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Responsiveness to Host Community Health Needs

There is near universal agreement within the scientific and ethics communities that a necessary condition for the moral permissibility of cross-national, collaborative research is that it be responsive to the health needs of the host community. It has proven difficult, however, to leverage or capitalize on this consensus in order to resolve lingering disputes about the ethics of international medical research. This is largely because different sides in these debates have sometimes provided different interpretations of what this requirement amounts to in actual practice.

The goal of the discussion that follows is to clarify the nature of this important moral requirement. The first section explains the requirement for responsiveness to host community health needs in the context of international medical research. The second section examines various formulations of this requirement as they are enunciated in some of the core consensus documents in research ethics. The third section then defends a particular interpretation of this requirement, and the final sections examine more liberal alternatives with the aim of highlighting points of agreement and assessing the significance of areas of disagreement.

Responding to the Developing World's Health Needs

The health inequalities that currently divide the developed from the developing world are not morally neutral. As the Ad Hoc Committee on Health Research Relating to Future Health Interventions of the World Health Organization (WHO) has noted, "The health of the world's peoples has improved more in the past four generations than in the whole of their history." [1] However, the size and extent of these gains have differed radically between populations of economically developed countries and impoverished nations of the developing world. In 1990, for example, more than a third of the global disease burden could be attributed to a handful of conditions that are virtually unknown in affluent nations of the developed world. These conditions include communicable childhood diseases such as pneumonia, diarrheal diseases, malaria, and various vaccine-preventable infections, as well as malnutrition and high rates of maternal and infant mortality arising from poor reproductive health.[1] Not only are these conditions more likely to occur in circumstances of social and economic deprivation, they are also more difficult to treat under such circumstances; and the devastating toll that they take on the populations in which they are endemic only reinforces the very conditions of deprivation in which such health problems flourish. As a result, the staggering health problems that plague many communities of the developing world play a major role in perpetuating a cycle of impoverishment, premature mortality, and underdevelopment.

The distinctive health problems of the developing world are inextricably bound up with poverty and other forms of social and political deprivation. Recently, however, the attention of scientists, ethicists, and policy makers has focused on what is increasingly viewed as a form of deprivation that occurs in the context of medical research. What is sometimes called the *10/90 disequilibrium* or the *10/90 gap* refers to the statistic that roughly 90% of the global burden of premature mortality can be attributed to diseases that primarily affect populations of the developing world, but only 10% of the annual global research budget of $50 billion to $60 billion is targeted at those diseases. Instead, 90% of the money spent each year on medical research across the globe focuses on the

health needs of populations in the developed world, which account for only 10% of the global burden of premature mortality.[1–3] To some degree, therefore, wealthy populations of the developed world have been able to use the fruits of scientific inquiry to safeguard and to secure their health needs so effectively because their needs have been the direct focus of the overwhelming majority of scientific inquiry.

Recognizing the morally problematic nature of the 10/90 gap has generated support for increasing collaborative research activities in the developing world. At the same time, however, such support is tempered by the awareness that too often in the past, when communities in the developing world have participated in research activities, they have not benefited from the fruits of those efforts. Instead, these benefits have been enjoyed primarily by more affluent populations of the developed world.[4] Such practices are now widely regarded as exploitative and, therefore, unethical. As a result, efforts to increase the involvement of the developing world in medical research have had to grapple with the difficult issue of how to achieve this goal while preventing the exploitation of those populations in the process.

One requirement that is intended to facilitate both of these goals is that cross-national collaborative research must be conducted in such a manner as to leave the host community better off than it was, or at least not worse off. This requirement supports another, namely, that international medical research must be responsive to the health needs and priorities of the host community. Together, these conditions constitute important moral constraints on permissible research, as well as substantive moral ideals toward which research should strive. Nevertheless, different interpretations of key concepts in these requirements have at times produced conflicting views about what these requirements amount to in actual practice.

