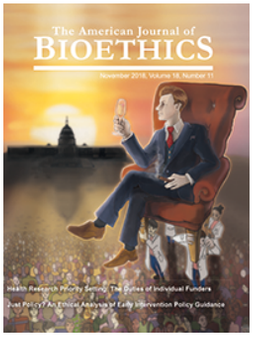

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Leah Pierson & Joseph Millum

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Health Research Priority Setting: The Duties of Individual Funders

Leah Pierson, Harvard Medical School
Joseph Millum, National Institutes of Health

The vast majority of health research resources are used to study conditions that affect a small, advantaged portion of the global population. This distribution has been widely criticized as inequitable and threatens to exacerbate health disparities. However, there has been little systematic work on what individual health research funders ought to do in response. In this article, we analyze the general and special duties of research funders to the different populations that might benefit from health research. We assess how these duties apply to governmental, multilateral, nonprofit, and for-profit organizations. We thereby derive a framework for how different types of funders should take the beneficiaries of research into account when they allocate scarce research resources.

Keywords: international/global health, pharmaceutical industry, rationing/resource allocation, research ethics

Research funding organizations must decide how to allocate their limited resources among multiple competing research programs. These allocation decisions affect which populations benefit from health research and when. For instance, publicly funded polio research led to the development of polio vaccines, benefiting millions of children who otherwise would have died or become paralyzed (Blume and Geesink 2000; WHO 2017). Children in high-income countries (HICs) benefited first from this research, but children in low- and middle-income countries (LMICs) subsequently benefited as well (WHO 2008). Conversely, research for Chagas disease, which can lead to cardiac failure and sudden death, has been woefully underfunded (Rassi, Rassi, and Marin-Neto 2010). Chagas disease continues to affect mostly poor and marginalized populations in Latin American LMICs (Tarleton et al. 2014).

The global distribution of research resources has been widely condemned as inequitable on the grounds that the majority of funding is directed toward developing interventions to benefit patients in HICs who are already, on average, better off (COHRED 1990; Røttingen et al. 2013). However, there has been little systematic work on what the individuals working at research funding organizations ought to do to change this.[1] Even if it is true that overall more resources should be directed to the conditions that most affect the global poor, it does not follow that any particular organization is obliged to take on this burden. Program officers at national research bodies may regard their remit as restricted to national health priorities, executives at pharmaceutical companies may think it legitimate to focus on marketable products, and employees of nonprofits may be focused on their organizational mission. Each may feel that it is not their job to achieve global justice.

In this article, we assess the strength of the duties of individual research funding organizations to the different populations that might benefit from the health research they could support. We begin by describing the ideal distribution of research resources. We argue that an allocator who had no obligation other than to bring about this optimal distribution would strive to maximize the social value of research. We then contend that all funders have general duties that require them to prioritize more socially valuable research. However, these general duties can be outweighed by special duties to particular populations. Finally, we analyze how these

1. Though see Callahan (2013, 240–258) and Dresser (2001, 73–90) for some discussion of research priority setting for U.S. government institutions.

Address correspondence to Joseph Millum, Clinical Center Department of Bioethics & Fogarty International Center, National Institutes of Health, 10/1C118, 10 Center Drive, Bethesda, MD 20892, USA. E-mail: joseph.millum@nih.gov

general and special duties might apply to each of the main categories of health research funders: government, multilateral, nonprofit, and for-profit organizations.

Ultimately, we take ourselves to be addressing individual agents. However, within each category of funding organization we start with the obligations that apply to the organization. The obligations of individuals working within the organization are largely derivative from those: Insofar as an individual has leeway to affect the distribution of research resources, she should do so in ways that improve the match between the overall organization's actions and its duties.

A key assumption frames our analysis: We take the amount of resources available for health research within an organization as fixed. That is, we assume that the individuals we are addressing at research funding organizations are neither able to devote more resources to research nor able to redirect funds earmarked for research to other uses.

GLOBAL SOCIAL VALUE AND THE OPTIMAL DISTRIBUTION OF RESEARCH RESOURCES

Before we can determine how the distinctive characteristics of different research funders shape their obligations, we must determine how resources should be distributed in the absence of special duties to particular populations. What would the optimal distribution of research resources look like? Two considerations are widely considered to be relevant to allocation questions like these.

First, the expected benefit of alternative allocations matters. All else being equal, if one individual would benefit more than another individual from a resource, she has a greater claim to that resource. Of course, it can be very difficult to determine who will benefit and how much from health research. For example, in the development of new pharmaceutical treatments for a specific condition, there may be great uncertainty about whether an intervention will result from the research, the degree of effectiveness any resulting intervention will have, who will get access to the intervention in the future, and so forth. This level of uncertainty stands in contrast to health care, where detailed data on the cost and expected effects of interventions are often available to help decision makers. Determining the expected benefit of alternative allocations of research resources is therefore a complex and highly technical matter. We set it aside here; such technical issues must be addressed by any research funding organization that seeks to allocate its funding in a data-driven manner. We note only that the uncertainty involved does not entail complete ignorance about who will benefit: Research on diabetes is much more likely to benefit people with diabetes than people with HIV; health systems research conducted in India is much more likely to benefit Indian patients than Japanese patients; and so on.

