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Health Research Priority Setting: Do Grant Review Processes Reflect Ethical Principles?

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ABSTRACT

Most public and non-profit organisations that fund health research provide the majority of their funding in the form of grants. The calls for grant applications are often untargeted, such that a wide variety of applications may compete for the same funding. The grant review process therefore plays a critical role in determining how limited research resources are allocated. Despite this, little attention has been paid to whether grant review criteria align with widely endorsed ethical criteria for allocating health research resources. Here, we analyse the criteria and processes that ten of the largest public and non-profit research funders use to choose between competing grant applications. Our data suggest that research funders rarely instruct reviewers to consider disease burden or to prioritise research for sicker or more disadvantaged populations, and typically only include scientists in the review processes. This is liable to undermine efforts to link research funding to health needs.

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Introduction

Most health research funding organisations ('funders') support only a small fraction of researchers who apply to them (Lauer, 2021; The Wellcome Trust, 2020). As a result, funding decisions often determine which health research is pursued. It is therefore critical that funders identify and support the most valuable research. However, researchers, clinicians, and activists have long criticised the health research agenda for failing to reflect the global disease burden (Røttingen et al., 2013; von Philipsborn et al., 2015). While the 'neglected diseases' that disproportionately affect people in low- and middle-income countries (LMICs) contribute 13.5 percent of global disability-adjusted life-years (DALYs) they received substantially less than 2 percent of global research funding in 2018 (Chapman et al., 2019; GBD Collaborators, 2018). In the United States, private and public research funders spend \$10,592 annually per patient with cystic fibrosis, a disease that primarily affects white patients, but only \$943 per patient with sickle cell disease, which disproportionately affects Black patients (Farooq et al., 2020). Last summer, the #ShutDownSTEM movement drew attention to racial disparities in research funding and called for research funders to reevaluate funding criteria and the processes used to make funding decisions (Kamai et al., 2020). Because funders are primary drivers of the health research agenda, they have a responsibility to remediate these disparities and to ensure their funding processes reflect ethical criteria for allocating limited resources.

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Most large public and non-profit funders provide the majority of their funding in the form of grants (Viergever & Hendriks, 2016). Grant applications are scored by reviewers, and funders rely heavily on these evaluations in making funding decisions. A minority of grant applications receive funding, and so the grant review process plays a critical role in determining how a funder's limited resources are allocated.

Often, calls for grant applications are relatively 'untargeted,' in that researchers working across a variety of topics and disciplines are eligible to apply for a given grant. For example, more than 75 percent of the new research grants funded by the U.S. National Institutes of Health (NIH) in 2017 were 'investigator-initiated,' i.e. grants that were not earmarked for a particular type of research (NIH, 2019). Within the mandate of the NIH or the broad topic areas of each NIH institute (e.g. cancer, mental health), these grants are largely funded on the basis of how they are scored during the review process. As a result, the criteria used to score these applications substantially affect how research funds are allocated across different methodologies, investigators, diseases, patient populations, and potential interventions. For example, one grant application might aim to investigate biomarkers for earlier detection of ovarian cancer. Another might propose a clinical trial testing an immunotherapy in patients with Kaposi's sarcoma. For funders that support investigator-initiated cancer research, which, if either, of these applications received funding would depend on how they were scored during review.

Though the question of which patient populations might benefit from research clearly has ethical dimensions, little attention has been paid to whether grant review processes adhere to ethical principles for research priority setting. To address this question, we analysed the criteria and processes that ten large government and non-profit funders use to evaluate grant applications. We compared the funders' criteria and processes to widely endorsed principles for research priority setting.

Methods

We selected the health research funders we would evaluate by reviewing healthresearchfunders.org (Viergever, 2014)—which lists public and philanthropic health research funding organisations—and identifying the ten largest funders that provide some of their funding in the form of untargeted extramural grants (Table 1).

