Journal of Health Care Law and Policy

Volume 20 | Issue 1 Article 2

Fair Benefits and Its Critics: Who is Right?

David Wendler

Seema K. Shah

FAIR BENEFITS AND ITS CRITICS: WHO IS RIGHT?

DAVID WENDLER*

SEEMA K. SHAH*

I. INTRODUCTION

Protecting participants from exploitation is one of the primary ethical challenges posed by clinical research.[1] This challenge is especially pressing for clinical trials that are conducted in lower-income countries by sponsors and investigators from higher-income countries.[2] For many commentators, the paradigmatic example of a problematic trial in this regard is one that evaluates in lower-income countries an intervention which will be marketed in higher-income countries only.[3] To address the potential for exploitation, it is widely agreed that the host communities and the individuals who participate in these trials should receive sufficient benefits.[4]

The Fair Benefits framework describes one possible way to realize this goal.[5] It argues that host communities and research participants should receive a fair level of benefits given the extent to which they contribute to the study in question and the extent to which they are thereby exposed to risks and burdens.[6]

---

1. Ezekiel J. Emanuel et al., *What Makes Clinical Research Ethical?* 283 JAMA 2701, 2701 (2000).

2. Marcia Angell, *The Ethics of Clinical Research in the Third World*, 337 NEW ENG. J. MED. 847, 848 (1997) (raising concerns about the standard of care in trials conducted in lower-income countries); Harold Varmus & David Satcher, *Ethical Complexities of Conducting Research in Developing Countries,* 337 NEW ENG. J. MED. 1003, 1003 (1997) (highlighting controversies over trials on how best to prevent maternal-infant transmission of HIV in developing countries).

3. Peter Lurie & Sidney Wolfe, *Unethical Trials of Interventions to Reduce Perinatal Transmission of Human Immunodeficiency Virus in Developing Countries*, 337 NEW ENG. J. MED. 853, 853 (1997) (discussing ethical issues about clinical trials conducted in lower-income countries to test antiretroviral drugs that, at the time, were not expected to be readily available in those countries because of cost).

4. Harold T. Shapiro & Eric M. Meslin, *Ethical Issues in the Design and Conduct of Clinical Trials in Developing Countries*, 345 NEW ENG. J. MED. 139, 139–40 (2001) (explaining that one of the ways to justify conducting clinical trials in developing countries is to address important health problems facing those countries).

5. Participants in the 2001 Conference on Ethical Aspects of Research in Developing Countries, *Fair Benefits for Research in Developing Countries,* 298 SCI. 2133, 2133–34 (2002) [hereinafter Participants 2002].

6. *Id.* at 2133.

Since it was first described in 2002, the Fair Benefits framework has been subject to a number of criticisms, leading some commentators to conclude that it should be rejected in favor of alternative approaches.[7] To assess whether this conclusion is warranted, the present manuscript describes the eight most prominent criticisms and evaluates their implications for how best to address the potential for exploitation in multinational research.

This analysis reveals that the prominent criticisms fall into three groups. First, several do not pertain to the Fair Benefits framework itself, but concern related issues that merit assessment in their own right.[8] Second, a number of the most prominent criticisms are mistaken.[9] Third, a few of the criticisms point to aspects of the Fair Benefits framework that require refinement and elaboration.[10] This third group of criticisms would support the conclusion that the Fair Benefits framework should be rejected if it is unlikely that the needed refinements can be realized, or there exists an alternative approach that does better in this regard. We argue that the nature of the needed refinements suggests future research will be able to address them. In addition, there does not exist an alternative approach which needs significantly fewer or even no refinements and addresses the potential for exploitation at least as well as the Fair Benefits framework. We conclude that the extant criticisms do not provide a reason to reject the Fair Benefits framework.[11] Instead, they point to the need for further research to refine the framework and thereby ensure appropriate protection for those who participate in clinical trials in lower-income countries.[12]

II. FAIR BENEFITS VERSUS REASONABLE AVAILABILITY

Conducting research in lower-income countries in order to develop medical treatments and interventions for higher-income countries has the potential to violate two of the fundamental ethical requirements for clinical research.[13] First, to the extent that these trials target individuals and communities in lower-income countries because they are poor and vulnerable, they violate the requirement for fair subject selection.[14] Research participants and research sites should be selected based on scientific and ethical considerations, not based on who is less able to protect themselves.[15] Second, participants and host communities in lower-

7. *Id.* at 2133; *see also* Udo Schüklenk, *Calling it a Day on Proceduralism in Bioethics?* 24 BIOETHICS ii, ii (2010).