Second, it matters how the benefits of alternative allocations are distributed. If all the funding were spent on patients who are already well off, it would generally be regarded as unfair, even if spending the money on them would maximize the total benefits generated by the research. We take this distributive concern into account by considering the degree of disadvantage of the beneficiaries.[2]

An individual's claim to benefit from research is greater the worse off that individual is. In assessing how badly off someone is we consider their expected well-being over a lifetime (Sharp and Millum 2018). Thus, populations with stronger claims to research resources will include those suffering from conditions that substantially reduce life expectancy, those who have serious chronic conditions, and those who are living in conditions of extreme poverty.

In the context of research ethics, the term *social value* is widely used to refer to the importance of the expected benefits of a research project (Emanuel, Wendler, and Grady 2000). Estimates of a project's social value can be used to assess whether it justifies putting research participants at risk and for research funding organizations to compare the importance of different projects they could fund (Barsdorf and Millum 2017). According to the arguments just given, a funder intending to distribute research resources optimally should aim to maximize global expected social value (or just social value for short), where social value is a positive function of both expected benefit and the degree of disadvantage of the expected beneficiaries.

GENERAL AND SPECIAL DUTIES

Agents may have three types of duty: general duties, constitutive duties, and acquired duties. These duties apply to research funding organizations and the individuals within them, and affect which populations they should direct their research to benefit. *General duties* apply to all funders and include duties of justice and beneficence. In addition to their general duties, funders may have special duties to benefit specific populations. Sources of special duties can be divided into constitutive and acquired duties. *Constitutive duties* are duties a funder has because of its societal role. By contrast, *acquired duties* arise through the actions of an individual funder when it makes a commitment to, has a reciprocal relationship with, or harms a particular population.

2. The alternative is to take it into account by focusing on equality. At the level of abstraction at which this article operates, the two will be more or less functionally equivalent: Distributions that give greater priority to those who are worse off will be those that reduce inequality and vice versa. What matter much more for our ultimate moral verdicts are questions such as: What constitutes disadvantage? (Or, what should be equalized?) How should priority to the worse off (or increasing equality) be balanced against maximizing benefits?

In this section, we describe each type of duty and show how each applies to the case of health research funding. We argue that funders' general duties are consistent with prioritizing the most socially valuable research. Constitutive and acquired duties may justify funders deviating from this maximizing approach to favor specific populations to whom they have special duties.

Among other things, justice requires that health research funders not discriminate between populations on the basis of irrelevant differences and not promote or exacerbate unfairness. It also imposes some positive duties to reduce existing unfairness. Health research can promote justice in three ways. First, when relevant laws and policies are informed by high-quality health research, they are less likely to inadvertently treat groups unfairly. Second, health research can motivate policy change by illuminating injustices. Finally, health research can promote justice by making people better off and thereby reducing inequality. In the context of funding research, we expect that positive duties of justice will typically favor supporting the research that is most socially valuable, since these duties usually oblige funders to prioritize research that will ultimately benefit disadvantaged groups. Although duties of justice could conceivably conflict with maximizing the social value of research, we think this is highly unlikely to occur in practice.

Duties of beneficence are duties to benefit others. They are typically divided into the imperfect duty of beneficence and the duty of easy rescue. The former is a duty to provide some benefits to others, but where the actor has discretion about exactly whom she benefits and how. This duty can be fulfilled by supporting socially valuable research but does not implicate any particular patient population as the appropriate beneficiary. Much health research falls into this category, as it is usually impossible to predict that a given amount of research resources will produce significant benefits: Projects often fail to complete, yield discoveries that have few implications for human health, or generate findings that go untranslated. The consequent low levels of expected benefit for specifiable individuals means individuals typically do not have a right to benefits that can only be generated through research. Thus, in the overwhelming majority of cases, research funding organizations' duties of beneficence are not owed to specific individuals (Callahan 2003).

However, according to the duty of easy rescue, if an agent could provide a great benefit to another at a low cost to herself or third parties, she has a duty to do so (Mann, Savulescu, and Sahakian 2016). For example, a person has a duty to rescue a child drowning in a pond even if doing so would involve muddying that person's clothes (Singer 1972). This duty is owed to specific individuals—those who could be rescued by the beneficent act—and so would direct research funders to benefit specific populations if it applied to them.