Eight of these organisations are government-run and represent seven countries, while two are private philanthropic organisations. These ten organisations funded approximately 15 percent of all health research in 2013 and accounted for 40 percent of the health research dollars spent by public and philanthropic organisations (Röttingen et al., 2013). For the largest eight of the ten organisations we analysed—NIH, European Commission (EC), U.K.'s Medical Research Council (UKMRC), US Department of Defense (DoD), Wellcome Trust, Canadian Institutes of Health Research (CIHR), Australia's National Health and Medical Research Council (NHMRC), and Deutsche Forschungsgemeinschaft (DFG)—the breakdown of funding between targeted and

Table 1. The Ten Largest Health Research Funders That Provide Funding Through Untargeted Grants.

Funder	Country	Annual research expenditures (millions of 2013 US dollars)	Type of Funder
National Institutes of Health (NIH)	USA	26,081.3	Public
European Commission (EC)	EU	3,717.7	Public
Medical Research Council (UKMRC)	GBR	1,321.5	Public
U.S. Department of Defense (DoD)	USA	1,017.7	Public
Wellcome Trust (WT)	GBR	909.1	Philanthropic
Canadian Institutes of Health Research (CIHR)	CAN	883.6	Public
National Health & Medical Research Council (NHMRC)	AUS	777.6	Public
Deutsche Forschungsgemeinschaft (DFG)	DEU	630.6	Public
National Natural Science Foundation of China (NSFC)	CHN	621.3	Public
Cancer Research UK (CRUK)	GBR	548.7	Philanthropic

untargeted grants is available. Four (NIH, Wellcome Trust, CIHR, NHMRC) provide extramural funding that is largely untargeted, three (EC, UKMRC, and DFG) rely substantially on both untargeted and targeted funding, and one (DoD) has a ‘smaller untargeted funding stream’ (Viergever & Hendriks, 2016). The breakdown of funding is not available for the National Natural Science Foundation of China (NSFC) and Cancer Research U.K. (CRUK), but they make clear on their websites that they largely fund investigator-initiated (i.e. untargeted) grants. While it is possible there are research funding organisations that provide more untargeted funding than DoD, NSFC, or CRUK, our analysis nonetheless provides insight into the criteria and processes used to prioritise a substantial portion of all untargeted funding.

We reviewed each funder’s website and downloaded the publicly available documents and web pages describing their missions and review processes, including guidance provided to reviewers.¹ We then reached out twice via email or online submission form to representatives at each funder to ascertain whether we had identified all of the relevant documents. We also inquired as to whether there are other documents or information the funders provide to reviewers that are not publicly available. DFG and NSFC primarily conduct business in German and Chinese respectively. We corresponded with English-speaking individuals at these organisations, who helped confirm that we had identified the relevant documents and provided versions of these documents in English. We used Google Translate to analyse a set of additional documents provided by an NSFC representative who also confirmed the general review criteria used for NSFC’s untargeted funding.

Separately, we reviewed four documents that describe the most commonly used systematic approaches for setting research priorities (Ghaffar et al., 2009; Montorzi et al., 2010; Okello et al., 2000; Rudan et al., 2006). To select these documents, we relied on an influential paper that used a literature review and expert interviews to identify four ‘commonly used comprehensive approaches’ to health research priority setting (Viergever et al., 2010). Each document suggests ethical principles for research priority setting, including substantive criteria upon which projects should be evaluated (e.g. magnitude of the health problem addressed by research) and principles pertaining to the process for selecting research projects (e.g. inclusion of relevant stakeholders). Based on the principles proposed in these documents, we developed a checklist for evaluating funders’ review criteria and processes (Table 2). We first listed every criterion from each of the four priority setting documents we reviewed. We each then individually classified related criteria (e.g. ‘Prevalence’ and ‘Urgency’) under broader headings (e.g. ‘Magnitude of the health problem’). We then conferred to remove duplicate criteria and reach consensus on the checklist. Finally, we supplemented the checklist with well-established procedural principles from the most commonly cited procedural approach to health *care* priority setting (Daniels, 2000; Gruskin & Daniels, 2008). A fair process for allocating health resources should be transparent, include a mechanism for appealing decisions, and include relevant stakeholders and experts (Daniels, 2004). We subsequently sought feedback on this checklist from a group of eight researchers, physicians, and ethicists who were familiar with health research and priority-setting to establish that it did not omit essential ethical considerations.