8. *See infra* Parts III.1 & III.2.

9. *See infra* Parts III.3 & III.4.

10. *See infra* Parts III.5 to III.8.

11. *See infra* Part IV.

12. *See infra Part IV.*

13. Emanuel et al., *supra* note 1, at 2704–06.

14. *Id.* at 2704 (explaining past abuses where vulnerable participants were selected to participate in research because they were relatively easy to enroll).

15. *Id.* (pointing out that fair subject selection involves making the scientific goals of the study the basis for selecting participants, not the vulnerability of the participants).

income countries contribute to and accept the risks of these trials, while all the benefits may go to individuals in higher-income countries.[16] These trials thereby have the potential to violate the requirement for an appropriate distribution of the risks and potential benefits of clinical trials.[17] Initial proposals to protect research participants in lower-income countries tried to identify additional requirements that might address these two concerns.[18]

The "responsiveness" requirement mandates that clinical trials in lower-income countries should not be designed to address the needs or priorities of higher-income countries, at least not exclusively.[19] Instead, they should address the health needs or priorities of the communities in which they are conducted.[20] This requirement helps to ensure fair subject selection by ensuring that there is a justification for conducting a given trial in lower-income countries, namely, the trial addresses the health needs of the host communities.[21]

The "reasonable availability" requirement was developed to address the potential for an inappropriate distribution of risks and potential benefits.[22] This requirement was first emphasized in 1993 by the Council for International Organizations of Medical Sciences ("CIOMS"), and is described in their revised guidelines of 2016 as follows:

Sponsors and researchers must "make every effort, in cooperation with government and other relevant stakeholders, to make available as soon as possible any intervention or product developed, and knowledge generated, for the population or community in which the research is carried out."[23]

Although the reasonable availability requirement received widespread support,[24] it fails to ensure an appropriate risk-benefit distribution.[25] Most importantly, many clinical trials, including early phase trials, observational studies, and trials testing products which prove to be ineffective, pose risks and

16. *Id.* at 2705.

17. *Id.* at 2704.

18. Alex John London, *Responsiveness to Host Community Health Needs*, THE OXFORD TEXTBOOK OF CLINICAL RESEARCH ETHICS 737, 737 (Ezekiel J. Emanuel ET AL. eds., 2008).

19. *See id.* at 738 (describing the standard view that if research is ethically sound it must respond to the health needs or priorities of the community hosting the research).

20. *See id.*

21. *See id.*

22. *See id.* (explaining that in order to prevent participants from participating in research and not realizing any of the benefits of said research, the researchers should provide health-related benefits to the host community).

23. COUNCIL FOR INTERNATIONAL ORGANIZATIONS OF MEDICAL SCIENCES: GUIDELINES, https://cioms.ch/ (last visited Jan. 1, 2018) (stating that the current guidelines call for governments and civil societies to make any possible intervention or product developed in a community available to that community within a reasonable amount of time).

24. *See* Participants in the 2001 Conference on Ethical Aspects of Research in Developing Countries 34 HASTINGS CTR. REP. 17, 17 (2004) (explaining there is general agreement that "reasonable availability" is imperative to preventing community exploitation)[hereinafter Participants 2004].

25. *Id.* at 19.

burdens, but do not yield a successful intervention.[26] And some clinical trials fail to recruit a sufficient number of participants or fail to yield meaningful results.[27] All of these trials fail to identify successful interventions or products and fail to generate knowledge which benefits the host communities. As a result, the reasonable availability requirement fails to ensure an appropriate risk-benefit ratio in these cases.[28] Given that trials which do not recruit a sufficient number of participants or do not yield a successful intervention may well represent the majority of clinical trials, it follows that reliance on the reasonable availability requirement fails to address the potential for exploitation in lower-income countries.[29]

With these concerns in mind, the Fair Benefits framework was developed as an alternative to the reasonable availability requirement.[30] It is based on the claim that the potential for exploitation traces not to the *types* of benefits that individuals receive, but to the *level* of benefits they receive.[31] In particular, conducting research in lower-income countries raises concern that the host communities and the participants might fail to receive a fair level of benefits.[32] The Fair Benefits framework was designed to address this concern by requiring that participants and host communities in lower-income countries receive a fair level of benefits.[33]