In rare instances, funders may have a duty to support research as a matter of rescue. Two requirements must be met for this to be the case: First, the research project must have a sufficiently high probability of providing a substantial benefit to some population; second, the funder must be able to provide the benefit at a relatively low cost. The first requirement can be easily met; many populations have serious health problems and so could benefit greatly from health research. The second, however, is much harder to satisfy. With regard to health research, the metaphorical pond often turns out to be a raging waterfall. For example, public officials famously underestimated the cost of developing an HIV vaccine by tens of billions of dollars (Markel 2005). Certain types of research projects—those where the cost of generating important results is known and insignificant relative to the amount of resources a funder has devoted to health research—are more likely to be implicated by the duty of rescue. Such research might include health systems research or comparative effectiveness research, wherein two standard treatments for a given condition are compared. In contexts where cost typically prevents some patients from accessing treatment, rescue research might also compare interventions that are thought to be similarly effective, but where one is much cheaper.

In any case, there will be little conflict between a funder fulfilling its duty of easy rescue and supporting research that maximizes social value. Those people who are most in need of rescue will be precisely those who are currently very badly off and would benefit greatly from assistance. That is, they are the people for whom assistance would have the highest social value.

Funders' general duties will usually be consistent with maximizing social value. However, according to most ethical theories, these duties are limited. For example, most people think that individuals have some discretion to benefit themselves or their loved ones even when they could produce more valuable benefits for strangers. Only if a funder were faced with sufficient easy rescues that its resources would be exhausted by them would such maximizing be required. We think this is unlikely. Thus, though funders' general duties are consistent with maximizing social value, they are unlikely to require it.

Constitutive duties are duties that a funder has in virtue of its societal role, that is, the type of organization it is. States, multilateral organizations, nonprofit organizations, and for-profit organizations are subject to certain duties that apply to all organizations that fall into each of these categories. To illustrate, many people think that states have constitutive duties to people living within the state because those people forfeit freedom—by paying taxes and abiding by laws, among other things—on the condition that the state will serve them (Blake 2001).

Thus, it might be argued that if a state uses tax dollars to fund health research, the population within the state should derive benefits from it.

Acquired duties arise in virtue of past interactions, rendering them specific to an individual funder (e.g., the Wellcome Trust, GlaxoSmithKline). They include duties of commitment (such as the duty generated by making a promise); duties of reciprocity (such as the duty to benefit someone who has benefited you in the past); and duties of culpability (such as the duty to compensate someone you harmed through deliberate or negligent behavior). For instance, a government that forcibly displaced a community to make way for a dam is culpable for the harms that result. If that community would benefit from health research, a state health research funding organization might partially fulfill the government's duty of culpability by funding such research. Admittedly, in most cases, research is not the best way to compensate harmed populations. However, as we explain shortly, research funders should allocate research resources as a matter of culpability if more appropriate agents will not directly compensate these groups.

In the rest of this article, we explore the extent to which each of these duties applies to the major categories of research funders.

RESEARCH FUNDING ORGANIZATIONS AND INDIVIDUAL DECISION MAKERS

Individuals within research funding organizations play different roles that grant them (limited) leeway to both set and implement the research funding agenda, and thereby affect which projects are pursued. These individuals might include a pharmaceutical executive responsible for deciding which lines of research continue and which are pulled, a National Institutes of Health (NIH) program officer writing a request for applications, or a nonprofit administrator on a committee that recommends research priorities.

Our ultimate interest is in what the individuals working within research funding organizations should do. That is, to the extent to which an individual's actions affect what research gets funded, how should they decide what research to support? We treat these individuals as institutional actors, in the sense that insofar as they are using institutional resources, their duties are largely derivative from the duties of the institution as a whole. Of course, almost no individual can unilaterally decide what her organization does. Thus, no individual can single-handedly fulfill her organization's duties. This should not detract from the usefulness of conceptualizing the problem in this way: Insofar as an individual has leeway to benefit one population or another, she should use that leeway to make the organization act in a way that is more consistent with its ethical obligations, rather than less.

Individuals also have duties that are separate from their institutional obligations. For instance, they have general duties to the global poor and special duties to their families. However, these duties never require individuals to support health research (rather than, say, donate to highly effective charities that distribute malaria nets). Moreover, these duties do not conflict with individuals' institutional obligations regarding health research. Thus, we set them aside here.

The duties of research funding organizations and their employees are sometimes expanded or restricted by nonideal circumstances. For instance, we might think that under ideal circumstances—that is, in a just world—a pharmaceutical company would not be obliged to fund health research as a matter of rescue. Perhaps multilateral organizations or states should be funding such research. But when these actors have failed to act as they should, it may fall to others, like private companies, to pick up the slack. Nonideal circumstances may also have implications for individuals within organizations. It might be that a pharmaceutical company ought to fund comparative-effectiveness research that would allow physicians to make informed decisions about when to prescribe that company's products. But if directing company funds towards such research would result in an executive's dismissal, it is plausible that she is not obliged to do this.

GOVERNMENT RESEARCH FUNDERS

Government research funders include institutions such as the U.S. National Institutes of Health (NIH) and the Indian Council of Medical Research (ICMR). Government institutions spend more than US$64 billion annually on health research, and fund a diverse array of research on clinical interventions, the basic sciences, health policy, and the social determinants of health (Røttingen et al. 2013).[3] Public-sector research investments in particular arenas can also spur private-sector research investments in those same areas, particularly with regard to basic research, high-risk projects, or research programs with very long time horizons (Sampat 2011). The government also supports health research indirectly: for instance, through tax breaks that benefit companies and nonprofits that conduct health research and through direct donations to multilateral organizations.

