided by the priority-setting team, and then the group is involved in a workshop applying the criteria to possible research options).

Ethical considerations for this activity include the following.

- It is sometimes appropriate to involve different groups in different ways. For example, some might be involved in decision-making and others simply surveyed for input on technical questions (see Stage 2c and Stage 2d). It is always important to connect **who** is included and **how** they are included to the reasons **why** they should be included.
- Of those who provide information, the different types of relevant knowledge they may have should be distinguished (for example, judgements about how likely it is that a research question can be answered should not be made by patients; judgements about the relative importance of reducing pain versus improving mobility should not be made by scientists who lack clinical or lived experience of a condition).
- In making decisions about the level of participation, the priority-setting team should consider with whom there is an obligation to share decision-making power. In particular, the following questions should be addressed:
  - To whom are the priority setters **accountable**?
  - How might sharing power improve the **social value** of the results of the exercise (for example, by ensuring that **equity** considerations are raised and heard, or by increasing the cultural relevance of the research options prioritized)?
  - On whom will the decisions being made have a substantial impact?
- The final process should be one that is justifiable to all interested parties – even those who are not included as collaborators.
- For **transparency**, participants should normally be asked to declare any potential conflicts of interests. Consider whether the process needs to be altered in any way to address conflicts of interests and whether any conflicts are serious enough to be exclusionary.

g. Collecting evidence

Effective priority setting requires gathering, analysing and organizing the relevant evidence that will be used as inputs into the process. Depending on the context, this might include information about *(59,61)*:

- the state of scientific knowledge on relevant biological mechanisms and pathology;
- existing interventions, including biomedical and behavioural modalities;
- public health needs, including current data on burden of disease, health system performance and access to the social determinants of health;
- disparities in health and well-being, such as how the disease burden is distributed among groups stratified by age, race or ethnicity, gender, sexual identity, disability, immigration status, geography and others;
- the research governance structures within a country;
- what research within the scope of the exercise has already been conducted or is ongoing;
- previous research priorities, identified through other priority-setting exercises, by identifying missing evidence when developing public health guidance, and in publications;

- how the health-care system operates; and
- what patients, carers, clinicians, policy-makers or other research users want.

At a minimum, gathering evidence will require reviewing the available scientific literature, databases, government reports and so on. Depending on the context, it might also require consulting subject-matter experts, clinicians or decision-makers, or even surveying research producers, users or beneficiaries. Note that many priority-setting exercises rely on the knowledge of the individuals involved in setting priorities (hence the **epistemic** reasons for inclusion – see Box 1). Not all knowledge gaps must be filled during the preparation stage.

In addition to gathering evidence, it is likely that the information will need some analysis and organization. For more extensive priority-setting exercises, a framework like the combined approach matrix may be helpful for identifying data needs and presenting the relevant information (see Chapter 4).

Ethical considerations for this activity include the following.

- The priority-setting team should consider whether the evidence that has been collected is sufficient for prioritization on the basis of **social value**. For example, if epidemiological data are not stratified by gender, socioeconomic status, geography or other potentially important characteristics, then it will not be possible to take into account **equity** regarding those characteristics. If the **costs** of different research options are not available to priority setters, then it will not be possible to allocate resources optimally.
- Where knowledge gaps are identified, whether it is possible to fill them or how to reduce their negative impact on the exercise should be considered. This might include, for example, flagging the gaps for participants, acknowledging them in reports and treating the gaps themselves as potential research priorities.
- Where participants in a priority-setting exercise will draw on data, the information should be presented in a way that they are able to access and understand. Information should be tailored to the needs of users. For example, if patients will be involved in priority setting, research options should be described so that they can be readily understood by non-scientists.

h. Deciding criteria for prioritization

An important component of any process used for setting priorities is the criteria that will be used to compare research options. Depending on the method chosen, these criteria may be set in the preparation or the prioritization stage (depending on whether the participants in the exercise are also setting the criteria). The four ethical principles discussed in Chapter 2 provide a framework for thinking about priority-setting criteria. However, they will typically be too general to use directly. Instead, they need to be specified in the form of criteria that reflect the context of the specific priority-setting exercise (for example, its topical and geographical scope, the types of research considered, whether it is thematic or project-based, and so on).

Ethical considerations for this activity include the following.

- Criteria should be included that capture each component of **social value** (see Annex 4 for further detail on how to define social value for a specific priority-setting context and operationalize the definition, and gives some examples of how this has been done):
  - the magnitude of potential benefits from research;
  - the degree of disadvantage of potential beneficiaries (according to relevant dimensions of equity);
  - the likelihood that a research project will be successful; and

- where relevant, the relative costs of different research options – for example, the amounts of resources that the research projects would require.

- For research that is more distant from translation into practice, including basic biomedical research, it will not be possible to estimate the effects on health and well-being that would result from a successful research project directly. In these cases, proxy indicators for the components of social value need to be devised (see Annex 4).
- The priority-setting team should consider whether **special obligations** justify giving greater weight to some research options over others – for example, a middle-income country governmental agency might give greater weight to benefits to its own population while still taking regional or global needs into account *(69)*.
- For exercises where the research options are likely to include **non-human animal research**, criteria should be included to compare options according to the harms they will cause to non-human animal subjects.
- The priority-setting team should consider whether **harms from research** to third parties are a plausible concern, given the scope and topics of the priority-setting exercise. If so, criteria should be included to flag research options that pose such risks.
- Consideration should be given to whether some criteria should be weighted to reflect their relative importance *(70)*.
- Consideration should be given to whether the criteria should be decided on by a wider group than the team leading the priority-setting exercise – i.e. whether this activity should take place during Stage 2a. Doing so **includes** more interested parties in setting the terms for the exercise. The ethical considerations regarding conducting surveys and running meetings may then apply (see Stage 2c and Stage 2d).

i. Generating research options

In order for priorities to be set, there needs to be a set of options to prioritize. In a few cases – for example, for a funder receiving investigator-initiated grant proposals – these options will already be given; for most priority-setting exercises, they will need to be generated. Generating research options involves listing potential research areas or research questions that the priority-setting exercise will rank or choose among. Depending on the method used, this can be part of the preparation stage or the prioritization stage. After an initial list of research options has been drafted, it can be refined by:

- making the research questions or potential areas of enquiry more precise;
- eliminating research questions that have already been answered (following a review of the scientific literature); and
- eliminating research options that are overlapping or duplicative.[3]

Ethical considerations for this activity include the following.

- If the research options are specific enough, **risk assessment** should take place. Consider whether any elements are likely to pose high enough risks of harm – directly or through the knowledge generated – to be of concern at this early stage. Some research options might be eliminated at this point; others should be flagged as needing particular attention during the prioritization stage.
- To ensure **inclusion**, the initial list of research options should be generated by a sufficiently diverse set of individuals. The priority-setting team might consider the following questions:

3 Chapter 6 of the James Lind Alliance Guidebook *(60)* provides a step-by-step guide to refining lists of potential research options.

- Should researchers from multiple disciplines be consulted?
- Are respondents geographically diverse?
- Should clinicians, carers and/or patients be consulted (noting that generating research options for a condition is not the same as finding out what matters most to people affected by the condition)?

- If research options are generated through surveys or meetings, Stage 2c and Stage 2d should be consulted.

Stage 2. Prioritization

The second stage is where priorities are actually set – that is, where selected criteria are applied to choose among research options to generate a list of priorities. In priority-setting exercises that centre around a workshop, this would be the activities that happen at the workshop. Other exercises will be more spread out over time. For example, the James Lind Alliance framework (see Chapter 4) involves interim prioritization via a survey, followed by final prioritization of shortlisted research options at an in-person workshop. The type and number of steps involved in setting priorities should be decided when selecting or designing the method. They will depend on the exercise's needs and resources.

Typical activities for the prioritization stage include:

a. Deciding criteria for prioritization

(if not completed as part of the preparation stage).

b. Generating research options

(if not completed as part of the preparation stage).

c. Administering surveys

Whether for preliminary data gathering, gathering research options or even setting final priorities, many priority-setting exercises involve administering surveys to participants.

Ethical considerations for this activity include the following.

- Considerations concerning **inclusion** can be very important when designing and administering surveys. It should be borne in mind, here as elsewhere, that the goal is not to simply include more people: what is needed is appropriate inclusion, so that the right people are asked the right questions to find out the information that is needed for ethical priority setting. Haphazard efforts to broaden inclusion can dilute the voices of the people whose opinions actually matter. Relevant questions to consider regarding surveys might include the following.
  - Should members of this group be surveyed rather than engaged in person? Surveying a group rather than engaging them in person typically means that its members have less power in the priority-setting process. However, it may make it possible to engage more people, and will generally be less resource intensive.
  - If the survey is online, will all members of the target population be able to access it? If not, are there alternative ways to administer the survey?
  - Is the survey written at a level that will be understandable to all respondents? Can those with visual or hearing impairments complete it?
  - In what languages will the survey be available?
  - Does the survey raise concerns about confidentiality, sensitive topics or other issues relating to participant protection?
- Comprehensive guidance on the ethics of survey research is outside the purview of this guidance and can be found elsewhere *(71)*.

d. Running meetings

Most research priority-setting exercises involve one or more meetings, which might be in person or online. It is usually at such meetings that final decisions are made about the research agenda or list of priorities that the exercise produces. Depending on the scope of the exercise and the resources available, it may be better to have independent trained facilitators to run meetings.

Ethical considerations for this activity include the following.

- Considerations related to **fair procedures** come to the fore when designing and running meetings.
- Meetings should be designed and run with the governing aim of ensuring **qualitative equality** among participants. This means that everyone has a fair opportunity to share their ideas and to influence the priority-setting process and outcomes. Relevant elements to consider include the following.
  - Consideration should be given to whether the process of decision-making raises concerns about **epistemic injustice**. For example, will patients be listened to, even if they do not use medical terminology? Will the views of scientists be given excess weight, even when they are speaking outside their technical expertise?
  - To mitigate power disparities, it is important to assess what types of power disparities exist between participants, and to apply strategies to reduce them – for example, setting ground rules that privilege speaking time for less heard voices, using facilitators skilled at drawing out less heard voices, and holding the priority-setting process in a location where less powerful participants feel comfortable *(72)*.
  - In some cases, it may be useful to employ a "stepped approach" to promote qualitative equality. This is a facilitation method where small groups meet first to deliberate. Then those small groups come together to deliberate about the topic.
- Consideration should be given to whether to hold several meetings with different participants. This can allow broader participation; it means that meetings can have different functions (for example, brainstorming research options versus applying prioritization criteria); and it can mitigate power imbalances by ensuring that particular individuals or groups do not dominate.
- Special efforts should be made to design the priority-setting process so that more disadvantaged and marginalized groups can participate effectively (see Annex 3).
- Resources should be secured to ensure participation (for example, to cover travel costs, accommodation or child care, as needed).

e. Applying criteria

Whether it happens as a survey response or during a meeting, the criteria used for prioritization have to be applied at some point. This can be done through developing consensus or through some metric-based approach, such as using an algorithm to aggregate participants' scores *(58)*. Either way, the process can involve several iterations of deliberation, feedback and scoring, depending on the method chosen.

Ethical considerations for this activity include the following.

- If research options are sufficiently specific to make judgements, projects that are likely to cause **unjustifiable harm** should be eliminated at this point. This might be because the suffering inflicted on non-human animals would be too great, or it might be because of potential third-party harms from the use of the results of the research.
- The criteria should be applied with the goal of **optimizing the social value** of research, consistent with any **special obligations** (see Stage 1h).
- Whether a consensus-based or metric-based approach is preferable for the context should be considered. Each has pros and cons. Consensus-based approaches require participants to take account of the views of others. However, they require careful facilitation to manage power dynamics. Metric-based approaches can ensure that every participant gets an equal say. However,

if the priority setters want participants to take account of others' opinions, then discussion and feedback needs to also be built into the process, prior to the final scoring.