To this end, the Fair Benefits framework endorses the responsiveness requirement, stipulating that clinical trials in lower-income countries should be responsive to their health needs.[34] Then, in place of the reasonable availability requirement, the framework endorses three conditions.[35] First, based on Alan Wertheimer's account of exploitation,[36] it stipulates that participants and host communities in lower-income countries should receive a fair level of benefits given the risks and burdens to which they are exposed, and the extent to which others benefit from their contributions to the study.[37] As participants and communities in lower-income countries are exposed to greater risks and burdens,

26. *See id.* at 20–21 (stating that the reasonable availability standard does not guarantee a benefit).

27. *See id.* at 26 (noting that many trials produce findings that are not significant or negative, and fail to demonstrate that the intervention was effective).

28. *Id.* at 18 (explaining that the potential exploitation of research participants is possible).

29. *See* Participants 2004, *supra* note 24, at 18.

30. Ezekiel J. Emanuel, *Benefits to Host Countries, in* THE OXFORD TEXTBOOK OF CLINICAL RESEARCH ETHICS 719, 725 (2008) (stating that the risk-benefit evaluation must be favorable in such a way that the potential benefits to the individual participants outweigh the risks).

31. *See* Participants 2004, *supra* note 24, at 19–20.

32. *See id.* at 18 (arguing that lower-income communities must derive potential benefit from the research they host).

33. *See id.* at 22.

34. *See id.*

35. *Id.*

36. *See id.* at 19–20 (discussing Alan Wertheimer's theory of exploitation as applied to cases where one party receives an unfair level of benefits).

37. *Id.* at 22.

they should receive a correspondingly greater level of benefits.[38] Similarly, the more others benefit from the contributions of individuals in lower-income countries, the more those individuals should benefit themselves.[39]

Second, the Fair Benefits framework endorses collaborative partnership, mandating that the benefits to be provided to participants and host communities in lower-income countries should not be determined solely by individuals from higher-income countries.[40] Instead, individuals in lower-income countries should be involved in determining what benefits they receive.[41]

Third, the Fair Benefits framework endorses a transparency requirement.[42] This requirement was based on recognition of the fact that it can be difficult to determine what level of benefits is fair in a given case.[43] To help to address this challenge, the Fair Benefits framework proposes a repository of prior trials that provided a fair level of benefits.[44] This record, which could be maintained by a reliable third party, such as the WHO, would provide a kind of case law against which new proposals could be evaluated to help to determine whether they are fair.[45]

The Fair Benefits framework was intended to provide a more flexible approach that helps to address the potential for exploitation across a broader range of trials compared to the reasonable availability requirement.[46] However, critics argue that the Fair Benefits framework suffers from a number of fundamental shortcomings which suggest that it fails to adequately address the potential for exploitation of participants and host communities in lower-income countries.[47] These critics conclude that the Fair Benefits framework should be

38. *Id.*

39. *Id.*

40. *See id.* at 23 (arguing that the population being asked to enroll should be consulted about whether the proposed benefits are sufficient and fair).

41. *Id.* at 23.

42. *See id.* (noting that transparency allows comparisons across similar interactions).

43. *Id.*

44. *Id.* at 23–24.

45. *Id.*

46. *Id.*

47. *See* Angela Ballantyne, *'Fair Benefits' Accounts of Exploitation Require a Normative Principle of Fairness: Response to Gbadegesin and Wendler, and Emanuel et al.*, 22 BIOETHICS 239, 240 (2008) (criticizing the utility of the fair benefits framework because it lacks a substantive principle of fairness, which she maintains is essential to the fair benefits account of exploitation); Reidar K. Lie, *The Fair Benefits Approach Revisited*, 40 HASTINGS CTR. REP. 3, 3 (2010) (arguing that the fair benefits approach is flawed because it is too vague, internally inconsistent, and judges individual research projects without taking into account that the goal of research is to develop knowledge that is most useful for society); *See* Alex John London, *Justice and the Human Development Approach to International Research*, 35 HASTINGS CTR. REP. 24, 24, 26, 29 (2005) (arguing that fair benefits advocates a "minimalist" approach, which does not adequately consider issues of background injustice); Alex John London & Kevin J.S. Zollman, *Research at the Auction Block: Problems for the Fair Benefits Approach to International Research*, 40 HASTINGS CTR. REP. 34, 37, 41 (2010) (criticizing that there are no specifics about how to engage in a process of collaborative partnership and that the practical result of a procedural approach to fairness is a race to the bottom); Joseph Millum, *Sharing the Benefits of Research Fairly: Two*

rejected in favor of some alternative approach that provides better protection.[48] To assess this conclusion, consider the eight most prominent criticisms.

