Setting Priorities in Global Child Health Research Investments: Universal Challenges and Conceptual Framework

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Increasingly, there is a need for national governments, public-private partnerships, private sector and other funding agencies to set priorities in health research investments in a fair and transparent way. A process of priority setting is always an activity driven by values of wide range of stakeholders, which are often conflicting. This process always occurs in a highly specific context (eg, agreed policies and targets in terms of disease burden reduction and time limit, defined geographic space, population and specific health problems).

Child Health and Nutrition Research Initiative (CHNRI) held a series of expert meetings during which a list of 20 universal challenges inherent to research prioritization was identified. Based on these challenges, several key concepts were proposed and defined, including the boundaries of health research, its main domains, and possible criteria for prioritization between competing research investment options. If accepted, these concepts could form a basis for a transparent decision-making framework for setting priorities in health research investments.

CHNRI first proposed that "health research" funded by public funds should be regarded as an activity undertaken to generate presently non-existing knowledge that will eventually be used to reduce the existing disease burden (or other health-related problem) in the population that provided funding. Three universal and non-overlapping domains of health research were proposed as follows: 1) research to assess the burden of disease and its determinants; 2) research to improve the performance of the existing capacities to reduce disease burden; and 3) research to develop new capacities to reduce the disease burden (or other problem). The focus on disease burden is aligned with internationally agreed goals, but it can also be changed to address differences in interests of the investors, such as patentable products for private sector. An approach to systematic listing of all competing research avenues, options, and questions is suggested along with a framework for identifying criteria that can discriminate between characteristics of research questions (eg, answerability, ethics, effectiveness, deliverability, affordability, sustainability, maximum potential impact on disease burden, equity, and others).

CHNRI proposes a new approach to undertaking health research priority setting in a fair and transparent way, respecting principles of risk-neutral investing. The process brings together the investors, a group of technical experts, and a larger number of representatives for various other stakeholders. Investors are a part of the process from the outset; they are assisted in defining the context, expected "returns" on the investments, and their risk preferences. The role for technical experts is to systematically list the competing research investment options and to use a set of criteria to discriminate between research options according to their likelihood of reaching the targets. The stakeholders can then weigh different criteria according to their system of values to inform the investors on research priorities.

It is estimated that more than US$130 billion are invested globally into health research each year and the amount has been increasing steadily over the past decade (1). Still, proposals for health research funding are far exceeding the available resources. Increasingly, there is a need to set priorities in health research investments in a fair and legitimate way, using a sound and transparent methodology. In 2005, CHNRI launched a project to develop a systematic methodology for setting priorities in health research investments and to apply it to child health (2). This effort was motivated by a notion that current research investment prioritization approaches suffer from many shortcomings, which may partly be responsible for the persisting high levels of mortality in children globally (3-5). Commission on Health Research for Development stated that "only 5% of global spending on health research in 1986 was devoted to health problems in developing countries, where 93% of the world's burden of 'preventable mortality' occurred" (6). Leroy et al (3) determined the proportion of research on childhood mortality directed toward better medical technology (ie, toward improving old technology or creating new technology) compared with research on technology delivery and utilization. They found

that 97% of grants were allocated to developing new technologies, which could reduce child mortality by 22% – a one-third reduction of what could be achieved if the existing technologies were fully utilized (3). Furthermore, in terms of financial support for health systems and policy research, the "10/90 gap" persists and health systems research receives very little funding (7). The World Report on Knowledge for Better Health: Strengthening Health Systems reported similar conclusions (8). All these sources implied that large disproportion existed between the investments in different types of health research, different diseases contributing to overall burden, and between the health needs of the wealthy and the poor.

One of the trends that have been observed is that certain type of research has persistently been awarded funds and, therefore, attracted scientists, while other crucial research, such as child health epidemiology, which many not be as attractive and likely to be funded remained neglected (5,9). Our concern is that the past several decades of rewarding new, attractive, and original ideas, whereby little concern was given to the usefulness of the generated new knowledge for reduction of persisting disease burden in the society, has led to a dramatic increase in the number of basic research studies and growth of impact factors of the journals that publish such research (5). This process inevitably led to an opening of many new and exciting research avenues, but there have been only few examples where the full potential of the new knowledge was realized at the level of public health, ie, used to meet the needs of the community/society. This is particularly unwelcome because the contributions from taxpayers are frequently the main source of funding for health research investments, and it may (to an extent) explain the ongoing lack of progress toward achieving substantial disease burden reduction across the developing world (3). Only recently, these issues have gained more attention (10-12).