Stage 3. Follow-up

Assuming that Stage 1 and Stage 2 were carried out correctly, the final priorities should be consistent with any special obligations, and unethical research options should have been eliminated. But the principles of **optimizing social value** and **following fair procedures** still have implications at the follow-up stage. Social value will not be optimized unless steps are taken to implement the priorities – whether by carrying out the highest priority research oneself or disseminating the priorities to others. **Accountability** will not be achieved without feeding back the outputs of priority-setting to participants, and assessing whether the priority-setting process itself was fair and achieved its goals.

If using the guiding questions for ethical research priority setting (Annex 6), the questions in part 7 should be answered now to inform the follow-up activities.

The following activities should be considered during follow-up.

a. Reporting the results

Reporting the results of priority setting includes all activities relating to publication, outreach and dissemination. Exactly what should be reported, in what form and to whom will depend on the nature of the priority-setting exercise and who carried it out.

Ethical considerations for this activity include the following.

- To **optimize social value**, where the results of priority setting might be of value to others, they should be made publicly available. Depending on the audience, this might be through academic publications, presentations, websites, social media, newsletters or direct communication (for example, to representatives of funders or government ministries) *(60)*. Timely reporting and effective dissemination are essential to getting uptake of the research priorities. They also reduce the chance of duplicative priority setting.
- **Transparency** is particularly important for larger exercises and those conducted by entities with special obligations to the public. The methods used in setting priorities should be reported as well as the findings. The REPRISE reporting checklist could be used to structure these reports *(65)*.
- There are ethical obligations based on **reciprocity** to share the results of priority setting with the parties who participated in any part of the exercise (just as there are obligations to share research findings with participants).
- **Accountability** may require not only that the methods and results of priority setting are made publicly available but also that plans for action based on the identified priorities are set out.
- In all cases, care should be taken to match both the method and content of communications to the intended audiences. For example, if priorities are being set for research with a specific patient population, the process and outcomes should be communicated in a way that is understandable and accessible to members of that population (including through translation into their preferred language, if necessary).

b. Acting on the priorities

The easiest way to ensure that a set of research priorities gets taken up is to use them oneself. Whether this is possible, and what form it will take depends on the priority setter – whether they conduct research themselves, directly support research or are simply developing an agenda for others to follow.

Ethical considerations for this activity include the following.

- Where possible, priority setters and other interested parties have ethical obligations to conduct research in line with the final priorities, or to directly support it in other ways. For example:
  - **funders** should consider directly commissioning high-priority research, earmarking funding for priority research areas, and/or designing grants programmes to encourage and give higher scores to applications that fit the priorities (see Scenario 3 in the companion casebook *(3)*;
  - **researchers** should consider carrying out the highest priority research, identifying funding opportunities consistent with the priorities, and/or finding training opportunities and collaborators that would enable them to carry out the research;
  - **governments** should consider whether there are changes to law, policy, sources of government support or other activities that would enable scientists to better pursue the priorities – for example, in addition to directly funding research, this might involve identifying bureaucratic barriers to priority research, and coordinating funders and researchers working in the country around the national priorities; and
  - **research institutions** should consider redirecting funding and other institutional resources towards the priorities, adjusting career incentives to match carrying out priority research, and hiring individuals working in priority areas.

c. Monitoring and evaluating

Priority setting is not a one-off exercise. After an exercise is completed, it is important to evaluate how it went so that lessons can be learned for future exercises. This includes what worked and what needs improving in the preparation and prioritization stages, as well as whether the overall process was, in fact, fair. The results and lessons learned from one exercise should feed into the next to improve the process of priority setting *(57)*. The priorities will eventually need to be revisited, as the landscape of health and research changes and as – hopefully – some of the high-priority research is carried out.

After the results of a priority-setting exercise have been published and disseminated, it is important to monitor its effects. In the short term, these might include measuring awareness of the priorities; in the longer term, these might lead to changes to what research is carried out, new interventions and impacts on well-being *(64)*.

Ethical considerations for this activity include the following.

- Anyone carrying out research priority setting should monitor and evaluate the process and results in order to ensure that the priority setting increases the **social value** of research. This includes monitoring dissemination, uptake and, eventually, whether and when research priorities need to be revisited. In areas where there is rapid change – for example, in the speed of innovation – priorities may need to be revised more frequently.
- Many actors – including governments and funders – have obligations of **accountability** and **transparency**, which mean that they should report on their monitoring and evaluation, as well as providing opportunities for interested parties to challenge or comment on the priorities *(57)*.
- Whether and how participants can be asked to evaluate the priority-setting process in which they were included should be considered.

4. Existing methods and guides

A number of methods for running research priority-setting exercises have been published and used extensively. This guidance is not intended as an alternative to these published methods, but it may help priority setters think about whether to adopt one in whole or in part. This chapter describes and discusses the most commonly cited methods for research priority setting.[5] Some methods are best thought of as components to be incorporated into a bigger priority-setting process. Others are complete methods in the sense that they prescribe how each stage of priority setting should be carried out. The following sections describe how the component methods can be incorporated into an ethical priority-setting process, and how this guidance can complement the complete methods.

In addition to the published methods, several guides provide helpful recommendations for priority-setting exercises without prescribing specific designs *(43,57,61)*. Existing WHO guidance on research priority setting is also available for WHO staff *(64)*. The final section of this chapter

5 Other methods not described here include Listening for Direction (73); adaptations of the Choosing All Together exercise to health research *(74)*; and Value of Information Analysis *(75)*.

discusses some overlaps and differences between that publication and this guidance.

In considering the use of an existing method for a priority-setting exercise, the following elements should be borne in mind.

- There is no one-size-fits-all method for research priority setting. Each method has pros and cons, and should be considered in the light of the exercise's specific circumstances, needs and resources.
- In many cases, designing their own process will be the best way for priority setters to ensure that they can set priorities in a systematic, evidence-based manner on the basis of sound ethical principles.
- Borrowing from different methods to create an adapted method that suits the exercise should be considered.
- Even if an existing published method is chosen, it is still essential to think systematically through the ethical considerations that apply to one's specific situation.

Component methods

The combined approach matrix (CAM) and the Delphi method are sometimes described as priority-setting methods in their own right. However, it may be helpful to view them instead as providing components for a priority-setting exercise. These components can be incorporated into a broader process designed by the priority setter.

The CAM

The CAM is a tool that is used to "classify, organize and present the large body of information that enters into the priority-setting process" *(59)*. The core of the CAM involves gathering data to complete a matrix with two dimensions (**public health** and **institutional**) or three (adding an **equity** dimension). The public health dimension includes information on disease burden, determinants of disease, the present level of knowledge about disease, the cost and effectiveness of existing interventions, and current resources flows. The institutional dimension is used to assign this public health information to different levels: individual, household and community; health ministry and other health institutions; non-health sector; and governance. When the equity dimension is included, this requires assessing whether there are also differences between social groups, such as gender and income groups.

There is no one-size-fits-all method for research priority setting

The completed matrix presents all the relevant information relating to a priority-setting process in a systematic way. In addition, it reveals knowledge gaps (and filling those knowledge gaps might be research priorities). According to the authors of the CAM, it can be used by "institutions, local or national governments, development agencies, academics and individual researchers" *(59)*. Practically, it requires gathering and synthesizing a lot of information, so whether it should be used will depend on whether all that information is needed and whether there are sufficient resources and time to complete it.

The following points should be borne in mind when considering the CAM and this ethics guidance.

- The CAM does not constrain the form that priority setting takes; it just guides the collection, analysis and presentation of data for a priority-setting exercise. A process using the CAM should therefore be designed in the light of the four ethical principles set out in Chapter 2, and taking note of the ethical considerations enumerated in Chapter 3 for each stage of priority setting.
- Given how data-intensive the CAM is, and

how much interpretation must be imposed on the data in order to populate the matrix, care must be taken to identify and defend any value judgements that are embedded in it.
- The applicable ethics guidance section in Chapter 3 is:
  - Stage 1g (collecting evidence).

The Delphi method

The Delphi method is a process through which information and opinions from a group of experts are gathered and synthesized. Originally developed for forecasting, the Delphi method is now used in various situations where information is limited so predictions cannot be based on models *(76)*. There are several variants of the method, but the basic idea is that priority setters convene a panel of experts who answer questions or rank options. Their responses, including their reasoning, are compiled and then circulated to the same panel of experts. The exercise is repeated one or more times. A Delphi exercise may aggregate the expert panel members' scores, or it may aim for consensus.

Research priority-setting exercises often incorporate some form of the Delphi method as one component. Usually, it is used for applying criteria to rank research options, but it can also be used for developing the criteria themselves and for generating lists of research options *(78)*.

The following points should be borne in mind when considering the Delphi method and this ethics guidance.

- Where the Delphi method is used for the prioritization stage of priority setting, special consideration should be given to how it relates to **fair procedures**. An application of the Delphi method is usually not replicable, which poses challenges for **transparency**. Care must also be taken that appropriate **inclusion** is not undermined, as in the following examples.
  - Solely including experts on a panel means that that part of the process will not include other voices, such as those of the users or beneficiaries of research. Thought should be given to how those voices will feed into the process.
  - Feeding back scores to the panel or having them discuss the pros and cons of research options has advantages in terms of critical engagement and knowledge exchange. However, it risks more dominant or powerful individuals having excessive influence on the results.
- The applicable ethics guidance sections in Chapter 3 are:
  - Stage 1d (identifying interested parties)
  - Stage 1f (determining interested parties' level of participation)
  - Stage 1h/2a (deciding criteria for prioritization)
  - Stage 1i/2b (generating research options)
  - Stage 2d (running meetings)
  - Stage 2e (applying criteria).

Complete methods

The Child Health and Nutrition Research Initiative method

The Child Health and Nutrition Research Initiative (CHNRI) method was developed by researchers to help set priorities for research into child health and nutrition. The method has since been used for various health topics and in different contexts *(79)*. The CHNRI process starts with a technical working group who define the context of the priority-setting exercise (for example, target population or target disease burden). The working group surveys a large sample of experts to identify a set of candidate research options. Depending on the context, these experts might include policy-makers and programme managers in addition to scientific researchers. The survey of experts generates "an exhaustive list of the competing research options by addressing main risk factors and possible interventions" *(80)*. After this list is cleaned up (for example, by removing duplicates and integrating related ideas), the experts are surveyed again. This time they score independently each research

option on a set of criteria. The CHNRI method provides five "standard" criteria for prioritization among research options: answerability, effectiveness, deliverability, maximum potential for disease burden reduction, and effect on equity. This is not set in stone, so the criteria used can be changed and, in practice, often are *(79)*. The criteria can also be weighted, so that more importance can be assigned to one criterion than another across the exercise. The weights are developed by surveying external stakeholders from the wider community. This allows these non-experts to give input regarding values. The weights are applied to the experts' scores, which are aggregated to rank all the candidate research options.

The following points should be borne in mind when considering the CHNRI method and this ethics guidance.

- The five standard criteria used to score research options can be mapped to the three components of **social value** (Annex 4). As noted, many CHNRI exercises have used different criteria – adding to or subtracting from the standard set. In all cases, care should be taken that the scores can realistically be interpreted as estimates of each component of social value (without under- or over-counting), and that the overall score makes sense as an estimate of social value.
- The standard CHNRI method does not include consideration of the relative cost of conducting the research projects being prioritized. Where possible, this should be incorporated into the process.
- The CHNRI method can be run and reported in a transparent manner, and in some respects is a model of procedural fairness – for example, it does not allow the opinions of any individuals to have outsize weight or, indeed, to influence what input others add to the process. However, the method is also predominantly driven by scientific expertise. It is therefore important to consider whether the priority-setting context is appropriate for such an exercise, by addressing the following questions.
  - Should there be input from non-scientific groups, such as clinicians, carers, patients or members of the public?
  - Will an exercise that does not include their perspectives reflect what matters to them?
  - Are there pragmatic reasons to involve non-scientists at some stage of the process?
- The applicable ethics guidance sections in Chapter 3 for the technical working group are:
  - Stage 1a (defining the context and scope)
  - Stage 1b (deciding on governance)
  - Stage 1d (identifying interested parties)
  - Stage 1h/2a (deciding criteria for prioritization).
- The applicable sections for the survey are:
  - Stage 1g (collecting evidence)
  - Stage 1i/2b (generating research options)
  - Stage 2c (administering surveys).
- The applicable section for the prioritization process is:
  - Stage 2e (applying criteria).
- The applicable sections for determining weights are:
  - Stage 1h/2a (deciding criteria for prioritization)
  - Stage 2c (administering surveys).