III. CRITICISMS AND ANALYSIS

A. Fails to Consider Background Injustice

The Fair Benefits framework is based on a transaction-specific account of fairness in the sense that it is designed to help to ensure a fair distribution of the benefits and burdens of individual trials.[49] What constitutes a fair distribution in this regard depends on the risks and burdens to which participants and host communities in lower-income countries are exposed by a given trial and the extent to which others benefit from their contributions to the trial.[50]

Some critics have pointed out that this approach ignores the fact that the circumstances in which individual trials are conducted in lower-income countries often are characterized by significant background injustice.[51] Individuals in lower-income countries frequently are comparatively worse off, due at least in part to prior unjust treatment, including unjust treatment by individuals, entities and governments of higher-income countries.[52] This history is problematic in its own right, and also raises concern that sponsors and investigators may benefit

Approaches, 38 J. MED. ETHICS 219, 219, 221–22 (2012) (arguing that the lack of consensus about what constitutes a fair agreement makes the fair benefits framework impractical; whereas the responsiveness requirement gives guidance as to the content of an agreement that is non-exploitative); Udo Schüklenk, *Calling it a Day on Proceduralism in Bioethics?*, 40 HASTINGS CTR. REP. ii (2010) (noting that one of the leading experts who initially helped create the fair benefits framework had changed his mind, and also agreeing that this framework is likely to result in a "race to the bottom" that produces unfair results).

48. Ballantyne, *supra* note 47 (summarizing critics' conclusions that the Fair Benefits framework should be rejected).

49. *See* Participants 2004 *supra* note 24, at 19–20.

50. *See id*. at 20, 22 (explaining that a fair level of benefits should be proportional to the amount of risks and burdens).

51. *See* James V. Lavery et al., *'Relief of Oppression: An Organizing Principle for Researchers' Obligations to Participants in Observational Studies in the Developing World*, 10 BMC PUB. HEALTH 1,2,4,6 (June 30, 2010) (advocating 'relief of oppression' as an organizing principle to help researchers address background conditions of injustice affecting their research participants); *see also* London, *supra* note 47, at 24, 45 (arguing that the ethics of international research has not adequately addressed background social justice); *see also* Lie, *supra* note 47, at 3 (noting that the fair benefits approach ignores background conditions of injustice).

52. *See* Lie, *supra* note 47, at 3 (unjust treatment by their own authorities and international institutions often contribute to the poverty and deprivation of host country communities); *see also* London, *supra* note 47, at 24, 25, 30 (explaining that the lower-income countries are more susceptible to illnesses, abuse and exploitation due to poverty and social deprivation, that was created in part by Western democratic nations who recognize the "international resource privilege."); *see also* London & Zollman, *supra* note 47, at 35 (pointing out that populations in low-income countries bear high burdens of communicable and preventable disease due to inadequate public health systems).

from it by being able to conduct trials faster and cheaper than would have been possible absent the unjust circumstances.[53]

It is further argued that this history generates an obligation on individuals from higher-income countries to provide benefits to individuals in lower-income countries as a way of compensating them for prior injustice.[54] When sponsors and investigators from higher-income countries conduct trials in lower-income countries, it is not sufficient, as the Fair Benefits framework supposes, to compensate the participants and the host communities for the risks and burdens they face and the extent to which others benefit from their contributions.[55] Sponsors and investigators also need to discharge their obligations to address the conditions of background injustice.[56] Rather than benefitting from the (unjustly) impoverished circumstances of host communities, sponsors and investigators have an obligation to help to remediate those circumstances.[57]

The history of injustice in international relations and the impoverished circumstances of individuals and communities represent some of the most pressing ethical concerns of our time. At the same time, it is unclear how these considerations represent an objection to the Fair Benefits framework. As noted, the Fair Benefits framework is intended to ensure a fair distribution of the benefits and burdens of individual trials. It does not claim that the provision of fair benefits in this sense satisfies all the obligations that sponsors and researchers might have to participants and host communities in lower-income countries. To make this a compelling criticism, advocates would need to show how the general obligations to address conditions of injustice in the world are relevant to an ethical analysis of individual trials.[58]

The challenge here is that attempting to address existing background injustice one trial at a time seems, at best, odd and inefficient.[59] To illustrate this

53. *See* London, *supra* note 47, at 24 (explaining that lower-income countries are more susceptible to exploitation because they have greater health needs, poverty and social deprivation); *see also* London & Zollman, *supra* note 47, at 35 (noting that sponsor nations might further impose risks and burdens on low-income nations for research that will only be relevant and valuable to the sponsor nations).