Different Expressions of the Requirement

Perhaps the clearest statement of the requirement that collaborative international research be responsive to the health needs of the host community is presented by the Council for International Organizations of Medical Sciences (CIOMS), in collaboration with the WHO, in its International Ethical Guidelines for Biomedical Research Involving Human Subjects[5] (see Chapter 16). Guideline 3 of the 2002 text governs "ethical review of externally sponsored research" and states in part, "The health authorities of the host country, as well as a national or local ethical review committee, should ensure that the proposed research is responsive to the health needs and priorities of the host country and meets the requisite ethical standards." The phrase *health needs and priorities* introduces two key concepts and raises the question of their relationship. In order to understand what this guideline requires, it is necessary to clarify (a) what constitute the *health needs and priorities* of the host community and (b) what is required to show that a research initiative is sufficiently "responsive" to the host community's health needs and priorities, so understood.

To begin with, *health needs* are concerns that are particularly important or urgent because of their close relationship to the ability of persons to be free from medical conditions that shorten their lives or prevent them from functioning in ways that are basic or fundamental to their pursuit of a reasonable life plan.[6] In this respect, health needs stand in contrast to health-related wants or desires, when these terms refer to things that may help to improve the functionality of persons but which lack this urgency.

Among the various health needs that exist within a community, some may be viewed as more urgent or important than others. For instance, prostate cancer and breast cancer may be health needs that are *represented* in a resource-poor community in the sense that a significant cohort of people may suffer from these conditions. Nevertheless, finding new means of treating these afflictions may not be a health priority of such a community if significantly larger numbers of people suffer and die much earlier in life from conditions such as malaria, tuberculosis, or HIV. When this is the case, the latter conditions might constitute health needs that are also health priorities of such communities. In other communities, however, finding new means of treating prostate or breast cancer may constitute important health priorities. Communities can differ, therefore, in their health priorities even when significant members of their populations have common health needs.

Every community is constrained to use its finite social, economic, and human resources to meet a wide range of basic needs of community members. As a result, communities may differ in their social priorities, giving greater or lesser priority to different needs, depending on their broader social circumstances. For example, fostering economic development through job growth may be a top priority in a community with high rates of unemployment and low per capita income levels. So might be expanding the country's infrastructure or improving national security. Different communities may therefore view health-related issues, such as preventing the spread of HIV and providing a wide range of childhood vaccinations, as more or less of a priority than other social or economic concerns.

These rudimentary distinctions raise an important question about the requirement for responsiveness to host community health needs: Should the requirement be understood in a fairly restrictive way, according to which collaborative research initiatives should be required to focus on health needs that are also health priorities of the host community? Or should it be understood in a more liberal way, according to which it is sufficient for research to focus on a health need that is represented in the host community, even if it is not necessarily a health priority, so long as the research is adequately responsive to other priorities of the host community?

Perhaps the most natural reading of CIOMS Guideline 3 is that it requires research to be responsive to those health needs *that are also health priorities* of the host community. In this view, it is not sufficient to establish that the health need in question is merely represented in the host community. Rather, the health need in question must be sufficiently urgent or important that finding the means of addressing it represents a judicious use of the community's scarce social resources.

On the other hand, a literal reading of Guideline 10 of the 2002 text appears to be consistent with the more liberal or permissive interpretation of this requirement. This guideline governs "research in populations and communities with limited resources," and holds the following:

> Before undertaking research in a population or community with limited resources, the sponsor and the investigator must make every effort to ensure that:
>
> - the research is responsive to *the health needs and the priorities* of the population or community in which it is to be carried out [emphasis added]; and

- any intervention or product developed, or knowledge generated, will be made reasonably available for the benefit of that population or community.

Because "the health needs" of the host community do not necessarily fall under the scope of "the priorities" of that community in this statement, a literal reading of this guideline is consistent with the more liberal view.

To illustrate the importance of the difference between these two positions, consider the double-blind, randomized, placebo-controlled trial proposed in 2001 by the pharmaceutical company Discovery Laboratories. This trial would have compared the company's new surfactant agent, Surfaxin, against a placebo in impoverished communities of Latin America. Surfactants are substances that are essential to the ability of the lungs to absorb oxygen, and roughly half a dozen surfactant agents are commonly used to save the lives of premature infants in countries of the developed world. In return for hosting this study, Discovery Labs offered to upgrade and modernize the intensive care units in which the study would take place, increasing the ability of host communities to provide neonatal care to premature infants. This study, however, provoked an outcry over its use of a placebo control, which critics charged violated the current standard of care for treating premature infants. But this study also raises a more profound question that must be addressed prior to concerns about standards of care. Namely, was this proposed project sufficiently responsive to the health needs of host community members?