The examples above point to the dangers of the status quo, inconsistencies, and imbalances in investing, relative lack of transparency, accountability to high-level goals and strategic directions, difficulties in determining where particular research fits in the process of knowledge translation, and similar issues. Since May 2005, CHNRI organized a series of meetings and workshops that involved more than 100 experts in global child health from different backgrounds. During those meetings, a review of existing principles and practice of research priority setting was undertaken (4) and a strategy of involving all the stakeholders in the process was defined (13). Those two papers were the first in the series of five papers describing the CHNRI methodology that was prepared as a result of the meetings.

The meetings also highlighted a need for defining some universally observed challenges and agreeing on several key concepts that could be helpful in resolving the challenges. A consensus over those concepts would enable systematic, transparent, and rational solutions to the challenges that were identified with respect to research investment priority setting. In this paper, which is the third paper of the series on CHNRI methodology, we exclusively focus on those universal challenges and propose a solution in a form of conceptual framework that should serve to surmount the challenges through the CHNRI priority setting process. Information on the historic approaches, current principles, and practice of priority setting, strategies of involving the stakeholders, specific guidelines for implementing the CHNRI methodology, and its validation and comparison with other similar methodologies can be found in other papers of this series (4,13), and these issues are not a focus of this particular paper.

Universal challenges in setting priorities in health research investments

Discussions between experts of different backgrounds were moderated by CHNRI at several meetings and workshops during 2005 and 2006. They highlighted some universal challenges that any priority setting exercise in health research investments will eventually have to face (Table 1).

Table 1. Universal challenges in setting priorities in health research investments identified by Child Health and Nutrition Research Initiative experts.

Challenges in setting priorities:
1. Deciding who should be involved in the process of setting research priorities
2. Defining what constitutes a health research investment option opportunity
3. Defining what constitutes the expected "return" on the investment
4. Defining what constitutes a potential "risk" in the investment
5. Finding a way of dealing with uncertainty of health research outcomes
6. Defining health research, its boundaries, and its levels of "depth"
7. Systematic listing of many competing research investment options
8. Defining what is meant by "priority setting" in the context of health research
9. Defining criteria relevant to priority setting in health research investments
10. Comparing different domains of health research using the same criteria
11. Development of a simple quantitative way to rank competing research options
12. Limiting the potential of personal biases to substantially influence the outcome
13. Ensuring that priority setting process is fully transparent
14. Ensuring that it can be repeated and validated
15. Ensuring that it is flexible and adjustable to all contexts and levels of application
16. Ensuring that it is iterative with a feedback loop, instead of a one-way process
17. Ensuring that it is perceived by the users as legitimate and fair
18. Ensuring that it is simple and intuitive enough to become popular among users
19. Linking quantitative ranks of research options with specific investment decisions
20. Involving stakeholders from the wider community into the process

The first challenge is deciding who should be involved in the process of setting research priorities. It was agreed that one important requirement should be that the priority setting process involves those who invest in health research from the outset. The shortcoming of several previously proposed methodologies driven by technical experts was that, although they resulted in sound recommendations, they were rarely implemented by the investors subsequently (4). It is therefore important that investors are involved in the process from the start. Still, they should seek assistance from technical experts and numerous other stakeholders to better understand the context in which investments are performed. This context involves time frame (long-term vs short-term expectations), space (geographic boundaries likely to be affected by investments), magnitude and urgency of the problem (ie, burden of disease, disability, or death), and existing and agreed investment policies and targets to which political commitment has been made.

Based on the understanding of the context, investors can make informed decisions in terms of expectations from their investments and their risk preferences. Discussions with technical experts and stakeholders should assist them in addressing further 3 universal challenges – defining what constitutes a health research investment option/opportunity; defining what constitutes the expected "return" on this investment; and defining what constitutes a potential "risk" in this investment. The CHNRI's solution to defining what constitutes a "research investment option" has been described in detail in our earlier work (2,5). We proposed previously (5) that an investment option in health research where public funds are used should be defined as a research activity that not only produces new knowledge but also incorporates a vision of implementation of this knowledge to reduce the burden of disease and disability and improve health. However, different investors will have different expectations on "returns" from such investment options. While those who are in charge of public funds may be interested in reduction of the persisting disease burden as an appropriate "return" of their health research investment, funders of academic institutions may be seeking "high impact," visible publications, while funders from the industry may

be primarily interested in patentable products that could have commercial value.

