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Danielle M. Wenner [a]
[a] Cleveland Clinic

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Discharging the Duty to Conduct International Clinical Research

Danielle M. Wenner, Cleveland Clinic

Pratt, Zion, and Loff (2012) correctly point out that most international clinical research (ICR) is not intended to address the vast inequities in access to health care between developed and developing populations. Given that such inequities exist, however, they ask whether there might be a moral obligation to conduct ICR in low- and middle-income countries (LMICs) grounded in duties of global justice.

Pratt and colleagues' approach is novel, insofar as they examine theories of justice operating at a broad, institutional level and attempt to apply them to specific questions regarding the conduct of ICR in LMIC settings. However, their analysis would benefit greatly from the recognition of three important distinctions. Explicit acknowledgment of these distinctions highlights how and where broad theories of justice can inform our thinking about the conduct of ICR, and where such analysis is problematic.

First, we should distinguish between:

(A) The duty to address global health inequities.
(B) The duty to address global health inequities *through the conduct of ICR*.

There are many ways to combat global health inequities, and the conduct of ICR is but one of them. Theories of justice in distribution such as Rawls's procedural account (1971) or its extension to the field of health care by Daniels (2008) may speak to duty (A) while nevertheless remaining silent with regard to the prescription contained in (B). For instance, it may be the case that there is a duty to address global health inequities, but that this duty could be discharged through the development of local infrastructure or the subsidization of interventions already available in wealthier markets. Procedural theories of justice such as these leave the determination of the best means of discharging this duty to deliberative processes. Similarly, a human rights framework such as Shue's (1996), which prescribes a mediating duty to aid those deprived of basic health care through institutional measures, may ground a duty to address global health inequities but fail to specify (B), given other, more direct options. These examples highlight that the theoretical bases for duty (A) often operate at the level of the basic institutional structure, and therefore may not provide helpful tools for assessing the legitimacy of claims regarding duty (B).

It is also important to distinguish between:

(B) The duty to address global health inequities through the conduct of ICR.
(C) The duty to address global health inequities through the conduct of ICR *of a certain type (or types)*.

(B) expresses a much laxer moral requirement than (C), and if we accept the claim that there is any type of ICR the conduct of which is morally impermissible, then it must be the case that any duty to conduct ICR (if such a duty exists) is of the form (C). This is because (B) *simpliciter* would generate a moral duty, the fulfillment of which could be accomplished through the conduct of a morally impermissible action.

Thus, we require some means of determining what kinds of research it is *permissible* to conduct in LMIC settings. And further, we need a way to determine, if there is a duty to conduct ICR as a means of addressing global health inequities, whether that duty can be discharged by

Address correspondence to Danielle M. Wenner, Cleveland Clinic, Department of Bioethics, 9500 Euclid Ave., JJ60, Cleveland, OH 44195, USA. E-mail: wennerd2@ccf.org

conducting any permissible type of ICR, or if the duty to conduct ICR is more specific. I return to these questions shortly, but I want first to introduce the third distinction bearing on the strength of Pratt and colleagues' analysis, which is that between:

(C) The duty to address global health inequities through the conduct of ICR of a certain type (or types).
(D) The duty to conduct ICR *in a certain way.*

This last distinction highlights the difference between the macro-level question of how to fulfill our duties of global justice (C) and the micro-level question of how to ensure that any ICR which is conducted is just in its own right (D). (D) governs individual interactions between identifiable actors (persons or institutions), regardless of whether those interactions are motivated by the duty to address global health inequities. It is unsurprising, then, that a theory such as Daniels's Accountability for Reasonableness or the cosmopolitanism of Pogge or Shue will not have much to say about the justice of such transactions, beyond perhaps the general caveat that such transactions should take place with respect for the basic rights of all involved and should not involve fraud, coercion, or force. Further specifications of the principles governing the just conduct of ICR are necessary before individual cases can be evaluated with regard to (D), and such specification is unlikely to find its root in broad political theory governing justice in distribution.

ICR AND SOCIALLY VALUABLE KNOWLEDGE

If there is a duty to address global health inequities through the conduct of ICR, then it must be the case that this duty is further specified as a duty to conduct ICR of a certain type (or types) (C). A full picture of the permissibility of ICR requires understanding consent, coercion, exploitation, and other concepts that might impinge upon the moral validity of a research endeavor (Wertheimer 2011). That permissibility is also impacted, however, by the nature of the research endeavor itself.

The justification for subjecting human subjects to risk of harm resides in the social value of the knowledge gained during the research enterprise: "The goal of biomedical research—promoting socially valuable knowledge about health, disease, and treatment—is ethically central" (Joffe and Miller 2008, 32). This tenet is so central to the ethical conduct of research that "only if society will gain knowledge . . . can exposing human subjects to risk in clinical research be justified" (Emanuel et al. 2000, 2703). If the social value of the epistemic outputs of clinical research is essential to its moral validity, then in determining what types of ICR are permissible, we must explore the further development of the concept of socially valuable knowledge.