We then individually evaluated each funder’s documents against this checklist. We independently assessed whether each checklist item was considered, where it was considered (e.g. in a mission statement or in instructions provided to reviewers), and the specific language used to describe each item. We then re-analysed any discrepancies in results.

Results

Substantive criteria

Magnitude: It is widely agreed in the priority-setting documents that the magnitude of a health problem in a population is relevant to how important it is to fund research into that problem. This may be justified on the basis of the expected benefits to the population from successful research projects. Reviewers can assess the magnitude of a health problem by considering the number of people

Table 2. Research Priority Setting Checklist.

Criterion (General)	Criterion (Specific)
<i>Substantive Criteria</i>	
Magnitude of health problem	Prevalence: Are reviewers instructed to consider the number of people affected by a disease? Severity: Are reviewers instructed to consider whether there are greater potential benefits associated with researching diseases that are worse for patients—that is, how bad a disease typically is for a given patient? Economic and social costs: Are reviewers instructed to consider the non-health burdens a disease imposes on patients, their families, communities, and society at large? Urgency: Are reviewers instructed to consider how important it is that the research proposal be funded <i>now</i> , e.g. because of future projected disease prevalence or demographic changes? Other: Are reviewers instructed (in any other way) to consider the size of the health problem the research proposal would address?
Equity	Medical disadvantage: Are reviewers instructed to consider whether the research will benefit sicker patients? Social disadvantage: Are reviewers instructed to consider whether the research will benefit patients who are socially disadvantaged, for example, the medically underserved, people with low socio-economic status, and otherwise marginalised groups? Priority for users: Are reviewers instructed to consider whether the research is considered a priority by potential beneficiaries, e.g. patients with the condition being researched?
Likelihood of meeting scientific aims	Scientific merit: Are reviewers instructed to consider the scientific merit of the research proposal? Quality of investigators: Are reviewers instructed to consider the credentials of the researchers sponsoring the proposal? Quality of institutions: Are reviewers instructed to consider whether the institution where the research would be conducted is well equipped to host the proposed research? Likely adoption: Are reviewers instructed to consider whether the research findings are likely to be translated into practice or policy?
Cost of proposed research Other benefits or harms	Cost: Are reviewers instructed to consider the cost of the proposed research? Social and economic effects: Are reviewers instructed to consider other social or economic benefits or harms that might result from the research (e.g. training of young investigators; economic growth associated with developing a new technology; harmful uses of potential research findings)? Innovation: Are reviewers instructed to consider whether a project is original or innovative?
Standing	Target populations identified: Does the funder identify particular populations with special standing, such as co-nationals?
<i>Process Criteria</i>	
Publicity	Criteria: Are the organisation's review criteria publicly accessible? Decisions: Does the organisation publicise which researchers and research projects it funds? Rationales: Does the organisation provide substantive feedback to applicants? Reviewers: Does the organisation identify some or all of the individuals responsible for reviewing applications and making funding decisions?
Inclusion	Scientists: Are scientists included in the review process? Patients: Are patients included in the review process? Community members: Are other lay representatives included in the review process?
Revisability	Revisability: Is there a process for appealing funding decisions?

affected by a disease, how bad a disease typically is for an individual patient, the additional burden a disease imposes on patients, their families, communities, and society, and whether there is an urgent need to fund a given kind of research (e.g. in the case of a pandemic). None of the funders consider the magnitude of the health problem addressed by the research in terms of prevalence, urgency, or economic and social costs (Table 3). Indeed, NHMRC explicitly instructs reviewers to disregard prevalence, stating ‘The significance of the study is not a measure of the prevalence/incidence of the health issue (e.g. cancer versus sudden infant death syndrome).’ Only one funder, CRUK, appears to consider the severity of an illness—that is, how bad it is per patient—in deciding whether to prioritise a research project. They write: ‘CRUK is particularly interested in proposals addressing cancers of unmet need (i.e. brain, lung, oesophageal and pancreatic cancer).’ Several funders express interest in the magnitude of health problems in less specific ways in their mission statements. For instance, the NIH aspires to ‘enhance health, lengthen life, and reduce illness and disability.’ Six others—UKMRC, CIHR, DoD, DFG, CRUK, and NHMRC—mention the magnitude

Table 3. Review Criteria Used by Funders.