A further universal challenge is finding a way of dealing with uncertainty of health research outcomes. This challenge reflects perceived difficulties in comparing long-term strategic basic research that offers great promise in reducing disease burden (although the final outcome is very uncertain) with short-term research in order to define more efficient means of delivering existing interventions that are known to be effective. At this point, it would again be reasonable for the investors to consult technical experts, whose knowledge and expertise can be used to assess likelihoods related to answerability of different research investment options (ie, the likelihood that the endpoints of the research can be reached) within a precisely defined context.

Further challenges include systematic listing of a seemingly endless spectrum of competing research investment options and comparing different domains of health research using the same criteria. Again, the CHNRI's solution to this problem has been described in detail in implementation exercises of CHNRI priority setting process in South Africa (at the national level) and for zinc as a risk factor (at the global level) (14,15) (Table 2). Potential profits and risks from investing in research options from epidemiological research, research on new interventions, or health systems and policy research can be compared to each other according to several criteria, which should always include (but are not limited to) their answerability, their usefulness (in terms of effectiveness, deliverability, affordability, and sustainability), potential impact on persisting disease burden, and effect on equity. A further challenge is deciding whether those most fundamental criteria need refinement or addition of some other criteria.

For example, in different contexts addressing of the "answerability" criterion may also require a separate assessment related to ethics, existing research capacity, or public acceptance of research results. The "usefulness" (relevance) criterion will, in different contexts, be split into criteria that will separately assess effectiveness, deliverability, affordability, sustainability, and whether a critical gap in knowledge is being addressed. The "potential impact" will occasionally not only assess the quantity of potential burden reduction, but also its quality– ie, whether this reduction is targeting those most heavily affected in the population. Table 3 lists some of the possible criteria that can be used for setting priorities

Table 2. Child Health and Nutrition Research Initiative's proposed framework for systematic listing of investment options in health research, which takes into account the varying "depth" of proposed research: the three most fundamental and mutually exclusive research domains; very broad research avenues within those domains; more specific research options; and very specific research questions

Research domain	Research avenue	Research option	Research question
Health research to assess burden of health problem (disease) and its determinants	Measuring the burden Understanding risk factors (in terms of their relative risks) Measuring prevalence of exposure to risk factors Evaluating the efficacy and effectiveness of interventions in place Measuring prevalence of coverage of interventions in place	Many research options within each of the avenues; research options should correspond to the level of 3-to-5-y research programs	Several very specific research questions within each of the research avenues should correspond to the title of individual research papers
Health research to improve performance of existing capacities to reduce the burden	Health policy analysis Health system structure analysis Financing/costs analysis Human resources Provision/infrastructure Operations research Responsiveness/recipients Improving existing interventions (their affordability and deliverability)		
Health research to develop new capacities to reduce the burden	Basic, clinical, and public health research to advance existing knowledge to develop new capacities Basic, clinical, and public health research to explore entirely novel ideas to develop new capacities		

Table 3. Some of the possible criteria and related questions proposed by Child Health and Nutrition Research Initiative that can be used to discriminate between any two (or more) health research options that compete for investments in order to set research priorities. The outcomes of the different criteria will necessarily conflict each other

Criterion	Question
Acceptability	How likely is the proposed research to be approved, taking into account any possible resistance based on ethical or political grounds and public opinion?
Affordability	How likely is it that the results will improve affordability of existing policies and programs?
Answerability	How likely is it that the objectives will be met given the current state of science and the size of the gap in knowledge?
Applicability	How likely is it that the results will be immediately applicable for guiding policies and programs?
Deliverability	How likely is it that the results will improve the delivery of existing policies and programs?
Equity	How likely is it that the proposed research will benefit those who are most vulnerable to poor child development?
Feasibility	How likely is it that the cost of the proposed research will be a feasible investment?
Potential effect on disease burden	How likely is the proposed research to lead to significant improvement in disease burden reduction?
Sustainability	How likely is it that the results will improve sustainability of existing policies and programs?
Usefulness	Given the quality of existing evidence, how likely is it that the proposed research will fill a critical gap in knowledge?
Existing research capacity	How likely is it that that the objectives will be met given existing research capacity?
Alignment with other policies	How well are the objectives aligned with other existing policies in the society?
Generation of commercial products	How likely is it that the proposed research will lead to patents and generate commercial products?
Competitiveness and publication impact	How likely is it that the results of the research will be seen as competitive against other ongoing work and be accepted for publication in the journals with the highest impact factor?

between different research investment options and questions about each option that could address these criteria well.