The most natural reading of CIOMS Guideline 3 supports the verdict that this research was not morally permissible because it did not target a health need that was also a health priority of the host community. Several effective surfactant agents are already widely used in developed counties, but these agents are not available in the impoverished communities that would host this trial. Moreover, Surfaxin was not specifically designed for use in the developing world. It therefore did not have properties that would make it more likely to be deployed in the developing world or more likely to be effective in that context than existing surfactants.

According to the weaker requirement that is at least consistent with a literal reading of Guideline 10, however, this research could be seen as permissible. It targeted a health need that was represented in the host community, and supporters argued that it was responsive to other priorities of the host community—such as strengthening the health-care infrastructure, training and educating medical personnel, and perhaps also fostering economic activity that would result from hosting the research.

Each of these views represents a different way of trying to satisfy the requirement in CIOMS that "the research project should leave low-resource countries or communities better off than previously or, at least, no worse off." In fact, the requirement for responsiveness to host community health needs can itself be viewed as emanating from the imperative in CIOMS that host countries should be left "at least, no worse off." As a result, the core consensus documents in research ethics have been more concerned with the relationship between access to benefits and the *responsiveness* clause in this requirement than with clarifying the relationship between the health needs and the priorities of the host community.

Similar tensions exist within the responsiveness clause of this requirement, however. In the CIOMS guidelines, under the section, "General Ethical Principles," for example, we are told that research in low-resource countries or communities, "should be responsive to their health needs and priorities *in that* any product developed is made reasonably available to them, and as far as possible [should] leave the population in a better position to obtain effective health care and protect its own health [emphasis added]". Here, responsiveness is equated with ensuring that the fruits of any successful research initiatives are made reasonably available in the host community. This statement also emphasizes the important role that medical research can play in helping communities safeguard their own health by discovering new diagnostic or therapeutic modalities. As I argue below, the requirement to ensure reasonable availability seems most appropriate when combined with the requirement that such research actually focus on health needs that are also health priorities of that community.

On the other hand, not all medical research is designed to vindicate a new diagnostic or treatment modality. Similarly, not all research that has this end succeeds in achieving its goal. However, research initiatives can be designed in such a way as to ensure that they provide host communities with indirect or ancillary benefits of various kinds.[7,8,3] For instance, researchers can provide vaccinations or rudimentary medical care to community members. They can train and educate local medical personnel and thereby contribute to enriching local research capacity. In this regard, the commentary on Guideline 10 again appears to be consistent with a more liberal view. There we are told, "It is not sufficient simply to determine that a disease is prevalent in the population and that new or further research is needed: the ethical requirement of 'responsiveness' can be fulfilled only if successful interventions *or other kinds of health benefit* are made available to the population [emphasis added]". Here it appears that the requirement of responsiveness can be met by providing other kinds of health benefits to the host community. As I argue below, this view seems most reasonable when conjoined to the somewhat weaker requirement that research need only focus on health needs that are represented in the host community as long as that enterprise is responsive to other priorities of that community. I will return to this point in the following section.

In some of the core consensus documents in research ethics the reasonable availability requirement eclipses entirely the debate over what is required in order to be adequately responsive to the health needs of the host population. The Declaration of Helsinki, for example, does not explicitly state that medical research must be responsive to the health needs of the host population (see Chapter 13). Paragraph 19, however, does state, "Medical research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the results of the research."[9] This paragraph, however, is often cited by commentators as an instance of the requirement that research be responsive to the health needs of the host community.[4,10]

In its report, *Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries,* the National Bioethics Advisory Commission (NBAC) affirmed that "Clinical trials conducted in developing countries should be limited to those studies that are responsive to the health needs of the community."[11] The NBAC derives the requirement of responsiveness to host population health needs from the values of beneficence and justice. Following the Belmont Report[12] and the U.S. Department of Health and Human Services' Common Rule, the NBAC holds that the requirement of beneficence is satisfied when the risks to research participants are reasonable in light of the prospect that the research initiative will generate either of two possible benefits: tangible

benefits to trial participants or increases in the "fund of human knowledge" (see Chapters 14 and 15). The NBAC then views the value of justice as requiring that "some of the benefits must accrue to the group from which the research participants are selected."[11]