Criterion (general)	Criterion (specific)	Canadian Institutes of Health Research	Cancer Research UK	Deutsche Forschungsgemeinschaft	U.S. Department of Defense	European Commission	Medical Research Council (UK)	National Health & Medical Research Council (AUS)	National Institutes of Health (USA)	National Natural Science Foundation of China	Wellcome Trust
Magnitude of Health Problem	Prevalence	X	X	X	X	X	X	X	X	X	X
	Severity	X	✓	X	X	X	X	X	X	X	X
	Economic and social costs	X	X	X	X	X	X	X	X	X	X
Equity	Urgency	X	X	X	X	X	X	X	X	X	X
	Other	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Medical disadvantage	X	✓	X	X	X	X	X	X	X	X
Likelihood of Meeting Scientific Aims	Social disadvantage	✓	X	X	X	X	X	✓	X	X	X
	Priority for users	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Scientific merit	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Cost	Investigators	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Institutions	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Likely adoption	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Other benefits or harms	Cost	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Social and economic effects	✓	X	✓	X	✓	✓	✓	✓	✓	✓
	Innovation	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Standing	Target populations identified	✓	✓	X	✓	X	✓	✓	X	✓	X
	Criteria	✓	✓	✓	✓	✓	✓	✓	✓	✓	X
	Decisions made public?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Publicity	Rationales shared with applicants?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Reviewer identities public?	✓	✓	✓	X	✓	X	✓	✓	X	✓
	Scientists	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Inclusion	Patients	✓	✓	X	✓	X	✓	X	✓	X	X

(Continued)

Table 3. Continued.

Criterion (general)	Canadian Institutes of Health Research	Cancer Research UK	Deutsche Forschungsgemeinschaft	U.S. Department of Defense	European Commission	Medical Research Council (UK)	National Health & Medical Research Council (AUS)	National Institutes of Health (USA)	National Natural Science Foundation of China	Wellcome Trust
Community members	✓	✓	✗	✓	✗	✗	✗	✗	✗	✗
Revisability	✗	✗	✗	✓	✓	✗	✗	✓	✓	✗

of health problems in their review criteria in non-specific ways. For instance, the UKMRC asks reviewers to assess the proposed research's potential 'contribution to relieving disease/disability burden and/or improving quality of life.' However, these criteria are vague, and funders do not appear to provide other guidance to reviewers on *how* to assess the magnitude of the health problem addressed by a given research project.

Equity: Reviewers can assess whether a research proposal will promote equity by considering whether the research will benefit sicker patients, will benefit patients who are more socially disadvantaged, or is a priority for a given patient population. Only CRUK explicitly prioritises research for sicker patient populations, or those with more lethal diseases, in their review criteria. CIHR and NHMRC are the only funders that prioritise research for socially disadvantaged populations, and they do so only for a subset of research funding applications—those that aim to benefit indigenous populations. The other funders do not encourage reviewers to prioritise research likely to benefit disadvantaged groups. Research that is a 'priority for users' is research that is desired by the patient populations likely to benefit from the research. Four funders—CRUK, DFG, DoD, and NHMRC—ask reviewers to consider whether the proposed research is a priority for users. Funders assess this consideration in different ways. For instance, in the criteria NHMRC uses to assess research for indigenous populations, they instruct reviewers to assess whether 'The proposal and potential outcomes address a need that is of urgent priority for Aboriginal and Torres Strait Islander communities.' Meanwhile, DFG evaluates this consideration less directly in criteria for clinical trial proposals, instead asking 'Is the effect size of the experimental intervention ... of significant clinical relevance for the patient?'