The Essential National Health Research strategy for priority setting

The Essential National Health Research (ENHR) strategy is a method designed by the Council on Health Research for Development for use in national priority-setting exercises *(81)*. The method starts with the team convening the exercise setting up a working group of stakeholders to decide how the exercise will be run and to conduct a "situation analysis" to gather relevant data. An initial list of research ideas is generated from the situation analysis and inputs from various stakeholders. The

working group also decides on the criteria and the scoring method for ranking research options, which are agreed by consensus. The final priorities are set at a national workshop. This workshop includes a larger group of stakeholders, who should represent the different groups with interests in health research in the country. These may include researchers, health service providers, communities, professional associations, industry, politicians, donors and international agencies. The workshop participants use the criteria to score the research ideas to produce a national research agenda.

The following points should be borne in mind when considering the ENHR strategy and this ethics guidance.

- In so far as this method is used to set national priorities, its focus will naturally be on what is most important to the citizens and residents of that country. However, consideration should still be given to the scope of the exercise given potential international obligations – for example, whether regional or global needs should be taken into account.
- The ENHR strategy emphasizes the importance of bringing together all interested parties. Including politicians, donors and representatives of the private sector may be highly valuable for getting full information and obtaining buy-in from key decision-makers. However, it raises many of the challenges concerning **inclusion** mentioned in Chapters 2 and 3. Particular care should be taken with regard to the design of the overall process and the workshop at which priorities are set, so that they do not disempower disadvantaged and marginalized groups (Annex 3).
- The applicable ethics guidance sections in Chapter 3) for the working group stage are:
  - Stage 1a (defining the context and scope)
  - Stage 1b (deciding on governance)
  - Stage 1d (identifying interested parties)
  - Stage 1e (building foundations with interested parties)
  - Stage 1f (determining interested parties' level of participation)
  - Stage 1g (collecting evidence)
  - Stage 1h/2a (deciding criteria for prioritization)
  - Stage 1i/2b (generating research options).
- The applicable sections for the national workshop are:
  - Stage 2d (running meetings)
  - Stage 2e (applying criteria).

The James Lind Alliance framework

The James Lind Alliance (JLA) brings patients, carers and clinicians together in priority-setting partnerships (PSPs) "to identify and prioritize the unanswered questions or evidence uncertainties that they agree are most important for research to address" *(60)*. These PSPs are comprised only of patient, carer and clinician groups – that is, only individuals with actual experience of the health area for which research priorities are being set – because these groups are thought to have special insight into what research evidence is actually needed by patients and their clinicians. The composition of PSPs is carefully balanced so that clinicians do not outnumber patients and carers. This is to ensure that the patient and carer voices are heard. Meanwhile, they exclude "representatives of the pharmaceutical industry, other commercial businesses or those in the research community who are not also clinicians, patients or carers". The JLA view is that these groups may bias the results of priority setting away from what really matters to the users and beneficiaries of research evidence, and that they already have opportunities to influence the research agenda.

The first stage of the JLA method involves the organizers of the PSP gathering "uncertainties" from existing guidelines and systematic reviews, and from surveys of patients or service users, carers and clinicians. These uncertainties are

checked by the organizers for whether they are in scope, overlapping questions are removed, and the remainder are stated in the form of "indicative questions". Questions that have already been answered in the literature are then removed to leave a longlist of questions. A survey of stakeholders is used to conduct interim priority setting, which reduces the longlist to a shortlist of 20–30 questions. Survey responses from patients and carers are given the same weight as responses from clinicians. The final stage involves a workshop of 12–30 patients, carers and clinicians. The participants aim to develop consensus on a top 10 list of priority questions through small group discussion and ranking exercises. The JLA guidebook states that "the aim of the Top 10 is to highlight important areas for research, but not necessarily to come up with the specific research questions".

The following points should be borne in mind when considering the JLA method and this ethics guidance.

- The JLA method is the most directive of the priority-setting methods discussed here. It therefore leaves less discretion to make adjustments according to the ethical principles described in this guidance. Of note, the method dictates which groups will be included, and decisions about which uncertainties merit highest priority are made using the criterion of what participants regard as most important (rather than, for example, through applying specific criteria corresponding to the components of social value). The relative costs of answering research uncertainties are also not considered in the JLA method.
- The key strength of the JLA method is that it is designed to identify what matters to those directly affected by a health condition, and to elevate the voices of those who might otherwise not be heard.
- In deciding whether to use the JLA method, priority setters should consider whether the key gap in knowledge needed for priority setting on a health topic concerns what matters to research users, carers and patients.
- For those interested in acting on the priorities generated by a PSP, it may be necessary to engage in further priority setting to incorporate the likelihood of success in resolving a research uncertainty and the cost of doing so. These considerations are in addition to the fact that the uncertainties in the top 10 priority questions are ranked as highly important for users and beneficiaries.
- The applicable ethics guidance sections in Chapter 3 for gathering and reviewing initial uncertainties are:
  - Stage 1a (defining the context and scope)
  - Stage 1b (deciding on governance)
  - Stage 1g (collecting evidence)
  - Stage 1i/2b (generating research options)
  - Stage 2c (administering surveys).
- The applicable sections for the survey to reduce longlist to shortlist are:
  - Stage 1d (identifying interested parties)
  - Stage 2c (administering surveys).
- The applicable sections for the workshop are:
  - Stage 1d (identifying interested parties)
  - Stage 1e (building foundations with interested parties)
  - Stage 2d (running meetings)
  - Stage 2e (applying criteria).

Guides

A number of useful guides summarize published methods and give practical advice on carrying out priority-setting exercises *(43,57,61)*. This ethics guidance should complement such guides.

WHO guidance on research priority-setting exercises

WHO has also issued guidance on research priority setting – *A systematic approach for undertaking a research priority-setting exercise*

(64). The target audience is WHO staff carrying out a priority-setting exercise. Such exercises are typically global in scope, and aim to delineate high-level priorities for a specific disease or health topic, such as tuberculosis, nutrition, or maternal and child health *(82)*.

A systematic approach divides priority setting into four phases – plan, implement, publish, and monitor and evaluate – and delineates key activities for each stage. This ethics guidance should complement the process of designing a method to match the context that *A systematic approach* recommends, to make sure that all the ethical principles are taken into consideration. Such a method might draw on some of the other research priority-setting methods described above. The four phases of *A systematic approach* are related to the three stages of this guidance as shown in Table 2.

Table 2. Comparison of phases and stages

A systematic approach	**This guidance**
Phase 1. Plan	Stage 1. Preparation
Phase 2. Implement	Stage 2. Prioritization
Phase 3. Publish	Stage 3. Follow-up
Phase 4. Monitor and evaluate	

The recommendations of this guidance are intended to be consistent with *A systematic approach*, while going into a greater level of detail and specificity regarding the ethical considerations at each stage. For example, where *A systematic approach* lists three categories of criteria for comparing research options (64), this guidance recommends four categories: magnitude of benefit, impact on equity, likelihood of success and cost (Table 3). This breaks "public health benefit" into two components to emphasize the importance of incorporating equity into judgements of social value from the outset.

Table 3. Comparison of categories for comparing research options

A systematic approach	**This guidance**
Public health benefit	Magnitude of benefit Impact on equity
Feasibility	Likelihood of success
Cost	Cost

As a publication for WHO staff, not all the recommendations in *A systematic approach* will apply in the same way to other actors involved in priority setting. For example, the ethical obligations concerning scope, the involvement of interested parties, and carrying out prioritized research vary from actor to actor.

5. Frequently asked questions

Ethical principles

What should be done when ethical principles conflict?
Sometimes the ethical principles will all point in the same direction, but often they may appear to conflict. For example, the research project that has the greatest expected benefit may not be the one that would most improve equity in a population. The components of social value must then be weighed against each other. Alternatively, one research project might have greater social value globally, while another would provide greater benefits to a funder's national population. The obligation to optimize social value would then have to be balanced with the funder's special obligations. As always in ethics, there is no formula, and reasonable people may disagree about the relative importance of different principles. Working out how to balance different considerations relies on the good judgement of those involved. Where participants in a priority-setting exercise have different views about values, they should be reconciled through an inclusive process, just as with any other part of the exercise where individuals' views matter (see Chapter 3 and Annex 3). Just as factual claims should be backed up with evidence, trade-offs between important values should always be made on the basis of justifiable reasons. More important decisions about trade-offs should be documented and reported transparently.

What if participants in a priority-setting exercise raise ethical considerations that are not mentioned in the guidance?
This guidance provides a framework for incorporating ethics into research priority setting,

but it does not claim to be comprehensive or to cover all situations. The ethical principles described will always need to be specified and interpreted for the particular context of a priority-setting exercise. Further, it is always possible that additional ethical considerations might be raised that apply to one specific context. If participants in an exercise agree that there are additional relevant ethical considerations, the process should be designed to take them into account.

How can research priority setting promote global justice?
The vast inequalities in the world will not be rectified through better priority setting alone. Nevertheless, setting research priorities explicitly, in a systematic way, and guided by the ethical principles described in this guidance should help to align the health research that is conducted towards the promotion of global justice. If priorities are set ethically and those priorities are followed, they should promote social value. Since social value combines concern for improving population well-being and equity, aiming at social value entails aiming at social justice.

Are these principles different from those found in other WHO guidance? Why the inconsistency?
Depending on the specific topic, guidance may emphasize different ethical principles or organize them in different ways. The ethical principles laid out in this guidance are not expected to be inconsistent with those that WHO sets out elsewhere. Nor are they radical (although the implications for research if they are put into practice might be dramatic). They are synthesized from widely accepted frameworks for setting priorities in health care and research, and for research ethics.

Social value

Does research priority setting mean there is no place for curiosity-driven research? Will research priority setting kill innovation?
Many important scientific discoveries appear to have been driven mainly by curiosity about how the world works. At the same time, a great deal of research – especially health research – is goal directed: that fact is reflected in the way current health technologies reflect population health needs to some degree. The correct balance to strike between these two is itself a difficult and important research question *(83)*. At the very least, priority setting should allow space for curiosity-driven research in so far as there is evidence that such research will lead to valuable discoveries: letting scientists follow their interests is likely ultimately to promote valuable goals.

Note that there is a separate question concerning how far decisions about research projects should be driven from the top down or from the bottom up. When funders decide what studies should be carried out and then look for scientists to carry out those studies, or when they specify criteria for grants very narrowly, this is top-down decision-making (or "strategic funding"). When funders provide support to researchers but leave it up to them what to investigate, or when they leave the eligibility criteria for grants very open, this is bottom-up decision-making (or "response mode funding"). Whether one way of making research decisions leads to more valuable research in the long term is an open question.

The social value of basic biomedical research is often not apparent or is hard to determine. Does it mean that it should be de-prioritized?
It is undeniable that basic biomedical research has led to many scientific breakthroughs that have been vitally important to improving human health; thus, some has very high social value. It is also true that the exact direction of scientific progress cannot be predicted, so it is hard to estimate the social value of specific projects. Because the ultimate effects of basic biomedical research are so hard to determine, estimates of the social value of basic science projects are more uncertain – that is, they have a wider margin of uncertainty. But that does not mean that this type of research has lower social value.

This guidance encourages efforts to prioritize among basic science projects on the basis of social value, in so far as that is possible. Suggestions for how to do so can be found in Annex 4. More research is needed on how to prioritize among basic science projects, and on how to balance research portfolios between basic and more applied science.

What does research priority setting mean for the humanities and social sciences?
Where they are not competing for the same resources as health researchers, the question of how to justify humanities or social sciences research funding or prioritize among projects is outside the remit of this guidance. However, research projects in the humanities and social sciences that constitute health research should be judged by the same broad criteria as other health research. Some social science projects have a greater prospect of ultimately leading to social benefits than others. To some extent this is predictable. Likewise, with health research in the humanities.