But in filling out (C), we are also interested in whether any or all of those permissible forms of ICR are sufficient to discharge duties to address global health inequities. To take this additional step, we must ask not only how to avoid harming the LMIC subjects and populations in which ICR is conducted, but moreover how ICR might benefit them. Given that the production of socially valuable knowledge is itself a benefit, additional development of this concept may be doubly valuable: first, in further specifying the limits of permissible ICR, but second, in also accounting for how the conduct of ICR is capable of discharging positive duties of justice.

To better understand the kind of benefit that socially valuable knowledge is, we should first note that it is context dependent. In order for the outputs of research to be *socially* valuable, it is necessary for those outputs to be practically applicable to the society in question. Research proving the efficaciousness of a new treatment for malaria cannot play the role of discharging a duty to address health inequities, if that new treatment is too expensive to be accessible to those we have a duty to aid. In the case of ICR conducted in LMIC settings, the social context from which research outputs are valued should reflect the population whom we are trying to benefit in discharging our duties of justice, but a more precise determination of who constitutes that "population" will require further work.

The initial account of socially valuable knowledge offered here is clearly insufficient to differentiate those types of ICR that would successfully discharge the duty to conduct ICR. A fuller understanding will ultimately provide us with greater insight into (C), if it is the case that (C) adheres. It is also at this stage of reasoning that the kind of analysis proposed by Pratt and colleagues is of greatest value. Assuming the authors have shown that at least some actors have a moral obligation to discharge duties of global justice through the conduct of ICR, the theoretical bases for the duty to address global inequity *simpliciter* should similarly help to highlight which inequities are most important to correct and in what contexts. The extension of political theory to the intersection of international research ethics and global health disparities represents an important contribution to ongoing discussions of these topics, but such an analysis must be buttressed by an explicit recognition of the analytically relevant distinctions between the kinds of questions being asked. Such recognition permits us to apply the appropriate kind of moral analysis at each level of obligation, and will ultimately generate a more coherent account of the moral duties arising as a result of global health inequity. ■

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Ethics, Justice and Community Participation in the Microbicides Development Programme (MDP) Phase III Trial in Mwanza, Tanzania

Andrew Vallely, London School of Hygiene and Tropical Medicine and National Institute for Medical Research

Shelley Lees, London School of Hygiene and Tropical Medicine and National Institute for Medical Research

Charles Shagi, African Medical and Research Foundation

Saidi Kapiga, London School of Hygiene and Tropical Medicine and National Institute for Medical Research

Sheena McCormack, Medical Research Council

Richard Hayes, London School of Hygiene and Tropical Medicine

The Microbicides Development Programme (MDP) Phase III efficacy and safety trial (MDP301) of the candidate vaginal microbicide PRO2000 (McCormack et al. 2010; Nunn et al. 2009) was a landmark study that used innovative participatory community engagement (Shagi et al. 2008; Vallely et al. 2007) and social science research strategies (Pool et al. 2010) to ensure this trial was conducted within a robust ethical and social justice framework (Heise, Shapiro, and West Slavin 2008; Vallely et al. 2009; Vallely et al. 2010). The MDP301 trial has informed the UNAIDS Good Participatory Practice (GPP) guidelines and established a benchmark for the conduct of HIV prevention trials among women and men in communities in resource-limited settings. The target article by Pratt, Zion, and Loff (2012) fails to recognize the processes and strategies adopted by MDP in the design and implementation of the MDP301 trial in Mwanza, and at other MDP sites in Africa. The authors' findings and conclusions warrant further explanation, contextualization, and reevaluation by MDP investigators who led the MDP301 trial in Mwanza.

WRONG PEOPLE, WRONG TOOL?

The authors, citing the paper by Nunn and colleagues (2009), state that the MDP301 trial was designed to meet the needs of women who are less sexually active and that "Microbicides are specifically not intended for women who engage in sex work because they are thought to make women more susceptible to HIV infection if used at a high frequency." The authors contend that "microbicides are likely to be more effective for women who are less sexually active, which limits their usefulness for sex workers. This means that the health needs of a large proportion of poor women in Tanzania will not be met by a microbicide, resulting in inequity."

These statements are inaccurate for several reasons. First, although MDP investigators were mindful about vaginal toxicity and excess HIV seroconversions in earlier microbicide trials, particularly the COL-1492 clinical trial of nonoxynol-9 conducted among commercial sex workers, they were confident that this potential risk was extremely

All authors have composed this commentary on behalf of the Microbicides Development Programme (MDP) investigators.
Address correspondence to Andrew Vallely, University of New South Wales, Kirby Institute, 45 Beach Street, Coogee, Sydney, NSW 2034, Australia. E-mail: avallely@kirby.unsw.edu.au