Non-elected individuals employed by government agencies should act in light of the obligations of the

3. Røttingen and colleagues (Røttingen et al. 2013) write that US$214 of US$240 billion spent annually on research, or 89.5% of research funding, comes from HICs. Of this, 30% is spent by the public sector. We estimated $64 billion by calculating 30 percent of $214 billion. However, this is likely to be an underestimate, because some research funding from LMICs ($26 billion annually) comes from government sources. All funding estimates are in 2009 U.S. dollars.

governments of which they are a part. The constitutive obligations of governments with respect to the distribution of scarce resources include to distribute the resources fairly, which means that they should pay attention to both the quantity of benefits and to how those benefits are distributed. Since governments distribute the collective resources of their citizens, they must do so in a just way. Unlike other agents, governments do not have a zone of discretion within which they can favor themselves if they prefer (Dresser 2001).

It is worth noting that the requirements of justice do not change when the people who run the government do. For instance, governments—and the individuals who work within them—have obligations to apply their laws in a nondiscriminatory way. These duties are not dependent on whether current political leaders want to be prejudicial in their enforcement of laws. However, government employees are sometimes instructed by their superiors to disregard the government's constitutive obligations. This situation is particularly problematic when elected officials encourage appointed officials to behave in ways that are unjust, leading to a conflict between procedural and substantive justice: If nonelected officials ignore the commands of democratically elected leaders, this undermines the authority of the democratic process. Fortunately, with regard to health research, this conflict is limited. Decisions about research funding are less politicized than other decisions governments make, for instance, about access to health care or whether to wage war. Elected officials may make some big-picture decisions about how research funds are spent, but rarely direct research funding organizations to act in unjust ways. Individuals working within state research funding organizations should therefore default to allocating resources in accordance with substantive principles of justice where this does not conflict with the explicit directives of their elected leaders.

The crucial question concerning the constitutive obligations of governments is who has standing with respect to distributive justice. Should a national government allocate resources preferentially to citizens (or residents), rather than counting all people's health needs in the same way?

Answering this question requires taking a stand on the debate between cosmopolitans and statists over global justice. According to *cosmopolitans*, the same principles of distributive justice apply internationally as apply within a state. On a cosmopolitan view, then, government research funders should make their decisions on the basis of an assessment of the expected global social value of the research. The general duties of a government will be subsumed under its constitutive duties. According to *statists*, the primary locus of principles of distributive justice is the state. For a statist, a government may have some weaker obligations to populations outside of its borders, but it has much more stringent obligations to those within. On a strong statist view, then, government research funders have constitutive duties to maximize the expected social value of the research they support for the population of that country.

For a statist, a government's duties of justice to noncitizens are weaker or nonexistent, and its duties of justice and beneficence may thus fail to coincide. Nonetheless, even the most ardent statists concede that governments have duties to populations beyond their borders, and moderate statists acknowledge these obligations can be significant. States have general duties to support just institutions elsewhere in the world, and they have obligations of beneficence that are grounded in desperate need no matter where the beneficiary is. For example, John Rawls, who denied that the same principles of justice that applied within states applied between them (or, as he described it, between "peoples"), nevertheless recognized a duty of assistance to "other peoples living under unfavorable conditions that prevent their having a just or decent political and social regime" (Rawls 1999).

Our sympathies lie with cosmopolitan views of global justice. First, for us, as for many political theorists, it seems unjust when people face differences in their life prospects for reasons that are morally arbitrary. But nationality is a morally arbitrary quality, as one exercises no control over where one is born. By this logic, nationality should have little bearing on the share of resources, including health research resources, to which one is entitled. Second, some philosophers argue that the requirements for distributive justice arise when people are subject to coercively imposed rules (Moellendorf and The Hegeler Institute 2011). Such rules can only be justified to the people they bind when the resulting social order is just. Although nation-states are the main proximate source of the legal regimes that govern people's lives, a number of binding international agreements also affect the life prospects of people around the world. Just like national legal regimes, these must be justified to the people they constrain, which requires attention to the global distribution of resources (Beitz 1999). Space does not permit an extensive defense of our cosmopolitan position here. It is therefore worth noting that—though there will be some divergence between what reasonable statists and cosmopolitans conclude—the divergence will not be as extreme as a simple statement of the views might suggest. Not only do statists have to consider the general duties of their states to poorer populations outside their borders, there are also practical reasons for statists to favor research that benefits populations abroad and for cosmopolitans to favor research that benefits people within state borders.