Likelihood of meeting scientific aims: A project that meets its scientific aims is not necessarily one that produces positive results, but one that achieves study objectives within the proposed time frame and budget. By assessing whether a project is likely to meet its scientific aims, funders may be better able to determine which projects will be more impactful. Every funder assesses whether the proposed research is likely to meet its scientific aims. To this end, each considers the scientific merit of the proposal, the quality of the investigators, and the resources available at the host institution. Moreover, funders typically provide reviewers with explicit and concrete instructions for assessing whether the proposed research will meet its scientific aims. For instance, EC asks reviewers to assess scientific merit by considering the 'Soundness of the concept, and credibility of the proposed methodology,' while the DoD instructs reviewers to evaluate 'The applicant's capabilities, related experience, facilities, techniques, or unique combinations of these.'

Every funder additionally evaluates whether a proposed research project is original and likely to generate changes in policy or practice. Funders also assess the likelihood of adoption in different ways. For instance, CIHR instructs reviewers to evaluate specific factors that might enhance translation of the proposed research, like the knowledge dissemination plan, while the Wellcome Trust more generally evaluates 'the likelihood of the outcomes leading to important and transforming discoveries.'

Cost: By assessing the cost of a research proposal and whether proposed costs are reasonable, funders may be able to achieve more of their ultimate aims with their limited resources. To this end, funders often ask reviewers to evaluate budget proposals to determine whether a research proposal's projected expenses are justifiable. Although each funder considers cost, they account for it in different ways. For instance, the EC states that 'proposals with a significantly inflated budget, taking into account cost efficiency considerations, will receive a lower score and may not pass the threshold,' while the DoD asks reviewers to consider 'How much will [the research] cost, and how long will it take?' without describing how this consideration affects a proposal's likelihood of receiving funding.

Other benefits or harms: Eight funders favour research that will generate benefits aside from the health benefits produced by the research results. The Wellcome Trust highlights research capacity building through training of 'high-calibre researchers.' The other seven funders all mention economic considerations. Typically, though, reviewers are not explicitly instructed to consider these

benefits in reviewing grant applications. For instance, the NIH's mission statement makes reference to research enhancing 'the Nation's economic well-being,' and part of the NSFC's mission is 'developing international cooperation and promoting socioeconomic development,' but neither funder includes these considerations among the list of criteria provided to reviewers. The exception is the UKMRC, which, under its 'Impact' criterion, asks reviewers to consider 'What is the potential economic and societal impact of the proposed research?' Most funders also explicitly mention 'innovation' as a consideration, which is plausibly valued because of its longer-term prospects of advancing science (Charlton & Rid, 2019). For instance, the NIH asks 'Does the application challenge and seek to shift current research or clinical practice paradigms by utilising novel theoretical concepts, approaches or methodologies, instrumentation, or interventions?' while NSFC simply asks 'Is the research innovative?'

Standing: The population that has standing is the population whose benefits (and costs) should be considered when making allocation decisions. Four funders identify specific target populations they hope to help in their mission statements or review documents: the NHMRC and CIHR aim to promote the health of Australians and Canadians, respectively; CRUK aspires to benefit individuals who have or may develop cancer; and the DoD directs its research towards members of the U.S. Armed Forces, their families, and veterans. Some funders, such as the EC, do not identify a specific population they hope to assist, but instead aim to promote 'better health for all,' while other funders are silent on this issue.

Process criteria

Publicity: Review processes are more public when the criteria used to make decisions, people involved in making decisions, rationales for decisions, and outcomes of decisions (including both which projects and researchers are funded) are publicised. Almost all funders publish information about the criteria they use to make funding decisions and the projects they fund (Table 3). Funders also typically share information about the review process with applicants. For instance, the NIH provides individual criteria scores and critiques from reviewers to principal investigators, and the DFG may forward comments made during the review process. Although applicants are typically not told which individuals reviewed their application, most funders publish a list of review committee members or leaders.