Does the principle of optimizing social value rule out research on rare diseases?
Rare disease research presents a challenging case for research priority setting. All else being equal, the social value of developing (for example) a new, accessible cure for a common disease is greater than the social value of developing one for a rare disease. In this regard, prevalence is relevant to social value, and more common diseases would get higher priority. However, there are several circumstances in which it may be reasonable to include rare diseases in priority lists.

- A condition may be underfunded even given its rarity because of the amount of funding going into more common diseases from other funders.
- A condition may be very bad for individual patients. This is true of a number of rare congenital conditions. There will be equity reasons to prioritize such diseases, as well as reasons based on the magnitude of the potential benefit from a transformative treatment or prevention modality.
- Rare diseases are themselves common, affecting an estimated 300 million people worldwide *(84)*. Research on rare diseases may have the prospect of benefiting many patients if it focuses on features that are common to multiple rare diseases, or if information gained about one disease is likely to be valuable for learning about other diseases (for example, if the research focuses on improving the diagnostic journey or treating symptoms shared by multiple rare diseases).

Is building research capacity a component of social value?
It is relatively common for those funding and those carrying out research also to support capacity-building – for example, through training technical staff and future researchers. The primary value of this capacity-building is that, in the long run, it will lead to more high-quality research being conducted, which will promote social value. Where priority setters are deciding what resources to expend on carrying out research versus building capacity, they are making a decision about the allocation of scarce resources. In such cases, it makes sense to include building capacity among the options to prioritize, and to treat it as a source of social value.

Special obligations

How should research collaborations deal with conflicting special obligations?
The different individuals, teams and organizations involved in research collaborations may not always perceive themselves as having the same obligations. For example, a government department might have as its primary obligation improving the health of the national population, while it partners with a philanthropic funder whose mission statement is both narrower (for example, specific to a disease) and broader (for

example, not geographically limited). To some extent their special obligations will be aligned, and to some extent they may pull in different directions. There is no one-size-fits-all solution to such potential conflicts. They should be identified and actively discussed as early as possible during priority setting. Ideally, the priorities developed should be consistent with the obligations of all. Where some compromise is necessary, the balance struck should be one that weights most highly the needs of the most disadvantaged populations, so that equity is not sacrificed.

Public–private initiatives are one common form of collaboration that merits special mention. Such collaborations will often involve one partner whose primary motivation is profit. This is not in itself ethically problematic. However, partners with other ethical obligations should not compromise on those obligations on the grounds that they are in such a collaboration. Agreeing to collaborate should be a way for all partners to achieve their ethically valuable goals, not an excuse for falling short of them.

Inclusion

How should potential participants who don't have the relevant knowledge to understand the research topic be engaged?
Priority-setting exercises typically involve some learning for all participants, so that they understand the methods and goals of the exercise, as well as any necessary technical information. Some participants may be less familiar with health research or with the underlying science than others. There is a substantial literature on good practice for patient and community engagement in research *(85–88)* and a wide range of ways in which interested parties can be involved in research priority setting *(89)* (see also Annex 3).

Time and resources are too limited to allow all the relevant interested parties to take part in the exercise. Does this mean that the results will not be valid?
All priority-setting exercises are constrained to some extent by limited time and resources. This does not invalidate the results. Even if it is limited, a good-faith effort to set explicit priorities systematically and ethically will lead to better decisions than no priority-setting exercise at all. In cases in which the participation that is possible falls far short of the ideal, priority setters should reflect on how this is likely to affect the results. For example, will it mean that the perspectives of patients or of members of more disadvantaged groups will not be heard? If so, how might this skew the results, and how can it be mitigated? Case 3 in the in the companion casebook (3) describes a priority-setting exercise that involved difficult decisions about what to do with the limited resources available for carrying out the exercise.

Animals and the environment

How does the environment relate to social value? Is the environment important only in so far as it affects human beings?
Health research can have negative (or positive) effects on ecosystems and the local or global environment. For example, a research project that develops a home-based care intervention that can substitute for hospital care might have a positive impact by reducing the emissions and other waste associated with hospital-based health care. This matters at least in so far as it affects humans and sentient non-human animals. Whether environmental effects matter further is a matter of debate among philosophers and ethicists. In all cases, caution should be taken in terms of the ability to estimate and compare the expected effects on the environment, which can be quite distant from the research being carried out.

How do non-human animals matter for research priority setting?
The suffering and death caused to non-human animals during research matters ethically, and should be taken into account at two points. First,

during priority setting, the harm to non-human animals matters when prioritizing among different research programmes that will involve different uses of animals. For example, one research programme might use a mouse model and another cultured human cells, or one might expect to use more and another fewer sentient animals. There are ethical reasons to give higher priority to research programmes that involve less animal suffering. For more discussion, see Chapter 2 and Scenario 1 in the companion casebook (3).

The other point at which harm to non-human animals should be taken into account is when researchers propose specific studies involving animals. Those should normally not be evaluated during priority setting; they should be assessed by ethical and scientific review committees according to national regulations and international ethical and scientific guidance.

Existing priorities

Research priorities for the country/topic/organization have already been set. Do they have to be revisited?
Before embarking on a new priority-setting exercise, it is always important to check whether priorities have already been identified by another party. If so, careful thought should be given to whether additional priority setting is warranted. Duplicative priority setting is wasteful, using resources that could be better spent carrying out research. Following a consistent set of priorities can also assist with the coordination of research efforts among different research actors within a country or a topic. That said, where circumstances have changed or the priorities set do not clearly apply to the work, it may be valuable to carry out another priority-setting exercise (possibly on a smaller scale).

The priority setters are already setting priorities ethically. Why do they need to use this guidance?
Many countries and organizations already carry out ethically sensitive priority-setting exercises. Some excellent examples can be found in the companion casebook (3). Even for those who believe that their process is exemplary, however, this guidance may be helpful in two respects as they plan their next exercise. First, it is valuable to reflect critically on a process to ensure that it includes everything that matters. The framework offered by this guidance can facilitate thinking through an existing priority-setting process in a systematic manner. Second, it is important to be explicit about the values that underlie the priority setting. Being explicit about values allows both priority setters and third parties – such as patients, researchers, policy-makers and the public – to understand where priorities came from and what justifies them.

Relationships

What happens when the research priorities of an international funder differ from the research priorities set by the nation where they are planning to conduct research?
Legitimate concerns have been raised about whether the priorities of international organizations, funders and high-income countries are driving the global health research agenda to the detriment of the health needs of people living in LMICs. Whenever health research is planned in an LMIC whose government has already set its national priorities, those existing priorities should be taken into account. Research that plans to deviate from national priorities merits special attention. If it is not responsive to the country's health needs or if it is likely to displace higher priority research, it should not be conducted (4). However, the fact that a topic or question does not appear on a list of national priorities does not automatically rule it out. First, some research questions might be locally important but not make it onto a list of national priorities. Second, some research might be an international priority – that is, a topic that is collectively important – without being a high priority for each individual country where people are affected by the condition or problem. Third, responsible priority setting

includes looking at the activities and priorities of other funders and research organizations. National priorities may be set in the light of what international funders are already planning to do, to avoid duplication and fill gaps.

How does the guidance address cases in which funding comes from a partnership with industry whose aim is profit?

For-profit actors also have ethical obligations with respect to priority setting. They should be carrying out socially valuable research consistent with their special obligations, assessing and justifying any harms to third parties, and following fair procedures. Where two entities with different ethical obligations are working in partnership, each should ensure that the joint activities are consistent with their own ethical obligations. For example, a government funder's obligation to optimize the social value of the research it supports should not be diluted by partnering with a for-profit company. The partnership should be entered into only if it will increase the overall social value of research the funder supports.

Using the guidance

Should health research priority setting undergo ethics review?

Since priority-setting exercises vary so much, no blanket statement can be made. At least some health research priority-setting exercises appear to constitute research involving human participants.[6] These should undergo prospective review by a research ethics committee whenever that is required by the legislation governing research with human participants in the jurisdiction in which the priority-setting exercise takes place.

Does research priority setting discourage innovation?

Some may worry that insisting that research reflects the results of priority-setting exercises will lead to more conservative science. They may think that the social value requirement, in particular, will emphasize applied research with more predictable benefits over more fundamental science whose ultimate implications for human health cannot be known in advance. While this worry is understandable, ethical research priority setting should not stymie innovation. It is perfectly consistent with optimizing social value to take a long-term view of what is socially valuable science – accepting that the benefits are most likely to be felt decades in the future. It is also consistent with optimizing social value to support research whose payoff is very uncertain but where the payoff would be huge if it resulted, or where the applications of the knowledge are unknown at present. Nothing about the obligation to set research priorities explicitly, in a systematic way, and guided by ethical principles entails preferring low risk-low reward research over high risk-high reward research.[7]

Does every research priority-setting exercise have to follow all the steps described in the guidance?

Research priority-setting exercises are varied – ranging from individual scientists planning their next lines of research to international bodies setting global research agendas. Any guidance that can apply to all these exercises has to be quite general. It aims to articulate shared ethical principles, but these principles have to be applied according to the individual context, which may look quite different from one situation to another. Many priority-setting exercises will follow all the activities described in Chapter 3. Some may not. Provided that decisions about what activities to

6 WHO defines research involving human participants as "any social science, biomedical, behavioural, or epidemiological activity that entails systematic collection or analysis of data with the intent to generate new knowledge in which human beings: (1) are exposed to manipulation, intervention, observation or other interaction with investigators, either directly or through alteration of their environment; or (2) become individually identifiable through investigators' collection, preparation or use of biological material or medical or other records" *(90)*.

7 For example, 2024 Nobel Prize winner David Baker was supported in his research on computational protein design by, among others, Open Philanthropy – an organization that transparently sets its funding priorities on the basis of estimates of how much good it can achieve with its limited resources *(91)*.

include in a priority-setting exercise are consistent with the ethical principles, no particular set of steps is prescribed.

Other guides to research priority setting are available. Why should I use this one and not the others?

This guidance is unique in its focus on the ethical considerations that should govern health research priority setting. It is not intended to replace other guides that focus on other aspects of priority-setting exercises (for example, how to organize and analyse relevant data, how to carry out Delphi and other techniques, and so on). The relationship between this guidance and some of the more popular priority-setting methods is described in Chapter 4. Some priority setters may wish to use an existing method; others can learn from these methods while designing their own process to fit their own context. In all cases, it is essential to reflect on whether the process is consistent with ethical principles.

How often should research priorities be revisited?

There is no fixed time period within which research priorities should be revisited. Nevertheless, it can be valuable to pre-specify a timeline, since that will affect the scale and scope of the priority-setting exercise. Whether to revisit priority setting outside that timeline, and how substantial any revision of priorities should be, will depend on the situation of the priority setter and on external events. For example, a transformative discovery in a scientific field or a sudden outbreak of a novel disease might mean that priorities need to be reconsidered at short notice. In deciding whether to revisit priorities and how extensive subsequent priority-setting exercises should be, the following guiding questions might be helpful.

- To what extent have the existing priorities been addressed?
- Have changes in the field rendered many priority topics obsolete?
- Does the priority setter need to respond to important external events, such as a disease outbreak, natural disaster, conflict or change in government?
- Has a key decision point been reached? For example, has a funder received an increase or decrease in funds to disburse, or has a research unit hired new personnel?

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Annex 1.
How this guidance was developed

Writing group members were selected on the basis of subject-matter expertise and diversity in backgrounds and locations. An outline of the guidance was drafted by the lead author with the assistance of the writing group on the basis of a comprehensive literature review, augmented as needed on the basis of writing group expertise (1). This was workshopped in consultations with relevant expert groups and a draft of the guidance written on that basis. That guidance was revised iteratively in response to feedback from a series of in-person and online consultations with various groups (see Acknowledgements). Relevant questions that were raised during consultations but not fully answered elsewhere in the guidance were compiled and answered in Chapter 5.