According to the NBAC's justification of the requirement for responsiveness to host community health needs, some members of the host community must benefit either from the increases in the fund of human knowledge generated by the research or from tangible benefits that come from research participation. Both interpretations of the responsiveness requirement outlined above, however, can be viewed as interpretations of the argument that the NBAC offers. Nevertheless, the NBAC finds that researchers and their sponsors have an obligation to take steps prior to initiating a research initiative to ensure that the fruits of any successful research will be made reasonably available to the host population. As I argue below, however, this requirement seems most reasonable when combined with an interpretation of responsiveness to host community health needs that requires research to focus on health priorities of the host community.

The Nuffield Council on Bioethics displays the clearest grasp of the existence of, and conflict between, the two views outlined above concerning the requirement for responsiveness to host community health needs. In paragraph 2.24 of its 2002 report, *The Ethics of Research Related to Healthcare in Developing Countries,* the Council notes that "in countries where nearly all research related to healthcare is externally funded, the priorities for research have been largely set by the external sponsors." [3] It also notes the existence of the 10/90 disequilibrium, or 10/90 gap, mentioned earlier. This leads the Nuffield Council to affirm, in paragraph 4.8, that there is a general moral duty to alleviate suffering; and this moral duty creates a more specific moral obligation to conduct research that deals with the health problems in developing countries. However, the Council stops short of requiring all externally funded research to target health needs that fall within the nationally defined health priorities of the host community. Its reason for this, articulated in paragraph 2.31, is that even research that does not target a local health priority can "offer considerable indirect benefits to host countries in the developing world because of the potential for strengthening the national capacity in research, in the form of improved infrastructure and training." At paragraph 2.32, the Council therefore emphasizes that although it is important to encourage research that does advance local health priorities, this is not a necessary requirement because "all research contributes to the development of local skills and expertise in research, quite apart from the inherent value in diversity of research."[3]

The Nuffield Council, therefore, explicitly recognizes the moral permissibility of externally sponsored, international research that does not focus on a health priority of the host community. Presumably, such research is morally permissible only to the extent that it targets a health need that is represented in the host community and conveys sufficient indirect benefit to the host community that it can be seen as advancing other priorities of that community, such as strengthening the local research capacity.

Focus on Health Needs That Are Health Priorities

The survey of core consensus documents presented in the previous section reveals two salient dimensions along which alternative positions concerning the responsiveness to host community health needs requirement can be distinguished. For our present purposes, the most important distinction concerns whether international research initiatives are required to target health needs that that are also health priorities of the host community or whether it is sufficient to target health needs that are simply represented in the host community, as long as the research is sufficiently responsive to other priorities of the host community. This distinction is represented by the rows in the matrix in Table 67.1. I have labeled the top row *Restrictive* and the bottom row *Permissive* to indicate that not only do views that fall into the lower row permit all research that would be permitted by views in the top row, they permit a wider range of research as well. Within each row, views may then be distinguished as more or less restrictive depending on whether they also endorse the reasonable availability requirement.

Because it is sometimes difficult to tell exactly which combinations of these views are being advocated in some consensus documents, it is worth briefly exploring the merits of these positions in their own right. The top row of the matrix in Table 67.1 represents a variety of views that have been defended by numerous commentators.[13–17] Although these positions differ in significant ways, they share several basic tenets.