54. *See* London, *supra* note 47, at 26.

55. *See id.* at 26, 28 (arguing that making the benefits proportional to the burdens imposed assumes that the host country does not have an entitlement to claim a higher baseline than the current status quo; London contends this acceptance of the status quo as a normative baseline in host countries is a critical issue with the fair benefits framework).

56. *See* Lavery et al., *supra* note 51, at 4 (advocating a framework called "relief of oppression" that aims to encourage researchers to recognize an obligation to address background conditions of injustice).

57. *See* London, *supra* note 47, at 24, 33–34 (highlighting the "10/90 gap"—namely, that the burdens of research participation are generally borne by lower-income nations while the benefits of successful research generally go to the top ten percent of the world's population).

58. *See* Participants 2004, *supra* note 24, at 19–20 (explaining that exploitation is a micro-level concern regarding discrete interactions, rather than about macro-level background social justice issues, and that the key issue is the obligation for a fair level of benefits between participants to the interaction).

59. *See* Jennifer S. Hawkins & Ezekiel J. Emanuel, *Introduction: Why Exploitation? Exploitation and Developing Countries,* 1, 10–11 (explaining that the implementation of a particular intervention is complex and not under the control of a single sponsor).

concern, imagine a sponsor proposes to conduct research on a life-saving drug in two lower-income countries and agrees to fulfill the reasonable availability requirement by making the drug free to everyone who could not afford it in those two countries. In contrast, the sponsor does not offer to make the drug available in any other lower-income countries.[60] This proposal satisfies the reasonable availability requirement, but it fails to address concerns regarding the impoverishment of other countries.[61] Put generally, if individuals from higher-income countries have positive obligations to help those in lower-income countries, they presumably have these obligations to all the individuals who live in impoverished circumstances, not simply to those who happen to live in the communities and countries where the sponsors and investigators conduct their studies.[62]

It is also not clear why these general obligations would need to be discharged through capacity building and/or provision of the interventions developed in a clinical trial.[63] Couldn't the investigators and institutions discharge their general obligations to address existing injustice by contributing to charities that work in lower-income countries and then design their clinical trials to ensure that they offer fair benefits? This approach has the advantage of satisfying investigators' and institutions' general obligations independent of the research setting and thereby allowing the ethical evaluation of individual studies to focus on the research-specific obligations that are generated through clinical trials with participants and communities.[64]

We will not attempt to develop an account for how the general obligations we all have to rectify background injustice translate into specific obligations on researchers and sponsors. But, it seems plausible that one could develop a supplementary account of the obligations of researchers and sponsors to remedy background injustice based on duties of global beneficence and/or commitments made by institutions or individuals.[65] This analysis would then constitute an effective criticism only if it turns out that the Fair Benefits framework is inconsistent in some way with sponsors and investigators satisfying these other duties.[66] We can think of no reason why satisfying trial specific obligations based on the Fair Benefits framework might conflict with investigators and sponsors

60. Rahul Nayak & Seema K. Shah, *Should Social Value Obligations be Local or Global?* 31 BIOETHICS 116, 116 (2017).

61. *Id.*

62. *Id.*

63. Emanuel, *supra* note 30, at 726 (arguing that the Fair Benefits framework requires a broader based assessment of benefits).

64. *See id.* at 726. (arguing that the needs of the community should be considered when assessing which benefits would be fair).

65. Nayak & Shah, *supra* note 60, at 124–125; Lavery et al., *supra* note 51, at 4.

66. *See generally id.* (arguing that the conduct of clinical trials obligates researchers to provide fair benefits, but not to relieve oppression, which is a supplemental obligation).

also satisfying their general or promissory obligations.[67] To us at least, these approaches seem complementary, not inconsistent.