Value judgements made in the guidance express views that are widely held and that withstood critical discussion during the writing and revision process. For example, the four ethical principles were identified through the literature review, and were supplemented by relevant widely agreed principles from research ethics, the ethics of health-care allocation, and good practice in patient and community engagement. Where there appeared to be reasonable disagreement about some matter of values, the guidance does not commit to a specific view. For example, there is widespread agreement that equity matters when deciding how to allocate resources for health research. There is not widespread agreement on either exactly how to measure equity or how societies should balance the goal of increasing overall social benefit with the goal of reducing inequality. Consequently, the guidance endorses the importance of reducing inequity but does not endorse a specific view about its nature or how to balance equity with other important values.

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Annex 2.
The research ecosystem

Research priority setting does not happen in a vacuum. Each actor whose decisions affect what research gets done operates within the existing global health research ecosystem. This ecosystem comprises many other actors who conduct and influence research. They all operate against a background of health-care systems that may use the products of research and legislation that shapes research. Tables A2.1 and A2.2 summarize key features of the research ecosystem relevant to priority setting: the actors who affect what research is conducted, the decision points at which allocation decisions are made, and the scarce resources that limit what health research can be conducted.

Table A2.1. Actors and their roles in the research ecosystem

	Who sets priorities	When/how
Actors	**Categories**	**Decision points**
Funders	Academic and other research institutions – for example: • All India Institute of Medical Sciences • Institut Pasteur • Kenya Medical Research Institute	• Establishing institutional priority areas • Designing funding schemes • Setting criteria for scoring grant applications
	Pharmaceutical and biotechnology companies – for example: • Aspen Pharmacare Pfizer Inc. • Sun Pharmaceutical Industries Ltd.	
	Private sector philanthropic foundations, trusts, nongovernmental organizations and corporate donors – for example: • Bill & Melinda Gates Foundation • Médecins Sans Frontières • Wellcome Trust	
	Public sector institutions – for example: • European Commission • Instituto Nacional de Salud Pública, Mexico • United States National Institutes of Health	
	Public sector multilaterals – for example: • Unitaid • World Bank • WHO	

Table A2.1. Actors and their roles in the research ecosystem (cont'd.)

Who sets priorities		When/how
Actors	**Categories**	**Decision points**
Research institutions	Universities Hospitals and health-care providers Nongovernmental organizations Government agencies that conduct research directly Pharmaceutical and biotechnology companies	• Setting institutional priorities • Designing internal funding schemes • Allocating resources for personnel • Monitoring departments and activities • Rewarding employees for research outputs
Policy-makers	Legislators and elected officials – for example: • ministers of health • parliamentarians	• Setting national priorities • Allocating funding to state agencies • Promulgating laws and regulations, such as intellectual property laws or tax breaks for research
	Multilaterals – for example: • Organisation for Economic Co-operation and Development • WHO • World Trade Organization	• Publishing guidelines and regulation
	Regulatory bodies responsible for the marketing approval of new drugs and devices – for example: • South African Health Products Regulatory Authority • United States Food and Drug Administration • European Medicines Agency	• Interpreting legislation • Issuing guidance
	Regulatory bodies responsible for health technology assessments – for example: • National Institute for Health and Care Excellence, United Kingdom • Health Intervention and Technology Assessment Program, Thailand	
Individuals and networks	Individual researchers or teams Research networks	• Making decisions about areas of specialization • Identifying research areas and research questions • Applying for funding • Making hiring decisions
Other actors	Journals	• Encouraging certain topics for submissions • Gathering editorial boards with certain areas of expertise • Publishing certain research findings
	Research ethics committees	• Stopping research that would violate participants' rights • Checking whether proposed research projects have sufficient social value to justify risks and burdens
	Patient organizations	• Lobbying for more research on certain diseases • Rasing awareness in society on certain topics • Soliciting patient priorities

Table A2.2. Resources allocated in the research ecosystem	
What is allocated	
Type of resource	**Scarcity in the ecosystem**
Funding	Money is essential for the success of almost every research project, and is always in limited supply
Facilities and equipment	Facilities and technical equipment can be the limiting factors on what research gets conducted in an institution, and so may have to be allocated as a scarce resource
Expert personnel and their time	The availability of qualified scientists, clinicians, grant administrators, grant reviewers and other professionals is limited but required to enable health research
Research participants	For some types of research – especially studies of rare conditions – not enough willing, eligible participants are available to power all the studies that might be conducted

Annex 3.

Recommendations for inclusive priority setting

As discussed in Chapter 2, particular efforts should be made to ensure that participants who are members of more disadvantaged and marginalized groups have a meaningful say during the research priority-setting process. If their valuable perspectives are to have an effect on what priorities are set, they must be included in ways that give them genuine representation, and give their representatives genuine voice. Tokenistic inclusion will not change the prevailing practices by which those with power and social status ultimately make the decisions nor prevent extractive research practices. Table A3.1 provides some guiding questions to help priority setters think through how to include members of more disadvantaged and marginalized groups meaningfully in health research priority setting. These are adapted from a research article (1) and from Research for Health Justice's ethical toolkit (2). Further details can be found in in the companion document to the toolkit available on the Research for Health Justice website.

Table A3.1. Including disadvantaged and marginalized groups in health research priority-setting: guiding questions

Stage	Questions
1. Before priority-setting	• How will relationships with disadvantaged and marginalized groups be built or strengthened before priority-setting starts? • How will members of disadvantaged and marginalized groups be supported to participate?
Who initiates and for what purpose?	
2. Leadership	• Will community partners be among those leading the health research priority-setting process? (Ideally, community partners represent and can access communities that are considered disadvantaged or marginalized in their diversity.)
3. Scope	• Will research priorities be solicited relating to all health problems experienced by disadvantaged and marginalized groups?
4. Empowerment	• Will the capacity of members of disadvantaged and marginalized groups to participate in research priority-setting be strengthened? • Who are the disadvantaged and marginalized groups within the project or programme's research setting or population?
Who participates?	
5. Representation	• Which of these groups will be engaged during priority-setting, and for what reasons? • Do organizations or individuals exist who can represent those groups? • For organizations, is there evidence that their memberships reflect the group's diversity and are regularly consulted about their health needs and priorities? • For individuals, do they collectively reflect the group's diversity and share lived experience with those they are representing? • Given the answers to the previous three questions, how will participants be chosen?

Table A3.1. Including disadvantaged and marginalized groups (cont'd.)	
Stage	**Questions**
6. Mass	• Will the number of participants drawn from disadvantaged and marginalized groups equal or exceed the number drawn from higher status groups in the project or programme's research setting or population? If not, what are the reasons?
	How they participate
7. Stage of participation	• Will members of disadvantaged and marginalized groups be involved from the start of the priority-setting process? If not, what are the reasons?
8. Level of participation	• Will members of disadvantaged and marginalized groups be involved as decision-makers? Is this level of participation acceptable to them?
9. Space	• What spaces exist in the host community that are not imbued with norms that silence disadvantaged and marginalized groups? • Will disadvantaged and marginalized groups be involved in selecting the space for priority-setting? If not, what are the reasons?
10. Ground rules	• Will disadvantaged and marginalized groups be involved in developing and approving the ground rules for the priority-setting process? If not, what are the reasons? • What ground rules will be included to ensure that disadvantaged and marginalized groups are not silenced during priority-setting?
11. Facilitation	• Will a locally based person facilitate consultations and deliberations? If not, what are the reasons? • How will the facilitation give participants an equal opportunity to speak at focus groups and deliberations? • How will the facilitation make disadvantaged and marginalized groups feel comfortable sharing relevant, personal stories about their community's health concerns?
12. Listening	• How will the research team ensure that disadvantaged and marginalized groups' ideas are listened to during consultations and deliberations?
13. Being heard	• Will the voices of disadvantaged and marginalized groups have equal or greater weight than other participants' voices? If not, what are the reasons?
	Compensation and follow-up
14. Resources and compensation	• How will disadvantaged and marginalized groups be compensated for participation?
15. Accountability	• What will be done to ensure that the final research priorities are acted upon? • How will the final research priorities be fed back to disadvantaged and marginalized groups who participated in priority-setting?

References[1]

1 Pratt B. Inclusion of marginalized groups and communities in global health research priority-setting. J Empir Res Hum Res Ethics. 2019;14(2):169–81 (https://doi.org/10.1177/1556264619833858).

2 Sharing power with communities in priority-setting for health research projects: a toolkit. In: Research for Health Justice [website]. Queensland Bioethics Centre; 2025 (https://www.researchforhealthjustice.com).

All references accessed on 11–20 March 2025.

Annex 4.

Operationalizing social value assessments

Health research priority setting should aim at two broad goals: maximizing the benefits of health research to patients and populations, and reducing inequity. These goals are encapsulated by the principle that health research priority setting should optimize the **social value** of research. As discussed in Chapter 2, social value is a function of:

- the likelihood that the research will produce knowledge that will ultimately benefit patients and populations;
- the magnitude of the benefits if they were to result; and
- the extent to which providing those benefits would reduce inequity (1).

These benefits cannot usually be measured directly. Instead, social value assessments must be operationalized through proxy indicators. This annex provides some further points to consider and examples to guide priority setters in operationalizing social value assessments.

Defining social value

The first step is to clarify exactly what social value means in the specific context of one's priority-setting exercise. This includes thinking about what counts as a benefit, who counts as a potential beneficiary, and how to conceptualize equity. Points to consider include the following.

- **Health research does not only lead to health benefits.** Health research typically aims (ultimately) to improve health. Yet health, narrowly conceived, is not the only thing that matters to people, and it is not the only benefit that can result from health interventions. For example, a study comparing a home-based intervention with an intervention that can only be administered in a health-care facility might be valuable in part because the former intervention would reduce disruption in patients' lives and lead to lower out-of-pocket costs. In line with WHO's expansive definition of health as "a state of complete physical, mental and social well-being" (2), dimensions of well-being that are not always thought of as components of health are still relevant to social value. Such dimensions might include protection from financial shocks, reduction in stigma, or an increased ability to engage in meaningful work and social activities. Where non-health benefits are likely to be substantial, consideration should be given to how they can be captured in assessments of social value.

- **The effects of health research go beyond patients and beyond humans.** The health-care interventions that are developed as a result of research can have indirect effects on individuals other than the recipients. For example, a treatment that improves patient mobility may also benefit carers. Where these indirect effects are predictable and substantial they should be considered when judging the social value of research (3). Health research can also lead to benefits and harms to non-human animals and the environment. For example, health research can generate information on how health-related sectors can mitigate their climate change impacts. On the other hand, new health technologies may have substantial

and potentially deleterious effects if they are energy and resource intensive (4). Again, where such effects are predictable and substantial, they should be taken into account. How much weight should be given to effects on non-human animals and the environment versus humans is contentious; this guidance does not take a stance on that question.

- **Equity is multidimensional.** According to WHO, "equity is the absence of unfair, avoidable or remediable differences among groups of people, whether those groups are defined socially, economically, demographically, or geographically or by other dimensions of inequality (e.g. sex, gender, ethnicity, disability, or sexual orientation)" (5). This encompasses not only health-related differences but also differences in other factors relevant to well-being (Box A4.1). For example, research into interventions to treat or prevent "neglected diseases" in LMICs may have high social value both because the magnitude of the potential benefits are large and because the people who suffer from these diseases are among the worst off worldwide (6). In most cases, this disadvantage is a matter not just of worse health but also of higher rates of poverty, stigma and discrimination and the like (7).

- **There may be trade-offs among the components of social value.** Sometimes the project that is most likely to lead to the greatest benefit is also the one that will most reduce population inequalities, but not always. This means that trade-offs may have to be made. Since there is no consensus in the literature on how these values should be balanced, this guidance does not take a stand, except to say that both matter. This is one reason it is important to have separate criteria for assessing **magnitude of benefit** and **equity improvement** – both will then be taken into account and trade-offs between them can be made explicit.