Inclusion: Review processes are more inclusive when experts and stakeholders, including both patients and appropriate community members, are included in the review process. Most funders do not elaborate on their process for choosing reviewers, but instead state that they invite scientists with relevant expertise to review grant applications. CIHR and CRUK additionally include patients in their review processes. These two funders and the DoD also invite other non-scientists—including policy makers, industry representatives, and clinicians—to participate in their review processes.

Revisability: Review processes are revisable when there is a process for appealing funding decisions. Four funders—DoD, EC, NIH, and NSFC—describe or allude to such a process, while the other funders are either silent on this issue or encourage applicants to apply for other grants instead. Several funders provide applicants with an opportunity to respond to reviewer comments during the review process or revise their applications in accordance with reviewer feedback. For instance, UKMRC states that 'In most cases, those applicants that pass through triage will have the opportunity to respond to all of the reviewers' comments before the board or panel meeting.'

Discussion

Funders go to great lengths to ensure they fund only high-quality science. To this end, funders provide reviewers with specific, concrete criteria for evaluating the scientific merit of grant applications, the qualifications of applicants, and the suitability of the host institution, as well as including reviewers with relevant scientific expertise. Funders also aim to support research that

will ultimately improve health. For this reason, reviewers are asked to assess whether proposed research projects are likely to be disseminated and translated into practice.

However, our data suggest that in their investigator-initiated grant review processes, most funders do not instruct reviewers to consider the magnitude of the health problems the research might address in specific, objective ways. For instance, while six funders instruct reviewers to favourably evaluate research that, as NHMRC puts it, ‘addresses an issue of great importance to human health,’ funders typically allow reviewers to exercise discretion in determining which issues are of great importance.

The fact that review criteria typically allude to disease burden—albeit in vague terms—suggests funders aim to support research addressing more significant health issues and believe reviewers ought to play a role in assessing this. Insofar as this is their aim, funders might increase the association between research funding and disease burden by having reviewers utilise whatever specific, objective criteria funders believe are important for assessing disease burden, e.g. DALYs or years of potential life lost (YPLLs). Relying on objective criteria for assessing the magnitude of health problems could help reviewers avoid inadvertently favouring research for particular diseases (for instance, those that are more prevalent in reviewers’ communities).

Funders could also ask applicants to explain the significance of the health problem their research aims to address in objective terms that allow comparison across applications—for instance, by describing its prevalence and severity. Investigators studying rare diseases might be invited to explain the implications their research could have for other patient populations. Researchers studying less severe illnesses (e.g. the common cold) might be asked to explain the broader social or economic benefits research might yield (e.g. increased economic productivity due to fewer days of missed work). Notably, some research funding organisations already invite applicants to comment on the importance of their proposed research; for instance, the NIH requires researchers to submit statements describing a given research project’s public health relevance. However, while these statements are ultimately made public after funding decisions have been made, they are not evaluated by reviewers during the grant review process. Giving reviewers the opportunity to review these statements would be a first step towards evaluating the magnitude of the health problem addressed by a research proposal.

It is possible that funders account for disease burden at a different stage in the funding process—for instance, by requiring projects for less severe ailments to attain higher scores from reviewers in order to receive funding—but we saw few examples of this in the documents we reviewed. For instance, the NIH’s National Cancer Institute writes: ‘NCI pays most grants according to merit (i.e. based on the percentile ranking and/or priority score, depending on the type of grant) as assessed by peer review. However, for high-priority areas, NCI funds some applications outside the payline through exception funding.’

Funders might also use targeted grants, rather than untargeted grants, to bring their overall funding into greater alignment with disease burden or to account for other ethical considerations deemphasized by the untargeted grant criteria. Several organisations that fund global health research, such as the Bill and Melinda Gates Foundation, only provide funding in the form of targeted grants. However, among the materials we reviewed, we found no evidence that the organisations in our study—which primarily support investigator-initiated research—use targeted grants in a systematic way to compensate for the possible misallocation of their untargeted grant funds. In addition, analyses of funding allocations at specific organisations suggest that they correlate only moderately with disease burden, and funding does not fluctuate with changes in disease burden (Gillum et al., 2011; Xu et al., 2014).