One shared tenet of views that occupy this row in the matrix is that an adequate understanding of a community's health needs must consider the important connections that exist between the health status of people and the operation of a variety of basic social structures. One social structure that is particularly salient in this regard is a community's local health-care system. As Jha and colleagues have emphasized, strengthening the *close-to-client* health system in developing countries would significantly increase the ability of local populations to access the effective medical interventions that already exist for some 90 percent of the avoidable mortality in low- and middle-income countries.[18]

The health status of individuals is also deeply affected by the way in which other basic social structures in their community allocate fundamental rights, such as who has access to literacy and education, including access to information about individual and public health; who has access to the means of productive employment; whose freedom of speech and association is protected; and whose sovereignty over their own person is respected. Whether or not the fundamental institutions of a community are directed at providing these social determinants of health can have a tremendous impact on the nature and extent of the health problems that members of that community face—as well as on the opportunities that are available to individuals to deal effectively

Table 67.1
Matrix of Models of Responsiveness to Health Needs

	Reasonable Availability Is Required	*Reasonable Availability Is Not Required*
Must target health needs that are also health priorities	Most restrictive	Less restrictive
May target health needs that are not health priorities	Less permissive	Most permissive

with those conditions that do arise. Communities that use their scarce social resources to invest in the basic capacities of community members have significantly greater success in staving off famine and epidemic disease. Those that do not direct community resources to these ends often create conditions in which starvation and disease flourish, sometimes on a massive scale.[19,20]

At the same time, sickness and disease themselves threaten important interests of individuals and communities alike. On the one hand, they impede the ability of individuals to function on an equal standing with others by restricting the full range of social opportunities that are available to them and often shortening their lives. In turn, the inability of individuals to take effective advantage of the full range of the social and economic opportunities available to them can significantly impact the ability of communities to advance important social and political goals such fostering education and economic growth.[21]

In light of these interrelationships, one of the views that occupies the top row of the matrix, the human development model, holds that various parties from developed countries, including government officials and the citizens they represent, have a duty to aid those in the developing world. It also holds that the duty to aid should be understood as a duty to assist those populations in developing and maintaining fair and equitable social structures that serve to safeguard and to advance the basic interests of community members.[17] What is required in order to discharge this general duty will differ for various stakeholders depending on their ability to influence different aspects of the social structures in developing countries. For example, the citizens of developed countries have a duty to support efforts to make better use of existing knowledge, resources, and interventions that could make a significant impact on the lives of those in the developing world. However, this view recognizes that even when a greater share of existing resources are directed toward advancing this goal, scientific research still has an important role to play in this process.

When this general duty to aid is applied to researchers and to research sponsors, therefore, the human development model translates the duty into an obligation to ensure that scientific research is responsive to host community health needs in a particular way. The model assumes that research can function as a powerful engine for creating the understanding and the interventions that are necessary to bridge gaps between the basic interests of community members and the ability of that community's basic social structures to safeguard and advance those interests. In order to bridge such gaps, clinical research must focus on health problems of developing-world communities that cannot be met more effectively or efficiently through the application of existing resources. Such health needs may be novel in the sense that there are no known means of treating or ameliorating them, or they may be health needs that have to be met under novel circumstances. That is, effective interventions may exist, but it may not be possible to deploy them within the host community on a sustainable basis. As a result, inquiry may be necessary in order to ascertain how to best to meet those needs under conditions that are attainable and sustainable within the host community. By focusing on health needs that cannot be met more effectively or efficiently through the application of existing knowledge or resources, and by doing so in a way that seeks to bridge the gaps between important health needs of community members and the ability of basic social structures in that community to meet those needs, collaborative research represents an important avenue through which the more general duty to aid may be discharged.

This view of the duty to aid, and the role of scientific research in advancing its goals, provides important guidance for selecting the criteria for determining which of a community's health needs should be given priority for research purposes. In particular, such criteria should be responsive to (a) the significance of the impact of a health need on the ability of individuals to access the full range of social opportunities that would otherwise be open to them, including their ability to cooperate in advancing important social goals, (b) the impact of these needs on equity and social justice in the host community, (c) the prevalence of these needs in the host population, and (d) whether they can be more effectively or efficiently met through the application of existing knowledge and resources. Some important steps have recently been taken in this regard by a variety of communities that have sought to define their national health priorities so that research can focus on what has been termed *essential national health research,* or ENHR.[1–3] ENHR refers to a strategy of systematic priority setting within which research questions can be identified and prioritized according to factors such as economic impact, cost effectiveness, effects on equity, social justice, and their contribution to strengthening research capacity in the host community.