Box A4.1. Types of inequity

The causes of inequity in health and well-being are multiple and interacting. Inequities may be experienced by groups defined in terms of age, race or ethnicity, gender, sexual identity, disability, immigration status, geography, and more. A group may be worse off – and so deserving of greater consideration on equity grounds – due to disparities in any of the following:

- health outcomes (including morbidity and mortality)
- access to health systems and services
- education
- income and wealth
- access to social protection (such as sick pay, unemployment protection or pensions)
- access to nutrition
- housing and transportation
- the physical environment (including air quality, sanitation and clean water)
- access to financial and judicial services
- the social environment (for example, discrimination and stigma)
- public safety.

Source: : based on Weinstein et al. (8); WHO (9).

Operationalizing the definition: choosing criteria

The second step is to identify criteria for comparing research options that will optimize social value according to the chosen definition. These criteria will vary according to context, as shown in the examples at the end of this annex. Priority setters may also choose to add other criteria, corresponding to the other ethical principles or to other constraints on what research options can be chosen.

Points to consider include the following.

The process for developing criteria

As discussed in Chapter 2, both the selection of criteria themselves and their use in a research priority-setting process may helpfully be informed by fair procedures that include other parties. Patients, carers, community members, clinicians, policy-makers, scientists and other groups often have insights into what constitutes social value in a particular context and how it might be measured or compared.

In developing criteria, care should be taken to minimize the risk of epistemic injustice. Epistemic injustice occurs when individuals or groups are treated wrongly as potential sources of knowledge *(10)*. This may be because they are treated as less credible (testimonial injustice) or because their experiences are not recognized in the dominant conceptual schemes used by science (hermeneutical injustice) *(11)*. More general information should not automatically be preferred to more locally relevant information; concepts from dominant ways of understanding the world – such as racial/ethnic categories and paradigms of mental illness – should not simply be assumed. Appropriate inclusion (see Chapter 2 and Annex 3), especially of disadvantaged or marginalized groups, can help reduce the risk of epistemic injustice.

Substantive considerations

The choice of criteria should capture each component of social value:

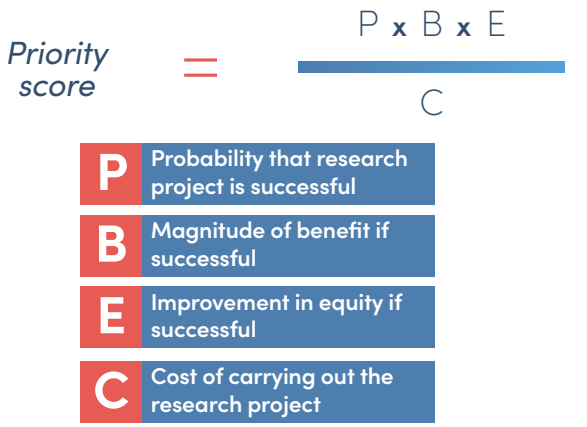
- the **likelihood** that benefits result from conducting the research
- the **magnitude** of the benefits if they result
- the extent to which providing those benefits would reduce **inequity**.

In addition, for project-level priority-setting exercises, the relative **costs** of research options should ideally be estimated. (For thematic priority-setting exercises this may not make sense.) For many priority setters, costs will be monetary. But the relevant scarce resource ("the cost") could also be the time of experts who would carry out the research, number of research participants, biospecimens, space in health-care facilities or access to specialized technologies.

In principle, it would be possible to assign numerical values to each of these components. A score could then be assigned to each research option, with higher scores indicating higher overall priority (Fig. A4.1). Such a calculation would parallel the use of cost–effectiveness analysis in health-care systems deciding which interventions to prioritize and the Reach, impact, confidence and effort method for product development *(12,13)*. In practice, this is not always practical. Nevertheless, it is valuable to keep the relationship among the components of social value in mind when deciding what criteria will be used for scoring research options and how the scores will be compiled.

> **In developing criteria, care should be taken to minimize the risk of epistemic injustice**

Fig. A4.1. The social value equation



In so far as direct indicators are available, they should be used. For example, it is often possible to estimate the cost of a research project (in monetary terms, staff time and so on). Where direct indicators realistically cannot be measured, proxy indicators should be used. These might include:

- **objective proxy indicators** –for example, the prevalence of a condition can be a partial proxy for the potential magnitude of benefit from successful research (see Case 2 in the companion casebook *(14)* for an example); or
- **subjective proxy indicators** – for example, asking scientists to estimate the probability of success (see discussion of the CHNRI method in Chapter 4).

Even subjective proxy indicators should be informed by data as much as possible. For example, there is no agreed measure of equity nor accepted view of how equity improvements should be weighted. At some point, subjective judgements will have to enter the picture. Yet the people making judgements about how to score alternative research options on the basis of equity can still be provided with relevant data (such as information on how different diseases are distributed among socioeconomic groups in a population). This makes their subjective judgements better informed.

Whenever numerical values are used in comparing the social value of research options, the inevitable uncertainties involved in calculating them should be explicitly acknowledged. Absolute precision is not to be expected.

Different types of research lead to social benefits in very different ways (Box A4.2). For more basic biomedical science, multiple possible paths might lead to social benefits. For example, there might be many possible uses for information about how different parts of the nervous system communicate or what happens when a particular gene is switched on. Whether any individual study ultimately benefits humans will depend on future research that itself cannot be mapped out easily. Basic science therefore poses particular challenges in estimating social value. This fact does not imply that it lacks social value; neither, however, does it mean that choices among basic science projects are completely arbitrary. The criteria used for comparing basic science projects can still usefully be mapped to the components of social value. Indicators for the likelihood of success may include factors that improve the probability that the research leads to knowledge (such as experimentalist skills, statistical soundness of study designs, recruitment plans, institutional support and so on) and factors that improve the probability of uptake (such as external validity, plans for publication and dissemination, coordination with other research groups, and so on). Sometimes plausible paths to social benefits can be identified (Box A4.2). Otherwise, indicators for magnitude may have to be more indirect – such as considering whether a topic is neglected, whether the results are potentially transformative, or the significance of knowledge gained for other scientific questions. Even when the ultimate beneficiaries cannot be known, equity can be considered (for example, focusing on diseases and environmental factors that affect worse-off populations, requiring that female animal models be used as well as male, pushing for collections of biological samples to be representative of the entire population, building research capacity in low-resource settings, and the like).

Box A4.2. Paths to social value

The path to social value for drug and vaccine candidates going into clinical trials is usually clear. But this is not the only path by which health research predictably leads to improvements in health and well-being. The following examples illustrate a small number of the many types of health research and the myriad paths to social value they can take.

Basic biological research

Widely used molecular biology techniques that have revolutionized the development of diagnostics, treatments and vaccines are derived from basic biological research *(15)*. Notably, although the discovery of the underlying mechanisms might be the result of "curiosity-driven" research, possible applications are often posited before or by the time the biological mechanism is identified. For example, decades before messenger ribonucleic acid (mRNA) vaccines against COVID-19 proved so successful, researchers explored whether mRNA could be delivered into human cells as vaccines for treatment or prevention *(16)*; Kary Mullis, widely credited as the inventor of the polymerase chain reaction knew immediately the practical importance it would have if it worked *(17)*.

Post-marketing drug studies

Studies of drugs that are already approved and prescribed to patients may reveal rare side-effects. These studies may be phase 4 randomized controlled trials (such as the Sibutramine cardiovascular outcomes (SCOUT) trial that showed sibutramine increased the risk of myocardial infarction and stroke *(18))*. They may also be database studies that review case reports from prescribing physicians (such as the reports of liver toxicity leading to Canada withdrawing approval for nefazodone *(19))*. If the drugs are withdrawn or contraindications are added to the label, patients are protected from risks.

Behavioural science

Concerns about rising rates of obesity in many high- and middle-income countries has led governments to look for policy solutions. Interventions ranging from sugar taxes *(20,21)* to restrictions on advertising to children *(22)* to the content and design of nutrition warning labels *(23)* have been informed by social science research. Importantly, it was often clear ahead of time which policies were likely to be under consideration, and therefore on what topics data from qualitative and quantitative research would potentially be sought.

For research that is closer to patients, the paths to social benefits can be relatively predictable. For example, a drug going into phase 3 trials will be expected to benefit the population suffering from the disease that it treats. Of course, even in these cases nothing is certain. The drug may not be effective, or it may turn out to be effective for a different disease in the end. Nevertheless, for clinical and public health research it often makes sense to capture **magnitude** through criteria such as prevalence and severity[1] and **equity** through measures of how disadvantaged potential beneficiaries of the research results are (or, more precisely, the predicted prevalence, severity and disadvantage at the future times when the research's benefits would actually be felt). The **likelihood** of success can be evaluated by looking at include factors that improve the probability that the research leads to knowledge and factors that improve the probability of uptake, just like for basic biomedical research. In addition, the likelihood will be increased where research has clear relevance to practice, will generate results that are usable by clinicians, and/or has actionable policy implications. In almost all cases, high levels of uncertainty will be associated with judgements of social value, and the degree of confidence that is warranted should be borne in mind when making use of scores or rankings.

Comparative judgements are easier the more similar the projects being compared. It is particularly difficult to compare high-quality research of different types – for example, comparing the social value of laboratory science with health systems research is extraordinarily hard. This is an important challenge for funders with broad portfolios, including many national funding bodies. It might be the case, for example, that social value would be optimized by investing in a mixture of basic and more applied research. More work is needed on the question of how to allocate resources across different types of health research.

Research that has no realistic prospect of generating benefits even in the long-term has no social value. Such research is wasteful and should be eliminated. Wasteful research is presumptively unethical because it uses up resources that could otherwise be put to better use. In addition, if it involves human or animal subjects, it may expose them to risks without justification, and it is likely to have a negative environmental impact. Wasteful research includes studies that ask questions whose answers are already known, research that will never be disseminated, "seeding trials" that are funded by companies just to promote an approved product, and studies that are underpowered or so poorly designed that they will not generate knowledge *(24)*. In general, for a research project to have non-zero social value there must be at least one plausible path to social benefits. Consideration should be given to actively identifying and eliminating wasteful research. For example, this might include requiring prior reviews of the existing evidence base to reduce the risk of unnecessary duplication or a study being predictably underpowered, ensuring that clinical trials are registered and their results reported even if negative, and so on *(25)*.

Three examples

Tables A4.1–A4.3 summarize three existing attempts to set out indicators for estimating the social value of research. They are presented here to illustrate how the concept of social value could be operationalized in a way that allows comparative judgements to be made. It may be valuable to consider how they could be adapted to your own priority-setting context, including – where appropriate – adding effects on non-human animals and the environment.

1 Prevalence is an indicator for the number of potential beneficiaries. Severity is an indicator for how large the potential benefits per patient could be.

Table A4.1. Social value indicators from Pierson & Millum's research priority setting checklist		
Social value component	**Criterion (general)**	**Criterion (specific)**
Benefit	Magnitude of health problem	• Prevalence: the number of people affected by a disease • Severity: how bad a disease typically is for a given patient • Economic and social costs: the non-health burdens of a disease on patients, their families, communities and society at large
Equity	Equity	• Medical disadvantage: whether the research will benefit sicker patients • Social disadvantage: whether the research will benefit patients who are socially disadvantaged • Priority for users: whether the research is considered a priority by potential beneficiaries (e.g. patients with the condition being researched)[a]
Likelihood	Likelihood of meeting scientific aims	• Scientific merit of the research proposal • Quality of investigators • Quality of institutions: whether they are well equipped to host the proposed research • Likely adoption: whether the research findings are likely to be translated into practice or policy
Cost	Cost of proposed research	• Economic costs • Human resources • Utilization of facilities

a This is also potentially a magnitude criterion.

Source: Pierson & Millum *(26)*.