Relatedly, most funders do not ask reviewers to assess how disadvantaged—medically or socially—the potential beneficiaries of a research project are. Just as the NHMRC review criteria for indigenous populations ask whether a research project will benefit Aboriginal and Torres Strait Islander peoples, funders might more generally ask reviewers to evaluate whether a proposal is likely to benefit sicker or more socially disadvantaged populations.

A few governments and non-profit funders have made efforts to redress research funding disparities by prioritising health research for disadvantaged populations at the organisational level. For instance, at its inception, CIHR created the Institute of Aboriginal Peoples' Health (now Institute of Indigenous People's Health) to focus on supporting health research for indigenous communities in Canada. However, there are multiple decision points at which allocation choices are made and which therefore present opportunities to improve the distribution of research funds without wholesale reorganisation.

In order to prioritise health research for disadvantaged groups, reviewers must be able to identify the populations likely to benefit from successful projects. One might be skeptical about whether this is possible, particularly for pre-clinical research. However, likely beneficiaries are currently identified in many grant applications.² Moreover, predictions about whether research is likely to affect policy and practice—which funders typically *do* assess—presuppose answers to the question of who is likely to benefit. Insofar as the existing criteria used to judge likelihood of meeting scientific aims are warranted, it should be no more difficult for researchers and reviewers to predict whether disadvantaged populations are likely to benefit from a successful research project.

Funders could also ensure that research is more responsive to societal needs by simply identifying the populations they aim to help and evaluating whether research proposals are a priority for these populations. Relatedly, provided that the research fits their broad criteria for relevance—e.g. cancer research—few funders give specific guidance to reviewers about which populations they hope to benefit through the research they support. This lack of guidance could confuse reviewers as to whom they should be prioritising research for.

Some funders who do identify the populations they aim to benefit make debatable decisions about whom to assist. For instance, NHMRC's mission, 'Working to build a healthy Australia,' makes clear that they support projects likely to benefit Australians, while CIHR aims to improve 'health for Canadians.' While we do not have space here to provide a thorough argument for funding research that benefits the global disadvantaged, we note that there are both ethical and practical reasons to believe that only supporting research for co-nationals is misguided, even for taxpayer-funded organisations (Pierson & Millum, 2018). Millions of people in LMICs die annually from illnesses like Chagas disease, tuberculosis, and malaria that have historically received less attention from research funders and continue to be underfunded (Chapman et al., 2019; Tarleton et al., 2014). Moreover, as the ongoing COVID-19 pandemic has shown, in our globalised world a disease in one nation can threaten the health of people worldwide, jeopardise the security of other nations, and lead to significant economic losses (Hutchinson et al., 2006; Letendre et al., 2010). There is therefore good reason to believe it would be both more ethical and more prudent for funders to support research likely to benefit people more widely, and, in particular, to prioritise research for patient populations that have historically been neglected by the research enterprise.

The processes funders use to review grant applications vary greatly. Some publicise nearly all aspects of their review processes—from the criteria they use to the reviewers responsible for scoring applications—while others disclose few features of their processes. Similarly, some funders offer ample opportunities for revising applications or funding decisions, while others do not. Some of these differences may be justified. For instance, there may be good reason to prohibit appealing funding decisions when other funding opportunities are readily available or applications are accepted every year, and an appeals process could reduce the efficiency of reviews.

Other differences in review processes seem less justifiable. For instance, there is little reason for funders to keep private the criteria they use to evaluate applications. Publicising review criteria would enable scientists and the public to better understand how grant applications are evaluated. It could also enable funders to learn from each others' review processes.

Finally, our data suggest that funders overwhelmingly rely on scientists to review grant applications. Unsurprisingly, when only scientists are included in review processes, they evaluate what they know best—in particular, whether the proposed project is scientifically valid and the investigators leading it have the relevant expertise to do so. Inviting individuals with diverse

perspectives—including clinicians, patients, public health practitioners, policymakers, and other stakeholders—might help research funders assess other important considerations, including the research priorities of potential beneficiaries.