On the one hand, conducting health research for populations outside the state may often promote the interests of people within the state. In an increasingly globalized world, an epidemic in one country may jeopardize the health of people worldwide. Moreover,

diseases that arise in one part of the world can undermine security in other nations or lead to significant economic losses (Hutchinson et al. 2006; Letendre, Fincher, and Thornhill 2010). On the other hand, funders may have a better sense of which researchers and institutions within their own countries are likely to produce high quality research. These researchers may in turn possess knowledge, connections, or infrastructure that render them better suited to study co-nationals. Research that benefits people within the state may also garner more public support over the long term, leading to greater investments in health research.

Governments may also acquire duties that government research funding organizations can fulfill. Governments sometimes incur such duties by making commitments to support health research that will benefit other states or people within their own state. For example, in 2005, the National Institute of Allergy and Infectious Diseases (NIAID), part of the NIH, agreed to help fund an International Center for Excellence in Research in Chennai, India (NIAID 2008). Research funders at the NIH consequently had a duty to follow through on this commitment.

A particularly important type of acquired duty for governments is the duty of culpability. If a government has harmed a population, then it has a duty to compensate it. The recent water crisis in Flint, Michigan, where the state piped leaded, bacteria-infested water into citizens' homes and then falsely assured them that the water was safe to drink, is an example of how states might incur duties of culpability to their citizens (Davey and Pẽrez-Pẽna 2016; Hanna-Attisha et al. 2016). States also incur duties of culpability to people outside of the state by engaging in conduct—like promoting trade agreements that disadvantage poorer countries—that causes poverty and ill health (Pogge 2002).

When a state harms a group, it can compensate that population in many ways, including through providing economic aid, building infrastructure, providing health care, or conducting health research. The optimal way to do so will depend on the situation. For instance, ideally families in Flint, Michigan, should receive free health care and housing repairs, among other goods, since these are the most direct ways to try to repair their harms. The optimal form of compensation will rarely be health research; even though most disadvantaged populations could be helped through research, its benefits are often diffuse and less immediate than those of other interventions.

However, it is often the case that a government is not planning to compensate a population in the optimal manner. Government leaders may deny responsibility or provide only token reparations. In such cases, other governmental actors may be able to fulfill the duties of culpability owed by the state. This could include providing benefits by sponsoring research. For instance, if other parts of the government of Michigan appear unlikely to provide the compensation owed to the population of Flint, individuals who make research funding decisions within the Michigan Department of Health and Human Services should help fulfill the government's duties. These individuals might do so by directing research funding toward projects that are likely to benefit Flint residents. As a matter of culpability, funders might, for instance, support research interventions that could mitigate neurological damage in children exposed to lead. Thus, when health research funders within the state set research priorities, they should consider which populations their states have harmed, and whether those populations have been fully compensated in other ways. If not, research funders should give higher priority to health research for those populations.

To summarize, there is debate around whether governments have greater constitutive duties to people within the state and so should give higher priority to their needs when funding research. In any case, governments, like all agents, have general duties to the populations most in need of health research, regardless of where these populations are located. Governments also have acquired duties, particularly duties of culpability. These duties may be owed to populations within the state or elsewhere that have been harmed as a result of government actions.

MULTILATERAL RESEARCH FUNDERS

Multilateral organizations are international organizations charged with resolving problems that individual states cannot adequately address. Multilateral organizations that fund health research include the World Health Organization (WHO) and the World Bank. These organizations collectively spend close to a billion dollars on health research every year (Viergever 2013; 2017). Multilaterals support several kinds of health research, including health systems research and translational research, and additionally devote significant resources toward building research capacity in LMICs (Lansang and Dennis 2004).

Multilateral organizations have constitutive obligations to states, which support multilateral organizations in the hopes of promoting a secure international order. Multilateral organizations play a crucial role in realizing justice in the international sphere. They do so by protecting human rights when states cannot or opt not to, by promoting democratic decision making, and by supporting international cooperation (Keohane 2006). They thereby carry out international obligations of states, including promoting peace and development. Individuals allocating funds for health research at multilateral organizations can best fulfill the constitutive obligations of those organizations by funding research for populations whose research needs cannot or will not be met by states or other agents (Letendre, Fincher, and Thornhill 2010). This may include helping LMICs

develop their own research infrastructure or supporting research that requires a coordinated international approach (Pratt and Loff 2014). In general, the populations who will benefit from this research are overwhelmingly disadvantaged, so the research multilaterals should fund in accordance with their constitutive obligations will tend to be highly socially valuable. Consequently, the general and constitutive obligations of health research funders at multilateral organizations will largely align.

Multilateral organizations have few acquired obligations, largely because they have a constitutive obligation to be impartial, and should thus strive to maintain neutrality (Keohane, Macedo, and Moravcsik 2009). Like all actors, they should follow through on their commitments, but these commitments will tend to reflect constitutive obligations. In some cases, research funders at multilateral organizations may have a duty to provide research resources because they are culpable for a population's ill health. For instance, United Nations (UN) peacekeepers caused an outbreak of cholera in Haiti in 2010 (Frerichs et al. 2012). If the population harmed by the epidemic would benefit from health research and is unlikely to be fully compensated in other ways, then research funders within the UN might have a duty to compensate Haitians by funding relevant health research.