Medical research that focuses on such health priorities has several important moral properties. Such research can make a strong prima facie claim to represent a just use of the host community's scarce social, economic, and human resources and to having significant social value because (a) these resources are being used to generate the knowledge, methods, and interventions necessary to expand the capacity of important social structures in the host community—such as the close-to-client health system—to address significant health needs of that community's members and (b) these needs could not be met more effectively or efficiently through the application of existing knowledge or resources.[17] As a result, such criteria represent a valuable means of identifying research questions that are essentially directed at closing the so-called 10/90 gap.

Although these criteria provide general constraints on what can count as a health priority in the research context, the actual health priorities of a community must be identified through the collaborative efforts of a number of parties. It is essential, therefore, that the process of identifying these priorities be transparent and open to public scrutiny. Similarly, it is essential that this process involve the participation of community representatives from local as well as national levels, including representatives of relevant minority groups. In this way, research can be responsive to on-the-ground factors that influence the prevalence of the condition in question, as well as factors that influence the ability to effectively treat those who are afflicted with it. The goal of these requirements is to ensure accountability and legitimacy as well as scientific and social responsibility.

The importance of ensuring such a transparent and legitimate process of democratic consultation has recently been emphasized by what is known as the fair benefits approach to international research.[7,8] This approach has also been a leading critical force in challenging the requirement of reasonable availability. Exploring the details of this approach and some of its possible variants will provide a clear context within which to evaluate positions that might fall into the cells in the Table 67.1 that are labeled "less restrictive," "less permissive," and "more permissive."

Less Restrictive Criteria for Permissible Research

The fair benefits approach has been critical of positions that require pretrial assurances of reasonable availability on the grounds that such requirements are overly restrictive and may actually work against the interests of developing world populations. This critical view of the reasonable availability requirement grows out of several concerns.

First, the fair benefits approach emphasizes that the reasonable availability requirement is relevant only to Phase III research. However, communities in the developing world might want to host Phase I or Phase II studies, or epidemiological studies, which are not designed to vindicate novel therapeutic or diagnostic modalities. Like the Nuffield Council, this approach also recognizes that there are numerous direct and indirect ways in which hosting a research initiative can benefit host communities. Such benefits might include the training of medical personnel, creating economic opportunities for employment, providing medical care, enhancing the local infrastructure, or enacting public health measures such as providing clean water. In fact, this approach holds that it might be possible for host communities to derive indirect benefits from hosting a research initiative that are more directly responsive to the larger priorities of that community than is the prospect of receiving access to the particular intervention being evaluated within that study. If this is the case, then requiring researchers and their sponsors to ensure reasonable availability puts an arbitrary roadblock in the way of research that might provide real benefits to developing world communities. It also paternalistically restricts the ability of host communities to bargain for the kind and amount of benefits that they desire most from a research initiative.

In its basic structure, therefore, the fair benefits approach represents an explicit defense of the more liberal version of the requirement for responsiveness to host community health needs identified in our survey of core consensus documents. Like those documents, this approach permits only medical research that is consistent with the values of beneficence and nonmaleficence. Research is permissible, therefore, only if there is a reasonable likelihood that it will leave the host community better off than it was, or at least not worse off. However, because the fair benefits approach views the reasonable availability requirement as overly restrictive, it adopts instead a mechanism of open deliberation and bargaining to achieve an exchange of benefits that is sufficient to leave the host community better off. Research initiatives must address "a health problem of the developing country population," and they must ensure that host communities receive a fair share of the benefits that are generated from research participation. Of course, decisions about how much of which kinds of benefits make hosting research worthwhile depend crucially on the priorities of the host community. So such questions are left for members of the host community to decide. These decisions would be subject to public debate, and a record of previous agreements would be used as a benchmark for fairness. Using this deliberative process to identify which kinds of benefit constitute a "fair" share in light of the host community's needs and priorities is meant to respect the autonomy of host community members and to ensure that the research has social value.