Limitations

This analysis was limited by our ability to access relevant documents. Although we reviewed the funders' websites and reached out to representatives at each to ensure we had evaluated all relevant documents, it is possible that reviewers are provided with evaluation materials to which we did not have access.

Many of the funders we analysed—such as CIHR, NSFC, and NIH—are comprised of multiple smaller entities. These entities may have additional review criteria (for instance, that pertain to a distinct mission or to a particular patient population) or separate review processes. We did not evaluate documents from sub-entities within the larger funders, and therefore cannot speak to additional criteria or processes they may employ.

There are also limits to the judgements we can render regarding even the ten funders included in our analysis. It is possible that some funders account for important priority setting principles at other stages. For instance, some funders direct targeted funding to disadvantaged populations when setting priorities for the organisation as a whole. Because we have analysed only one decision point at which funding decisions are made, we cannot conclude that the overall distribution of research resources by these funders is not justifiable. However, prior research has shown that the scoring of grant applications is a critical step at which funding disparities arise. For instance, NIH grant applications written by Black scientists receive lower impact scores and are less likely to be discussed by reviewers, even after controlling for the applicant's training, country of origin, employer characteristics, and prior scientific success (Hoppe et al., 2019). This disparity is explained in part by differences in topic choice, with Black researchers more frequently applying for funding to study health disparities and patient-focused interventions, topics that are funded at lower rates. Other decision points—for instance, institute directors' final decisions regarding grant funding—neither compounded nor redressed funding disparities between Black and white scientists. These findings suggest that the scoring of grant applications is an especially important decision point and that modifying grant review criteria could therefore reduce funding disparities.

Finally, our goal was to assess the extent to which funders adhere to widely established research priority setting criteria. However, the process of creating a checklist necessitated making empirical and normative judgments in defining, categorising, and consolidating criteria. Some empirical assumptions may be mistaken, e.g. that investing in more severe diseases produces greater benefits on average. Some criteria may not be normatively justifiable for research priority-setting, as discussed above. For these reasons, we encourage other researchers to pursue additional empirical and normative work assessing the processes funders use to allocate limited research resources.

Conclusion

The grant review stage is an important decision point for the allocation of scarce research resources, particularly for untargeted grants. Our data suggest that the largest public and philanthropic research funders do not explicitly take several important considerations into account in reviewing grant applications. In particular, few funders explicitly instruct reviewers to consider the magnitude of the health problem a research project addresses nor which populations will benefit. As a result, it is unlikely that reviewers systematically consider them. This is liable to undermine efforts to link research funding to health needs.

Several changes to the review processes could align them better with the ethical principles we identified. When making grant funding decisions, research funders could encourage reviewers to consider which populations are likely to benefit from research. Data relevant to the prevalence,

severity, and other measures of the magnitude of disease burden, as well as the situation of potential beneficiaries could be used in scoring grant applications. Relatedly, reviewers could be instructed to evaluate whether the proposed research is a priority for the relevant patient populations. Funders should consider inviting non-scientists—including patients, clinicians, and policy makers—to participate in their review processes and train these individuals to assess grant applications.

If major research funders took steps to bring grant review criteria into greater alignment with the global burden of disease, patients' research priorities, and the other ethical considerations this analysis highlights, it could have positive and far-reaching implications. Researchers, who select specific research topics in large part on the basis of funding opportunities, would likely respond to these changes by directing their research toward more pressing health problems and more disadvantaged populations. They would similarly make a greater effort to assess and respond to patients' health needs. At a minimum, investigators would need to address these criteria in writing grant applications and would thus be incentivized to consider how their research could be designed to benefit larger, sicker, or more socially disadvantaged patient populations.

Notes

1. Supplementary Table 1 lists the relevant documents.
2. To verify this, we reviewed 100 successful NIH grant applications from NIH's ten top-funded institutes. Of these, 88 specified a population the research was most likely to benefit (Supplementary Table 2).

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Disclaimer

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