NONPROFIT RESEARCH FUNDERS

There are thousands of nonprofit organizations (NPOs) that fund health research, including a large and diverse array of philanthropies and charities. These organizations are defined by the fact that they work toward a particular goal—for instance, furthering research for a given disease or promoting the health of a specific population—and use their revenue to realize that objective. NPOs vary greatly in their funding sources. Some, like the Bill and Melinda Gates Foundation, receive the vast majority of their funding from a handful of donors, while others, like the American Heart Association (AHA), receive much of their funding through small donations (O'Hare 2014). NPOs spend approximately $21 billion annually on research (Røttingen et al. 2013).[4]

NPOs have constitutive obligations to states and to their donors. They have constitutive obligations to states because states conditionally subsidize their existence through generous tax policies. Some of the money that goes to NPOs is therefore money that would otherwise have gone to the state. The state, which could have used this money to pursue socially valuable projects, grants tax exemptions to NPOs on the condition that these organizations will pursue such projects. Thus, NPOs should fund the most socially valuable research they can, consistent with their other duties.

These organizations should only prioritize more socially valuable research within the confines of their mission statements, which represent their constitutive duties to donors and duties of commitment to populations with which they are concerned. In adhering to their mission statements, NPOs should not accept donor money on false premises, and should be able to justify their funding choices to donors. For the most part, we expect that NPOs will be able to follow these constitutive duties consistent with their general duties of beneficence and justice.[5] For instance, the AHA's mission is "to build healthier lives, free of cardiovascular diseases and stroke." The AHA has a strong duty to fund cost-effective cardiovascular disease and stroke research that will benefit the neediest populations. Indeed, such research should be of highest priority. But the AHA has no constitutive duty to fund equally pivotal, low-cost research that lacks a plausible connection to the AHA's mission.

Some NPOs may also have duties of culpability or reciprocity. For example, if an NPO is part of a larger organization that knowingly engaged in harmful behavior, it may acquire a duty to compensate affected populations. In rare cases, NPOs may also have duties of reciprocity to other NPOs and the patient populations those organizations represent. These duties may arise when organizations collaborate on research projects.

To summarize, NPOs can usually best fulfill their general duties, constitutive duties, and duties of commitment by simply funding the most socially valuable research that is consistent with their mission statements.

FOR-PROFIT RESEARCH FUNDERS

Pharmaceutical, biotechnology, and medical device firms spend more than $128 billion on research annually (Dorsey 2010; Moses et al. 2005; Røttingen et al. 2013). These organizations have the goal of funding profitable health research in order to generate returns for shareholders.[6] The constitutive obligations of for-profit organizations (FPOs) will vary substantially depending on the regulatory framework and background justice of the

4. Røttingen and colleagues (Røttingen et al. 2013) write that of the $214 billion spent annually by HICs on research, "10% comes from other sources (including private, non-profit organizations)." We estimated $21 billion by calculating 10% of $214 billion. However, this estimate is very imprecise. It might be low because some funding from LMICs (26 billion annually) likely comes from NPOs. Alternately, this estimate could be high because "other sources" might include organizations that are not NPOs.

5. The exception would be rescue cases. But the likelihood that an NPO is faced with a rescue situation that requires research, would be low cost for that organization, and yet is outside of the organization's remit strikes us as low. We therefore do not address here the difficult question of how rescue obligations should be balanced against conflicting special duties.

6. We deal here with the paradigm case of a stock-issuing corporation, since such companies fund the vast majority of for-profit health research.

societies in which they operate. Under ideal circumstances—wherein states and multilateral organizations would ensure the fair distribution of goods produced by the market—private-sector actors would have no obligation to consider the distributive effects of their actions. As we argue, this is not the case in the context of market failures and inadequate governmental action in which FPOs actually operate.

In theory, markets excel at producing efficient outcomes, while governments are meant to ensure that efficiency is appropriately balanced with fairness. Research funders within the private sector therefore operate under somewhat different moral constraints than other agents. As Joseph Heath points out, basic moral norms, like the golden rule, do not always apply to private-sector actors:

> Before kicking in the winning field goal, we do not want football players to be thinking, 'How would I like it if the other team did that to me?' Similarly, before lowering prices, we do not want gas-station owners to be thinking 'How would I like it if the station across the street did that to me?' (Heath 2007)

Private-sector actors may not be subject to some moral rules in light of the special moral rules that obtain in the market. But outside actors—like states and multilateral organizations—have the authority to regulate the market and redistribute the goods it produces. There is empirical and normative debate regarding the extent to which regulators should constrain market forces to produce a just distribution of goods. Nearly everyone agrees that regulators should, at a minimum, promote Pareto-optimal market efficiency by preventing market failures (Heath 2004). However, regulators frequently fail to regulate the market effectively, creating conditions that are inefficient. Regulators often additionally fail at fairly redistributing goods produced by the market. These two facts prompt the question of how private-sector actors should behave when regulatory failures lead to an unjust distribution of important goods.