The next challenge is development of a simple quantitative (and intuitive) way to score and rank all competing research options while addressing all relevant criteria. CHNRI recommends that appropriate questions to address the chosen criteria need to be developed and then posed by the investors to technical experts, who will then answer them independently from each other. In this way, their expertise will be used to discriminate between competing research options based on strictly defined criteria and their collective optimism toward compliance of each research option with each criterion will be measured. It will also limit the potential of personal biases to substantially influence the outcome, which was seen as another universal challenge.

Namely, personal opinions of members of research panels and the undue influence of certain members of the panel can have large effect on the decision-making process on research grant awards. The proposed conceptual framework for CHNRI methodology ensures that technical experts provide their input independently of each other, and that the final scores for each competing research option are computed in a highly structured, transparent, and systematic way. This ensures that priority setting process is fully transparent and that it could be repeated and validated. Through application of agreement statistics methods, the CHNRI methodology can also identify controversial issues (ie, responses with a large variation in scores among experts).

The above characteristics of the CHNRI process should also deal with several other universal challenges. The flexibility in the choice of criteria should ensure that the methods are adjustable to all contexts and levels of application. They also enable a feedback loop, as the process can be repeated after some preset periods of time and priorities will then change with the changing context. Its transparency and clarity of the necessary steps should ensure that it is perceived by the users as legitimate and fair.

Finally, the following proposed solutions should eventually ensure that the process is seen as simple and intuitive enough to become popular among its users. Many experts from different backgrounds should undertake scoring independently from each other and intermediate scores for each investment options could then be expressed as the percentage of maximum possible points to get awarded for each criterion. The final score can then be computed as a

mean value of the five intermediate scores, expressed as a number between 0 and 100%. This simple and intuitive quantitative score assigned to each research investment option to capture its overall value can easily be presented to policy-makers to guide their decisions and can also be combined with the proposed cost of research to assess cost-effectiveness of all possible research options and derive optimal mix of funded options through program budgeting and marginal analysis (16). This is a way of linking quantitative ranks of research options with specific investment decisions.

The final challenge, identified as "universal," was how to address opinions and systems of values of stakeholders other than investors and technical experts (such as government representatives, health workers, journalists, legal experts, recipients from the wider community, and others). While stakeholders' representatives may lack technical expertise to list and score research options, they could still prioritize between the chosen criteria by setting specific weights on intermediate scores for each research option, based on their perception of the relative importance of each priority-setting criterion in comparison with others. The rank orders of competing research avenues may change with the modifying of weights. These can also be revised as a result of a feedback process or substantial changes in the dynamic environment in which the priority setting process is being performed. The problem of involving stakeholders is a very complex one and CHNRI have recently published a separate paper that presented different strategies to involve stakeholders into health research priority setting process (13).

Conceptual framework for setting health research priorities proposed by CHNRI

CHNRI experts agreed that all identified challenges could eventually be dealt with in a satisfactory way through introduction of a new and systematic methodology for setting priorities in health research investments. However, a prerequisite for such a methodology/process is that an agreement is reached on a very limited number of key concepts. We present these concepts in further text, as they form the basic framework of the CHNRI priority setting method.

Defining health research

In the framework proposed by CHNRI, health research is defined as "any activity that is undertaken to generate presently non-existing knowledge that will eventually be used to reduce the existing disease burden (or other health-related problem) in human population." This definition is intended mainly to guide the investments of public funding and not-for-profit organizations. Instead of disease burden, the endpoint may also be another health problem, such as health promotion necessary to address improvements in child development. For private donors, however, the endpoints may be patentable products that would have commercial value.

The definition of health research stated above, which applies to public funding, should be carefully considered, because it has two important implications as follows:

1) It defines disease burden reduction as the perceived "return" of investments in health research. This is because the agreed targets and policies for spending public and not-for-profit funds are typically defined in terms of burden of disease reduction within a specified time frame. This methodology assists investment choices to reach those targets in an effective way.