Table A4.2. Social value indicators for controlled human infection studies

Social value component	Consideration	Explanation or illustration
1. Magnitude of health benefits (at the time the research results could lead to health benefits)		
Benefit	1.1 Magnitude of health-related harm from the disease	• Loss in health-related quality of life or life expectancy per affected patient or individual at risk of infection
	1.2 Magnitude of health-related benefit from the research	• Potential gains in health-related quality of life or life expectancy that an affected patient or individual at risk of infection might make
	1.3 Number of potential beneficiaries	• –
Equity	1.4. Priority of potential beneficiaries as a matter of justice	• For example, level of disadvantage experienced over their lifetime
1. Magnitude of health benefits (at the time the research results could lead to health benefits)		
Likelihood	2.1 Novelty and innovation of research question(s)	• Possibility of addressing the research question(s) based on existing or expected future evidence, as summarized in complete and systematic reviews
	2.2. Quality of research question(s)	• Maturity of the research question(s) given the existing evidence
	2.3. Rigour of research design and data analysis	• Suitability of the given human challenge model for addressing the research question(s) • Generalizability of findings from controlled human infection studies to larger clinical trials and the field (external validity)
	2.4. Feasibility and rigour of research conduct	• Consistency of the research with national research priorities (if any) • Quality and timeliness of community and public engagement • Quality of the research team (e.g. training, prior experience, conflicts of interest, institutional support, access to wider research community) • Quality of the research sites (e.g. equipment, management)
	2.5. Quality of reporting and dissemination of results, and scope of data, sample and challenge strain sharing	• Quality of the publication plan • Quality of the stakeholder and public engagement plan • Quality of the research team • Quality of plans to share data and samples, and challenge strains
	2.6. Influence on future research with the potential to lead to health benefits	• Influence of the results on different fields of research • Feasibility of generating comparable information by using alternative research methods
	2.7. Influence on clinical or public health practice	• Feasibility of implementing the interventions • Acceptability of the interventions

Source: adapted from Rid & Roestenberg *(27)*; Rid et al. *(28)*.

Table A4.3. CHNRI method criteria		
Social value component	**Criterion**	**Explanation**
Likelihood	Answerability	Likelihood that research option would be answerable in ethical way
	Effectiveness	Likelihood that resulting intervention would be effective in reducing disease burden
	Deliverability	Deliverability, affordability and sustainability of resulting intervention
Benefit	Disease burden reduction	Maximum potential of intervention to reduce disease burden
Equity	Equity reduction	Effect of disease burden reduction on equity in population

Source: Rudan, El Arifeen & Black *(29)*.

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Annex 5.

Useful resources[1]

Priority-setting methods

WHO maintains a webpage with publications describing experiences and approaches in setting priorities for health research.

- Priority setting methods. In: World Health Organization [website]. World Health Organization; 2025 (https://www.who.int/observatories/global-observatory-on-health-research-and-development/resources/methods/priority-setting-methods).

Coordinating research efforts

WHO's Global Observatory on Health Research and Development is a source of information on what health research is being conducted globally.

- Global Observatory on Health R&D. In: World Health Organization [website]. World Health Organization; 2025 (https://www.who.int/observatories/global-observatory-on-health-research-and-development).

In addition, several international organizations coordinate health research and identify gaps. ESSENCE on Health Research promotes coordination among donors and funders of health research.

- ESSENCE on Health Research. In: World Health Organization [website]. World Health Organization; 2025 (https://tdr.who.int/groups/essence-on-health-research).

The G-FINDER project tracks investment in research and development for "new products and technologies to address priority global health challenges", including by industry.

- G-FINDER data portal: tracking funding for global health R&D [online database]. Impact Global Health; 2025 (https://gfinderdata.impactglobalhealth.org/).

The Global Research Collaboration for Infectious Disease Preparedness (GloPID-R) focuses on pandemic preparedness and response.

- Global Research Collaboration for Infectious Disease Preparedness (GloPID-R) [website]. Charité – Universitätsmedizin Berlin; 2024 (https://www.glopid-r.org).

Collaborative research projects

Tools and expert assistance on developing equitable research partnerships – especially in collaborations between research institutions in high-income countries and in low- or middle-income countries – can be found through the Research Fairness Initiative.

- Research Fairness Initiative [website]. Council on Health Research for Development; 2020 (https://rfi.cohred.org).

Further resources for including communities in research priority setting can be found in Annex 3 and the linked toolkit.

2 All references accessed on 18 March 2025.

- Sharing power with communities in priority-setting for health research projects: a toolkit. In: Research for Health Justice [website]. Queensland Bioethics Centre; 2025 (https://www.researchforhealthjustice.com).

Research ethics

Resources relating to the ethics of research with human participants can be found through WHO's Health Ethics and Governance Unit.

- Health Ethics & Governance. In: World Health Organization [website]. World Health Organization; 2025 (https://www.who.int/teams/health-ethics-governance/governance/research).

The following are two canonical sources of guidance.

- Declaration of Helsinki: medical research involving human participants. Ferney-Voltaire: World Medical Association; 2024 (https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/).
- International ethical guidelines for health-related research involving humans, fourth edition. Geneva: Council for International Organizations of Medical Sciences; 2016 (https://doi.org/10.56759/rgxl7405).

The following are two nuanced discussions of the ethics of research with non-human animals.

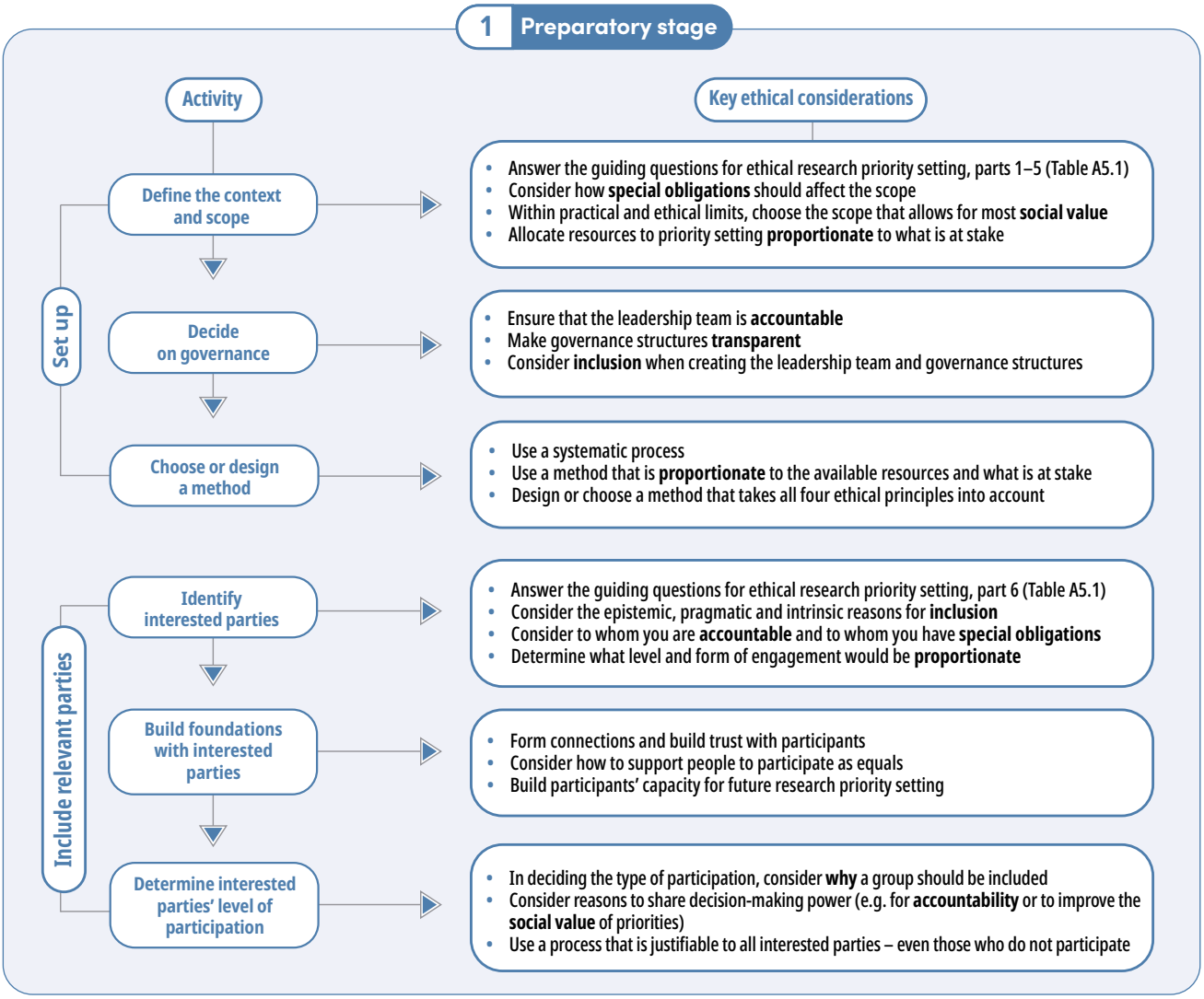
- The ethics of research involving animals. London: Nuffield Council on Bioethics; 2005 (https://www.nuffieldbioethics.org/publication/the-ethics-of-research-involving-animals/).
- Beauchamp TL, DeGrazia D. Principles of animal research ethics. Oxford: Oxford University Press; 2019.

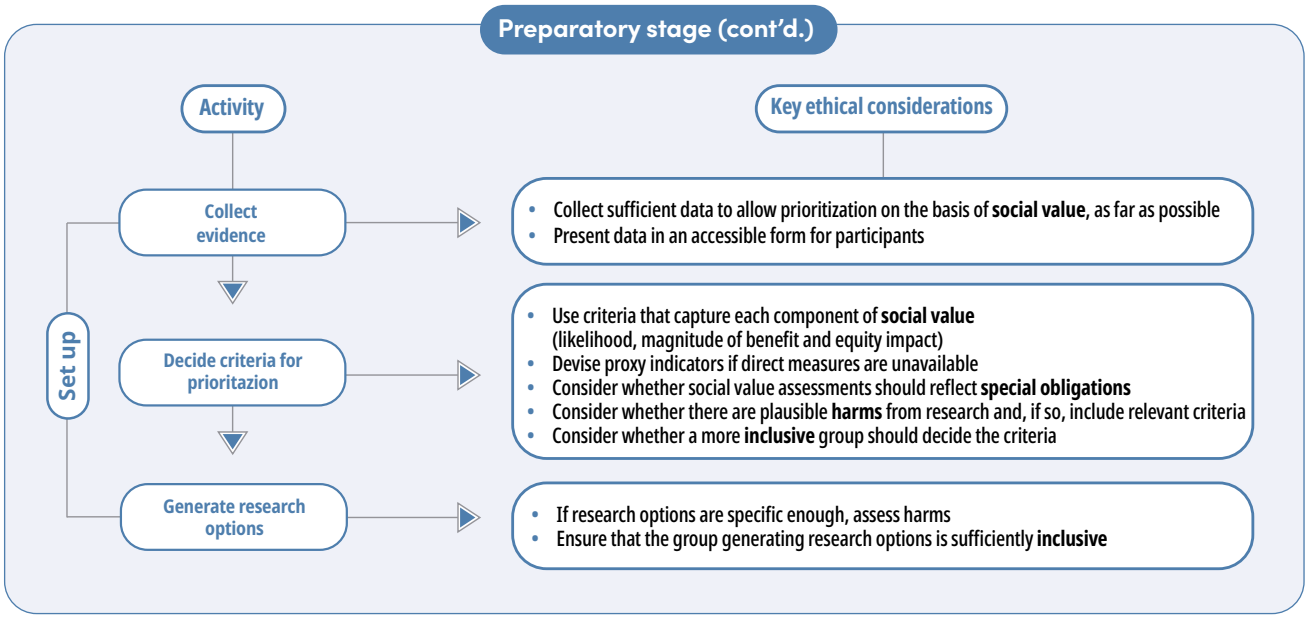
Annex 6.