An example illustrates this point. In 2000, Pfizer sold fluconazole, a medication used for treating AIDS-related opportunistic infections, for more than 28 times as much in South Africa as a generic version of the drug was sold for in Thailand (Perez-Casas et al. 2000). The high cost of this medication left millions of South Africans without access to a potentially lifesaving therapy. Pfizer did not need to make a significant profit on fluconazole in order to recoup research costs: Pharmaceutical companies, including Pfizer, have historically enjoyed profit margins that dwarf those of nonpharmaceutical Fortune 500 companies (Angell 2004). In the context of Pfizer's massive profit margins, the high price of fluconazole in South Africa represents a market failure, albeit a legal one (the World Trade Organization [WTO] Agreement on Trade-Related Aspects of International Property Rights [TRIPS] permitted Pfizer to hold its patent on fluconazole for 20 years) (Light and Lexchin 2012). But it was not only Pfizer or the WTO that was responsible for South Africans' inability to access this essential treatment. The South African government might have lowered the price of fluconazole by threatening to invoke emergency powers enshrined in the TRIPS agreement, as other countries had done. For instance, the Brazilian government had successfully negotiated a lower price for fluconazole by threatening to produce or import generic versions of the drug (Barnard 2002). Unlike the Brazilian government, the South African government failed to prioritize expanding access to HIV treatment. In this case, a market failure occurred, government actors failed to intervene, and South Africans were dying as a result. What were Pfizer's obligations?

To answer this question, we need to understand the obligations of pharmaceutical companies more generally. Clearly, firms have a constitutive duty to their shareholders: They must attempt to make a profit. Ethicists disagree on how stringent this duty is. Some argue that businesses have a duty to maximize profits for their shareholders (Friedman 1970). Others contend that duties to shareholders exist alongside duties to other stakeholders, including customers and communities (Freeman 1994). Both sides provide consequentialist justifications for their positions, arguing that their respective moral theories promote efficiency. But the extent of firms' duties to their shareholders can only be properly understood once we understand the justification for firms' existence in the first place.

States allow firms to incorporate and grant firms privileges on the premise that an efficient market, in conjunction with sound regulatory and redistributive policies, will tend to produce a better distribution of goods than a planned economy would. Firms thus have constitutive duties to states, which support firms through legal regimes that provide limited liability, tax policies, and patent protections, as well as subsidized research (Heath 2004). Under ideal circumstances, the constitutive obligations of firms to shareholders and to states should align. Heath writes: "If all companies fully internalized all costs, and charged consumers the full price that production of their goods imposed upon society, it would be impossible to make the case for any further 'social responsibility' with respect to, for example, the environment" (Heath 2004). But firms' obligations to shareholders and states diverge when regulatory failures produce a market rife with inefficiencies.

When market failures occur, firms' constitutive obligations to states trump their obligations to shareholders. Firms' obligations to shareholders arise from the fact that an efficient market benefits society: In a well-regulated market—where deception, for instance, is prohibited—private-sector actors promoting shareholder interests will enhance access to goods (Heath 2004). However, firms cannot have an obligation to make money for their shareholders when doing so requires exploiting or exacerbating market inefficiencies. After all,

the ultimate justification for the existence of firms is the promotion of an efficient market that—when tempered by the government's regulatory and redistributive efforts—leads to a more just distribution of goods.

Pharmaceutical companies often do take advantage of market failures; for instance, they sell lifesaving medications at astronomical prices while achieving massive profits and use these profits to lobby politicians to permit more market inefficiencies (Chon 2016). These actions leave some populations worse off than they should have been. Because firms have a constitutive obligation to not take advantage of market failures, when they do so, this generates a duty to rectify the social injustice that they have exploited and are aggravating. It is not always clear how this duty should be fulfilled. In some cases, altruistic behavior on the part of firms might exacerbate harms by further compromising market efficiency. However, in many cases, a firm can best fulfill its social role—to help generate a just distribution of goods—through targeted research. For instance, pharmaceutical companies can usually do more good by reinvesting a larger portion of profits in socially valuable research than they can by maintaining double-digit profit margins.

When a firm can identify populations that it has made worse off, it has a duty to compensate those populations. For instance, when Turing Pharmaceuticals, led by Martin Shkreli, bought pyrimethamine from Impax and immediately raised the drug's price by more than 5,000%, it was clear who suffered as a result: immunocompromised patients with toxoplasmosis, a potentially life-threatening infection (Rubin 2016). In this case, Turing Pharmaceuticals should have compensated these patients. However, given the many actors involved and the challenges in specifying the requisite counterfactuals, it will usually be difficult to identify precisely which populations were made worse off by market failures. For example, a company that reaps massive returns on a drug as a result of TRIPS might not have invented that drug if the international patent regime were different. Consequently, firms should generally fulfill their constitutive obligation to states by supporting socially valuable research projects, rather than by trying to determine exactly which populations were harmed by their actions.