2) It sets limits to what should be considered health research. Setting these limits may also attract criticism, but it is an essential first step that eventually enables a constructive and fair priority setting in health research invest-

ments in the real world. For example, a number of activities in construction, environment, and communication technology could eventually prove to have considerable positive collateral effects on population health. However, if it was not possible to envisage and predict these effects on disease burden reduction at the time when the activities were proposed for funding, then they should not be considered health research. Also, research on genetics of drosophila flies or yeast can bring fascinating new insights. However, if there is no vision at all (if even a blurred or distant one) on how the new knowledge generated by those activities can be used to achieve disease burden reduction in human populations, then those activities cannot be considered health research and should not be considered a funding priority by the organizations that invest in health research.

Defining main domains of health research

It has already been proposed by the Commission on Health Research for Development that, with respect to their potential to reduce existing disease burden, there are 3 broad and general domains of health research: 1) health policy and systems research, 2) research on improvement of the existing health interventions, and 3) research on development of new interventions (6). The recent work by CHNRI has shown that these domains of health research, although very useful, are neither mutually exclusive nor universally applicable, which would both be desirable properties for a research domain (2,4,5,14,15).

For example, if the health research proposed for funding is relevant at the global level, such as improvement of existing vaccines to increase coverage, then a domain "health research to improve deliverability or affordability of an existing intervention" will only be relevant to some countries, but not the others, depending on their contexts and level of investment in health care. Also, "improving of the effectiveness of existing interventions" cannot be entirely addressed through health policy and systems research, as suggested in the previous conceptual frameworks (6). Furthermore, epidemiological research features all 3 domains, and it is a necessary and important component of health research needed to inform any priority setting process, but it did not receive enough attention.

Much of the "improvement of the existing interventions" is reliant on the issues of deliverability or affordability. This qualifies it as the question for health systems and policy research, which is a different research domain from "improvement of existing interventions." Finally, development of new interventions is not always achieved through identifying an entirely novel line of research, but also through scientific advancements on the existing lines of work, which overlaps with the domain of "improvement of existing interventions."

Because of those limitations in the existing framework (6), we propose an extension of that framework in which there are 3 universal and non-overlapping domains of health research as follows:

1) Health research to assess burden of health problem (disease) and its determinants;

2) Health research to improve performance of existing capacities to reduce the burden;

3) Health research to develop new capacities to reduce the burden.

By capacities we consider any means of conducting health research – from health facilities and other infrastructure and equipment to available interventions and human resources. We believe that these three domains of health research are universally applicable in all contexts and also mutually exclusive. All possible health research questions should be easily categorized under one of the three domains, which is the advancement over previous approaches. For practical reasons, the sec-

ond general domain could be further split into "health policy and systems research" and "research to improve the existing interventions."

Defining priority setting (rationing, resource allocation)

In most human communities, ranging from the nuclear family to global human population, the needs and demands of the individuals or groups are greater than the resources that are available to fulfill them. Therefore, setting investment priorities for meeting those needs and demands becomes one of the most important issues for the development of any policy. Because not everyone can immediately get their demands fulfilled, some will be fulfilled immediately with existing resources, while others will be delayed.

These choices are especially difficult to make in developing countries, where delaying investments often means that a price would continue to be paid in human suffering, illness, and death. Because of this, priority setting requires transparent, legitimate, and fair approaches and explicit debate about the principles and criteria that would be used to make such difficult decisions. Some authors define priority setting as "who gets what at whose expense." The "what" can be either organs from donors, available drugs, or, most commonly, funding for different suggested activities. Although there is growing interest in priority setting, there is little consensus on the best way to carry it out in a fair and legitimate way at different levels (individual, community, national, or global) (4,17,18).

An important concept that we propose here is understanding that priority setting is not an exact science, process, or method. The reason for introducing this concept are the experiences with alternative priority-setting methods, such as Combined Approach Matrix, "value of information" approach, or the tools used by Council on Health Research for Development (4). These methods have all been carefully developed and validated with the aim to become very exact, consistent, and repeatable. However, the variety of contexts in which priority setting occurs and "returns" on investments expected by different donors are so large, that we believe it would not be possible to develop a "one-fits-all" method with a fixed set of criteria and processes. The successful method that will have a chance to become accepted and popular will need to show very large flexibility in design to be readily tailored to different contexts and purposes. Priority setting is a "science" intending to serve the needs of a community or a society at a specific point in time, within given policy, context, time limit, and financial constraints. It is value-driven and there are many interested stakeholders who will necessarily promote a diverse set of opinions and values. There are also many possible criteria according to which priorities could be set, some of them conflicting each other.