Because this approach requires that host community members receive a fair share of benefit from research that addresses "a health problem of the developing country population" without clarifying whether the problem must be a health priority of the host community, several different versions of this position can be constructed. If "a health problem of the developing country population" is understood as referring to a health priority of the host community—which would place it in the top row of the matrix in Table 67.1—then it can provide a rationale for what I have labeled a "less restrictive" approach to international research. It is less restrictive in the following sense: In addition to permitting all of the research that is permitted by positions in the "more restrictive" cell, it also permits research that targets a health priority of the host community without requiring pretrial assurances that any fruits of that study—if there are any—will be made reasonably available to members of the host community. Such projects are morally permissible, however, only as long as they do provide members of the host community with a fair package of ancillary benefits.

This version of the fair benefits approach overlaps to a considerable degree with the human development approach. Both require research to focus on a health priority of the host community but this version of the fair benefits approach rightly emphasizes the importance of ensuring that the indirect benefits that can attend research participation are coordinated so as to be responsive to priorities of the host community. This is especially important in cases in which the research is not designed to vindicate a new diagnostic or therapeutic modality. After all, Phase III research must often build on prior epidemiological research and on Phase I and Phase II studies. When it is appropriate to carry out such studies in the developing world, the research should be justified according to the requirements of this version of the fair benefits approach. Here, too, the criteria outlined above for prioritizing a community's health needs might also be used within the context of democratic consultation with host community members to determine which of the indirect benefits of research would best advance the community's larger social priorities.

Tensions arise between this version of the fair benefits approach and other views that occupy the most restrictive cell in the matrix in the context of Phase III research. Proponents of the fair benefits approach worry that research sponsors and other funding agencies will be unwilling to commit themselves to funding interventions whose therapeutic or diagnostic properties have not been clearly established. They therefore worry that such reticence may hinder the conduct of valuable research.

In contrast, proponents of the reasonable availability requirement worry that without prior commitments, the knowledge that is gained from collaborative research will not have a material impact on the health needs of host community members. For instance, many commentators who were critical of the short-course AZT trials in the developing world were explicitly rejecting a view that would fall into the "less restrictive" area of the matrix in Table 67.1. In particular, they argued that it is not sufficient for research to target a health priority of the host community if members of that community never benefit from the application of the knowledge generated by such trials. After all, effective interventions exist for many of the most pressing health problems in the developing world, and many of these interventions were vindicated by research that was carried out in such populations. Nevertheless, many of these interventions have not made a significant impact on disease burdens in these communities because they are largely unavailable there. As a result, critics hold that the position labeled "less restrictive" does not go far enough toward advancing the health interests of developing world populations.[4]

To a large degree, such tensions reflect the difference between pragmatic and aspirational approaches to international research. The pragmatic approach gives priority to generating knowledge that can be used to advance the health needs of developing world populations, leaving the problem of how to make these advances materially available to be dealt with later. The more aspirational approach emphasizes that host community members will benefit from medical research only to the extent that the fruits of that enterprise are used to expand the capacity of local social structures to meet the needs of the community. From this standpoint, one component of the requirement for responsiveness to host community health needs includes having reasonable assurance that the research enterprise is part of a social division of labor in which the knowledge that it generates will actually be applied to advance the interests of host community members.

Careful consideration of the criteria for responsiveness that were articulated in the previous section can mitigate the tensions that exist between these views. In particular, within the human development model, a fundamental part of identifying research initiatives that are capable of closing gaps between the basic health needs of a community's members and the capacity of basic social structures in that community to meet those needs is identifying target interventions that can be effectively deployed under conditions that are attainable and sustainable in the host community.[22] An important aspect of advance research planning, therefore, should be matching communities with research initiatives with the goal of ensuring that (a) the research target represents a health priority of the host community, (b) when research is designed to vindicate a therapeutic or diagnostic modality, there is a strong likelihood that any fruits of the research could be integrated into the basic social structures of the host community, and (c) the research initiative can provide an anchor for indirect benefits that are responsive to the broader priorities of the host community.

In all cases, research protocols should be accompanied by an assessment of the likelihood that the study intervention could be implemented in the host community, including an assessment of conditions that would need to be in place in order to increase this likelihood. Evaluations of whether pretrial assurance of reasonable availability is necessary should involve an explicit assessment of the likelihood that any knowledge generated could be used to expand the capacity of social structures in the host community to meet the basic health needs of community members—including an assessment of the extent to which the support of governmental, nongovernmental, or private entities is necessary to attain and sustain the conditions required for this goal.