To summarize, firms that fund health research have constitutive obligations to their shareholders, and so should fund health research that will be profitable. However, they should not take advantage of market failures in order to maximize profits. When a firm has taken advantage of market failures, its employees should ideally prioritize research that will benefit populations that suffered as a result. If research funders within the firm are unable to determine which populations were made worse off, they should fulfill their constitutive obligations to the state by instead pushing the firm to fund more socially valuable research.

OBJECTION: WHY MAXIMIZE SOCIAL VALUE

Our argument has implicitly assumed that, except insofar as other duties apply, research funders should support the most socially valuable projects. One might object that this is too strict. Provided that a project has some social value and is not expected to be harmful, why shouldn't funders have discretion to support whichever projects they choose?

We reject this contention as it applies to states. Governments have limited discretion in the use of their resources because they acquire these resources through taxation. A government can only legitimately redistribute resources in this way when it does so in accordance with principles of justice. Research funding is no different from other allocations of resources in this regard: Except as other moral constraints apply, the ultimate aim should be a balance between maximizing benefits and improving the situation of those who are disadvantaged. Thus, in the case of health research, public funders of health research should aim to maximize the social value of that research. In some cases, a government's duties of justice might be trumped by special obligations—for instance, to a particular population the government has harmed. But these special obligations are simply overlaid upon a government's baseline obligation to pursue the most socially valuable projects. The discretion of multilateral organizations is similarly limited by the fact that they are almost exclusively funded by states (and thus indirectly by taxpayers).

Because nonstate actors do not acquire their resources through taxation, they are entitled to more discretion in deciding how to allocate health research resources. This discretion is nonetheless limited for two reasons. As previously discussed, governments support NPOs and firms in myriad ways, including through generous tax policies and subsidized research. The obligation of states to support the most socially valuable research is thereby transferred to these other organizations, just as it is to multilateral organizations. But while multilateral organizations are largely funded by states—and therefore by taxpayers—NPOs and firms are not. We might then think that their discretion is limited only to the extent that they benefit from state support.

However, the discretion of nonstate actors is additionally constrained by the moral importance of health research, as health research is inextricably linked to several human rights. These include the rights to health care, the social determinants of health, and the benefits of scientific progress (Daniels 2001, 2008; London, Cox, and Coomans 2016). A suboptimal distribution of research resources renders an unjust distribution of these other health resources far more likely. Conversely, when research resources are used well, they can greatly improve or extend the lives of individuals who benefit from them. For this reason, nonstate actors that fund health research are not entitled to the degree of discretion they would be entitled to if they were distributing

Table 1. The duties of individual research funding organizations.

Type of funder	Constitutive obligations	Other key obligations
Government—cosmopolitan	Maximize global social value	Compensation for harms
Government—statist	Maximize local social value	Compensation for harms Global duties of assistance
Multilateral	Maximize global social value	Compensation for harms
Nonprofit organization	Maximize social value consistent with mission statement	Commitment to patient groups
For-profit organization	Conduct socially valuable research consistent with reasonable returns	Avoid taking advantage of market failures

other kinds of goods. Nonstate actors that fund health research should therefore similarly default to prioritizing socially valuable projects unless they are bound by special obligations.

CONCLUSIONS

In this article, we have analyzed which populations different research funding organizations ought to benefit. Our conclusions are summarized in Table 1. A funder intending to create an optimal distribution of research resources would maximize social value. The general duties of an individual research funding organization will also tend to favor maximizing the social value of research, but special duties may lead them to deviate from this baseline principle of allocation.

Government research funders have constitutive duties to distribute resources fairly, which are likely to be consistent with maximizing social value. The key question for them is whether they should give greater priority to the health needs of people within the state. Government research funders often also have acquired duties, and, in particular, duties of culpability to populations the state has harmed. Multilateral research funders have constitutive duties to prioritize the globally most socially valuable research, except in the rare cases when they have duties of culpability to specific populations. Nonprofit organizations are bound by their mission statements, which represent their constitutive duties to donors. In some cases, nonprofit organizations may also have duties of commitment to specific patient populations. Within these confines, nonprofit organizations' general obligations should lead them to prioritize more socially valuable research. Finally, for-profit organizations have constitutive obligations to shareholders. However, when market failures occur, firms' constitutive duties to states require that they not exploit these inefficiencies (even if doing so would benefit shareholders). When firms take advantage of market failures, they acquire a duty to support socially valuable research to help rectify the social injustice they are taking advantage of.

Individuals working within research funding organizations should consider which populations their organizations have duties to, and should strive to create greater alignment between these duties and their organizations' research funding agendas.

The gap between what health research is needed and what research is funded remains a pressing problem in global health. In order to create greater alignment between global health needs and the research funding agenda, we must be clear on the obligations of research funders to populations that might benefit from research. This article lays the groundwork for considering what role different types of research funders should play in redressing research funding disparities.

DISCLOSURE STATEMENT

The views expressed are the authors' own. They do not represent the position or policy of the National Institutes of Health, the U.S. Public Health Service, or the Department of Health and Human Services. ■

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