The community of health researchers is already used to the process of priority setting in which they submit their research proposals for funding and most of them get rejected or delayed until some later point in time. Only the minority of "priority research projects" get funded. Therefore, priority setting for investments into health research is already implemented for many decades by governmental and private donor agencies. The key question is whether it can be done in a more legitimate, fair, transparent, and replicable way (19).

Choice of relevant criteria for priority setting in health research investments

The decisions made regularly by investors in health research on supporting some of the proposed research grants are based on some criteria that separate priority projects, that get funded from those that get delayed or rejected. The key question is how much those criteria are compatible with what priority setting

should be about within our conceptual framework, ie, "serving the needs of a community or a society at a specific point in time, within given policy, context, time limit and financial constraints."

We have witnessed a publication of several millions of research papers as a product of investments in health research over the past several decades. Have those papers really been what society needed most in order to reduce its present disease burden? Did they really generate the new knowledge that was most needed and useful in reducing the persisting disease burden? Have they eventually led to reductions in disease burden over the past several decades that justified the immense investments made into health research over that time period? The criteria most often used by panels of experts evaluating the research grant proposals is answerability (mainly by judging track record and capacity of the group suggesting to undertake the research) and attractiveness of the new knowledge that is proposed to be generated (mainly in terms of potential for later publication in journals with high impact factors). Very rarely the panels judge the usefulness of the knowledge proposed to be generated in terms of its potential to contribute to reduction of the persisting disease burden in the society, although this should be one of the main criteria within CHNRI's conceptual framework for health research priority setting. The stakeholders can then weigh different criteria chosen by the investors and applied by technical experts. This weighing will reflect their system of values and guide the investors' decisions on research priorities. The technical aspects of the weighing have been addressed in detail in our previous work (13).

Conclusions

CHNRI proposes a new approach to undertaking health research priority setting in a fair and transparent way, respecting principles of maximizing the returns in terms of burden of disease reduction for invested funding. The approach is systematic and it attempts to overcome a larger list of universal challenges through introduction of several key concepts and proposal of a process that could become useful and popular among the users. It is transdisciplinary and it incorporates principles ranging from medical (eg, public health reasoning), social (eg, concern about equity), public opinion (eg, respecting stakeholders' views), ethical ("accountability for reasonableness"), and economic ("program budgeting and marginal analysis") disciplines. The agreed desirable elements of this new process are summarized in Table 4.

Table 4. Elements of the Child Health and Nutrition Research Initiative methodology for setting priorities in health research investments – it is a process driven by the investors and assisted by technical experts and numerous stakeholders, that results in the following seven outcomes.

Elements
1. Understanding the context in which investments are performed (by the investors)
2. Agreeing on expected profits and risk preferences (by the investors)
3. Defining main criteria for priority setting (by the investors)
4. Systematic listing of many competing research investment options (by the experts)
5. Transparent valuation of each research option against each criterion (by the experts)
6. Adjustment of this valuation according to values of the society (by the stakeholders)
7. Combining this adjusted valuation with predicted cost, expected profits and risk preferences to decide on the optimal investment strategy (by the investors)

Target audience for the proposed CHNRI methodology are national governments, public-private partnerships, international not-for-profit agencies, large research funding donors, and policy-makers, but it can also be adapted to the needs of private sector. We hope that these concepts will lead to improved accountability and increased attention to evaluation of returns on health research investments. In principle, it should be possible to evaluate the outcome of investment prioritization using a framework such as CHNRI's vs an alternative framework (eg, continuation of existing prac-

tices or using some alternative priority-setting tool). The countries increasingly measure and quantify their disease burden in metrics such as disability adjusted life years. If a reduction in disease burden is agreed as a target that could partly be achieved through health research investing, then the design of randomized controlled trial should be applicable in assessing the reduction in this burden achieved through different investment practices – those guided by priority setting tools vs alternative approaches. After a time frame of 5-10 years, the differences should become apparent and detectable. At that point, if a substantial advantage of the use of framework such as CHNRI's could be demonstrated, investing in health research could become a discipline guided by sound, transparent, and fair methods and practices.

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