Weakening the Criteria for Permissible Research

Significantly more liberal approaches to international research can be generated if the requirement in the fair benefits approach that research address "a health problem of the developing country population" is interpreted as permitting research that focuses on a health need that is merely *represented* in the host population. In such a view, as long as the ancillary or indirect benefits associated with the research are viewed as a fair return by members of the host community, then this position views positions that occupy the top row of the matrix as overly restrictive of important medical research and as paternalistically limiting the ability of developing world populations to advance their various interests and priorities.

Of the two cells in the permissive row, the less permissive view is conceptually unstable and perhaps incoherent. From the standpoint of the human development approach, it represents an inefficient way of advancing the fundamental interests of host community members, because it requires local governments and other funding agencies to spend scarce resources on interventions that do not necessarily address priority health problems of the host communities. From the standpoint of the "most permissive" view, the requirement of ensuring reasonable availability would only serve to prevent some research from taking place that would have otherwise offered benefits to host community members that they would have been willing to accept.

Although it seems clearly problematic in the abstract, this ad hoc approach is what appears to result from simply imposing the requirement of reasonable availability on all international research. As the Nuffield Council points out, most externally sponsored research in the developing world is driven by the priorities of the sponsoring entities. To the extent that the consensus documents canvassed earlier endorse the requirement of reasonable availability without clearly requiring research to focus on a health priority in the host community, these documents leave themselves open to withering criticisms from both more permissive and more restrictive perspectives.

The "most permissive" interpretation of the fair benefits approach is internally coherent and rationally compelling. It permits all the research that is permitted by views that occupy other cells in the matrix, while also permitting any research initiative that addresses a health need that is represented in the host community—so long as the host population receives what it views as a fair package of benefits in return. From this standpoint, hosting clinical research that generates significant indirect benefits for the host community, but which targets a disease problem that is not a priority in the host community might be seen as analogous to hosting a commercial plant that produces products that are enjoyed primarily by members of another community but which provides significant indirect benefits to the host community.

This view, however, raises a number of troubling concerns. To begin with, it is so liberal that it permits the continued use of developing world populations to answer questions that primarily address the health goals and priorities of the developed world. In this respect, it threatens to perpetuate or even to exacerbate the 10/90 gap. Second, the ancillary or indirect benefits that can be generated from research are unlikely to address root causes of disease in the developing world in a sustainable way. In particular, the disparities in bargaining power between research sponsors and host communities, combined with constant pressures to limit the costs associated with individual research projects, make it likely that there will remain a fairly low ceiling on the kind and extent of indirect benefits that host communities can access through the bargaining process.

Third, although it is true that medical research should be carried out so as to produce important indirect benefits, its most significant value lies in its ability to discover information necessary to improve the capacity of important social structures to minister to the health needs of community members. One of the critical reasons for the sharp gains in longevity and quality of life in the developed world over the past four generations has been the success of these nations in understanding health problems from a scientific standpoint and integrating that understanding not just into their respective health-care systems, but into the education

and lives of community members more generally.[1] In light of the profoundly urgent and pervasive health needs of the developing world, combined with the disparities in research representation represented by the 10/90 gap, strong reasons support changing funding priorities and creating incentives for governmental, nongovernmental, and private entities to focus more directly on priority health problems of developing world populations.[13–17] This process can be guided, at various stages, by understanding the requirement for responsiveness to host community health needs as holding that clinical research (a) must take health needs that constitute health priorities of the host community as the occasion for inquiry, and (b) must function as part of a social division of labor in which the fruits of such increased understanding have a high likelihood of being used to expand the capacity of that community's health-related social structures to meet the most pressing needs of community members.

Conclusion

When properly planned, scientific research can be a conduit for myriad direct and indirect benefits to host community members. The true social value of scientific research, however, emanates from its capacity to generate the knowledge, methods, and interventions necessary to enhance the ability of important social structures in the host community to address the most significant health needs of that community's members. Collaborative research initiatives should therefore be required to justify their responsiveness to host community health needs in these terms.

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