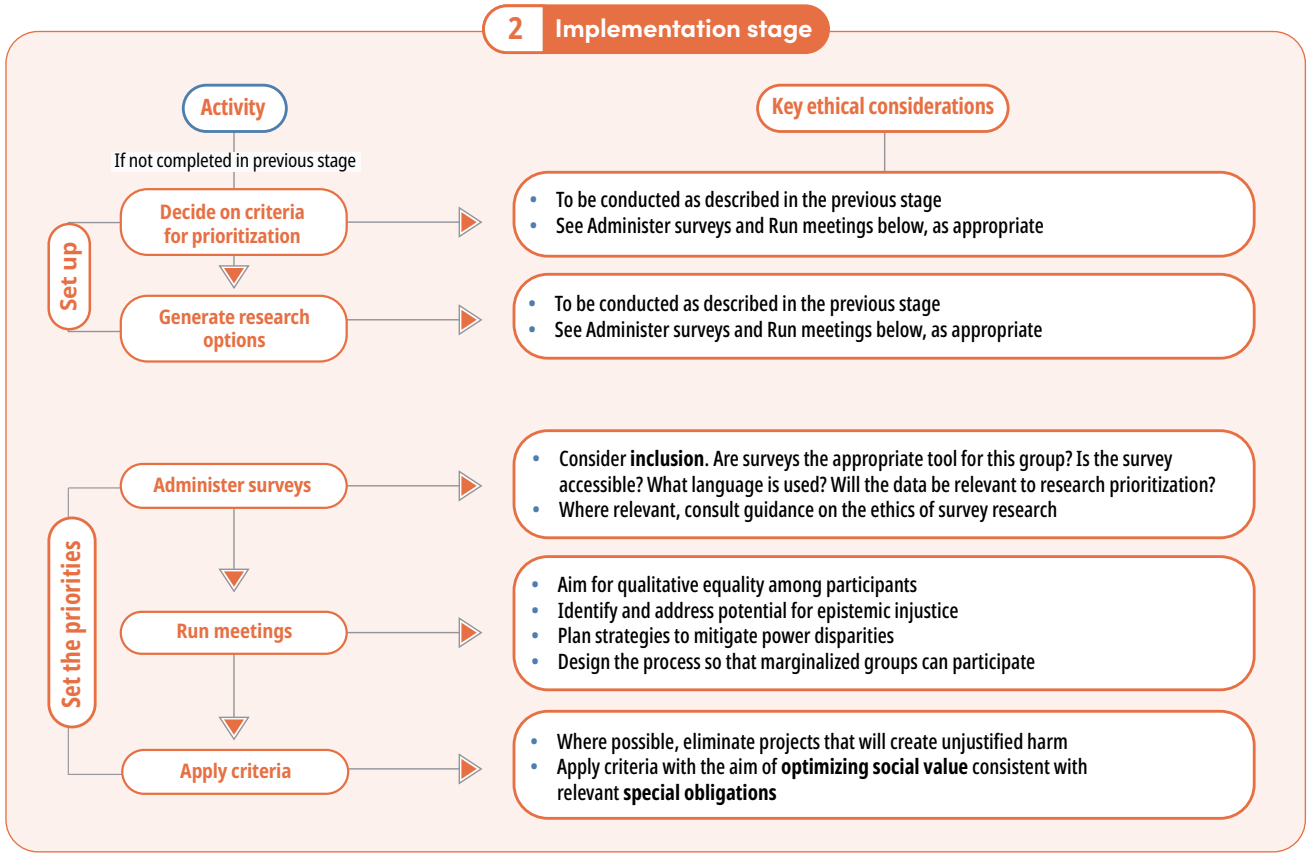
Tools: flowchart and guiding questions for ethical research priority setting

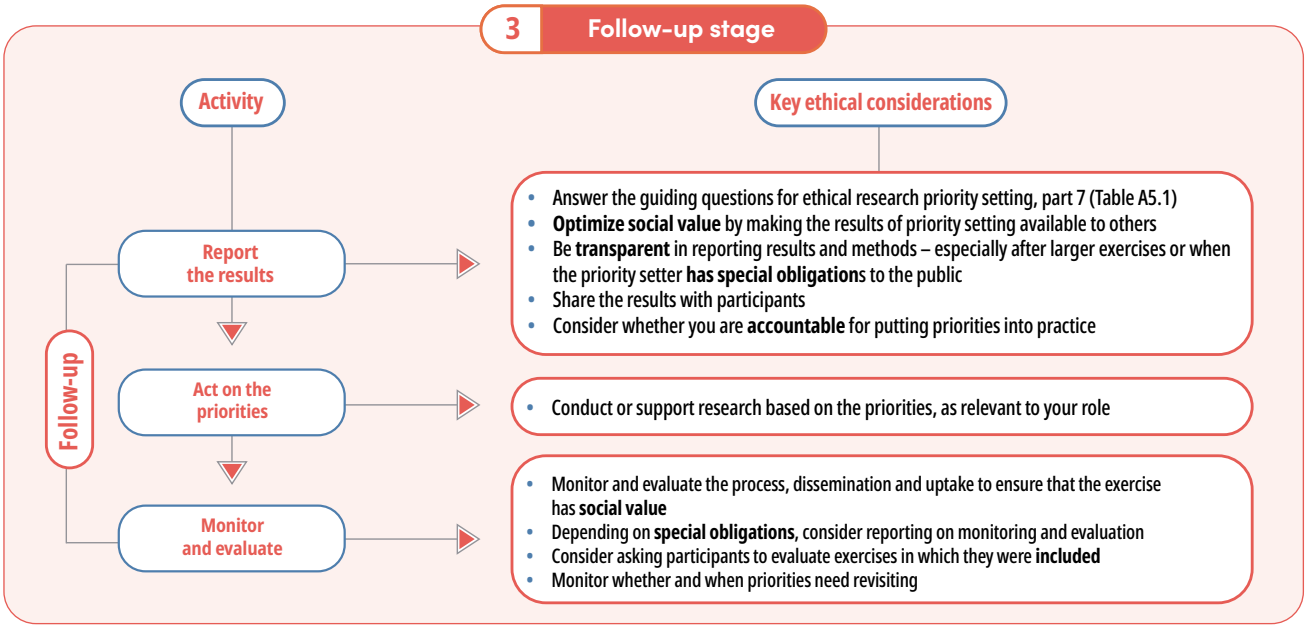
The flowchart in Fig. A6.1 illustrates the key activities involved in research priority-setting exercises, and the ethical considerations that are particularly relevant for each. For more details on each activity and how the ethical principles apply, consult Chapter 3.

Fig. A6.1. A flowchart of key activities and associated ethical considerations




Preparatory stage (cont'd.)
Activity
Key ethical considerations
Set up
Collect evidence
Collect sufficient data to allow prioritization on the basis of social value, as far as possible
Present data in an accessible form for participants
Decide criteria for prioritazion
Use criteria that capture each component of social value (likelihood, magnitude of benefit and equity impact)
Devise proxy indicators if direct measures are unavailable
Consider whether social value assessments should reflect special obligations
Consider whether there are plausible harms from research and, if so, include relevant criteria
Consider whether a more inclusive group should decide the criteria
Generate research options
If research options are specific enough, assess harms
Ensure that the group generating research options is sufficiently inclusive


2 Implementation stage
Activity
Key ethical considerations
If not completed in previous stage
Set up
Decide on criteria for prioritization
To be conducted as described in the previous stage
See Administer surveys and Run meetings below, as appropriate
Generate research options
To be conducted as described in the previous stage
See Administer surveys and Run meetings below, as appropriate
Set the priorities
Administer surveys
Consider inclusion. Are surveys the appropriate tool for this group? Is the survey accessible? What language is used? Will the data be relevant to research prioritization?
Where relevant, consult guidance on the ethics of survey research
Run meetings
Aim for qualitative equality among participants
Identify and address potential for epistemic injustice
Plan strategies to mitigate power disparities
Design the process so that marginalized groups can participate
Apply criteria
Where possible, eliminate projects that will create unjustified harm
Apply criteria with the aim of optimizing social value consistent with relevant special obligations



Guiding questions for ethical research priority setting

Incorporating the ethical considerations into each activity will be facilitated by answering the following guiding questions ahead of time (Table A6.1). The prompts are intended to help ensure that ethical considerations are incorporated into the design of the priority-setting exercise. Answers to these questions will help to determine which activities should be included in the exercise, and how. Parts 1–6 are essential to addressing ethical considerations during the preparatory stage. Part 7 is essential to the follow-up stage. Ideally, these questions should be considered throughout the design and implementation of the exercise.

Table A6.1. Guiding questions for ethical research priority setting

Part	Guiding questions

1. Scope	• How should the scope of this priority-setting exercise be set (taking into consideration the practical and ethical aspects)?
	• What themes, subject areas or types of research could realistically be included?
	• Within the limits of what could be included, do any ethical obligations affect the scope of what should be done?
	  • To whom are the priority setters accountable (e.g. the public, specific communities, funders)?
	  • What is the exercise's mission?
	  • Are there specific populations who should be prioritized (see also Part 5)?

2. Proportionality	• What time and resources will be devoted to priority setting?
	  • How is the exercise likely to be used (e.g. how many and how important are the decisions that will be informed by the results; how urgently are priorities needed)?
	  • What resources are available for priority setting?
	  • What is needed to carry out priority setting well in this context?

Table A6.1. Guiding questions for ethical research priority setting (cont'd.)	
Part	**Guiding questions**

3. Social value	• Within the scope identified, how is social value defined (recalling that social value is a function of the likelihood that research leads to benefits, the magnitude of those benefits, and their impact on equity)?
	  • In what ways might the research lead to benefits? What type of benefits?
	  • In what ways might the research lead to benefits that improve equity?
	  • What would make these beneficial impacts more likely?
	• Given the answers to the previous questions, what criteria (chosen with the aim of optimizing social value) will be used to assess the social value of alternative research options? Priority setters should consider:
	  • likelihood criteria (e.g. scientific merit, novelty, answerability, likelihood of adoption of findings into practice);
	  • magnitude criteria (e.g. burden of disease, potential benefit from successful intervention, potential for broad application or transformative findings);
	  • equity criteria (e.g. expected affordability of intervention, disadvantage of beneficiaries, consideration of gender, race/ethnicity and so on); and
	  • cost criteria (whether this priority-setting exercise will consider the relative costs of different projects – in money, time, personnel and so on – and if so, whether criteria should be included to estimate and compare the costs of research options).
	Annex 4 provides more guidance and examples of criteria appropriate to different types of research
	• Further questions to consider include the following.
	  • What process should be used to generate and compare research options using these criteria?
	  • Do the activities need to be coordinated with others (e.g. for funders – what are other funders doing)?
	  • Might the criteria for social value or the process by which they are selected reinforce epistemic injustice? If so, how can this be addressed?

4. Risks	• Are there risks to non-human animals or third parties that plausibly might result from any of the research options under consideration?
	• If harms are likely, the following questions should be considered for each case:
	  • What would minimize the harms?
	  • What would justify the harms?

5. Other special obligations	• In addition to scope restrictions, are there other ways that special obligations should be taken into account? Priority setters should consider:
	  • **substantive considerations** (e.g. should the process give greater weight to the health problems of specific groups – such as a national population or particular patient groups?); and
	  • **procedural considerations** (e.g. whether specific groups have a right to be included and in what way? – see Part 6)

Table A6.1. Guiding questions for ethical research priority setting (cont'd.)	
Part	**Guiding questions**

6. Inclusion	• Why might other parties need to be involved in this priority-setting exercise? Priority setters should reflect on:
	  • epistemic reasons – including others to increase accuracy (e.g. because they have lived experience or specific expertise);
	  • pragmatic reasons – including others to increase impact (e.g. to build trust or gain buy-in); and
	  • intrinsic reasons – including others because they have a right to be in-volved.
	• Based on this reflection, priority setters should consider who should be in-volved.
	  • How can the exercise aim for sufficient range and numbers so that it can collectively represent the diversity of interested parties who should be in-cluded?
	• Consideration should also be given to how they should be involved.
	  • Has the process been structured so that everyone has a fair opportunity to contribute and to influence the results?
	  • Has the design been checked to ensure meaningful participation from mar-ginalized and disadvantaged individuals who are included (see Annex 3)?
	  • How can priority setters aim to build the capacity of participants to partici-pate in this and future priority-setting processes?
	  • How will conflicts of interest be identified and managed?

7. Follow-up	• How will the process and results of priority setting be communicated, and to whom?
	  • To whom are the priority setters accountable?
	  • Who participated?
	  • Who might put the results into practice?
	• What other steps can be taken to ensure that the results of the priority setting are acted on?
	• When or under what conditions will priorities be revisited?

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