A similar line of reasoning applies to sponsors who benefit from the impoverished circumstances of host communities (e.g. by saving on the costs of conducting trials).[68] A wide range of individuals in higher-income countries benefit from the impoverished circumstances of individuals in lower-income countries, from tourists who save money on hotels to consumers who save money on clothing.[69] What is needed, then, is an analysis of the extent to which realizing such benefits creates an obligation to help individuals in lower-income countries, even when those who benefit are not responsible for the unjust circumstances which account for the savings.[70] Given the absence of such an account, it is difficult to be certain to what extent there are such obligations. However, here too we do not see any reason to think that satisfying trial-specific obligations based on the Fair Benefits framework might conflict with investigators and sponsors also satisfying whatever obligations they might have in this regard.[71] We conclude that concerns regarding background injustice are important, but distinct from the concerns addressed by the Fair Benefits framework. Hence, they constitute a criticism only in the sense of highlighting the fact that the Fair Benefits framework on its own does not enable sponsors and investigators to discharge all of their ethical obligations to individuals in lower-income countries.

B. Does Not Require Best Use of Resources

The Fair Benefits framework does not mandate that studies in lower-income countries must be designed to use resources in the way that offers the greatest benefits for host communities.[72] While this has been proposed as a criticism of the Fair Benefits framework, it is not clear that there is any conflict between these two approaches.[73] Specifically, if this is an appropriate requirement for clinical trials, lower-income countries and communities could charge ethics committees (or other oversight bodies) with ensuring that any trials conducted in their jurisdiction offer the best use of available resources.[74] The clinical trials that

67. *Id.*

68. Angela Ballantyne, *HIV International Clinical Research: Exploitation and Risk*, 19 BIOETHICS 476, 484–86 (2005) (explaining that it is cheaper to conduct trials in developing rather than developed countries).

69. Robert Schrader, *What Third World Travel Has Taught Me*, HUFFINGTONPOST (Apr. 24, 2012, 7:27 AM), http://www.huffingtonpost.com/robert-schrader/what-third-world-travel-h_b_1446745.html.

70. London, *supra* note 47, at 24, 33–34.

71. Emanuel, *supra* note 30, at 726.

72. Lie, *supra* note 47 (utilizing an example of the Thai Havrix case, where the research contributed to the local health infrastructure despite the drug not being particularly useful for the native population).

73. *Id.* (stating that critics have argued that the use of research resources to study conditions which pose a high disease burden in the host country could most benefit the host nation).

74. S.R. Benatar, *Reflections and Recommendations on Research Ethics in Developing Countries*, 54 SOC. SCI. & MED. 1131, 1137–38 (2002) (discussing research ethics committees, which already work to monitor and audit research, and provide accountability in lower-income countries).

satisfy these requirements would then be subject to the Fair Benefits framework, suggesting that this issue too represents a possible supplement to, rather than a criticism of the Fair Benefits framework.[75]

C. Does Not Require Health or Study Related Benefits

Some commentators have criticized the Fair Benefits framework because it does not mandate that the benefits provided to participants and host communities should be related to the study, or to health more generally.[76] This argument is difficult to assess because the critics typically do not explain why the benefits provided to participants and host communities should be subject to these limitations. One possibility would be to appeal to what is often referred to as a 'separate spheres' argument.[77] Applied to the present context, the claim would be that the benefits offered as part of an activity should be limited to those that define the purpose of the activity.[78] Since clinical trials are intended to identify interventions to improve health, the benefits that individuals in lower-income countries receive as a result of participating in these trials should likewise be health-related.[79]

Even if one endorses this view, provision of interventions that are found to be effective is not the only way to provide health benefits to a community.[80] Staffing a medical clinic can provide important health benefits, as can access to potable water.[81] Thus, even if one agrees that the benefits provided to ensure a fair trial must be health-related, it does not follow that they must be limited to the interventions that the trials identify as safe and effective.[82]

Proponents of the reasonable availability requirement might respond that benefits should be *study*-related, thereby prohibiting provision of potable water or staffing of a health clinic.[83] Yet, it is even less clear why this might be the case.[84] Clinic nurses are crucial to conducting clinical trials and they should be

75. *Id.*

76. *See* London & Zollman, *supra* note 47, at 35 (arguing that due to differences in income between nations the research conducted may not be focused on the relevant health priorities of low-income countries).

77. Anat Rosenberg, *Separate Spheres Revisited: On the Frameworks of Interdisciplinary and Constructions of the Market*, 24 L. & LITERATURE 393, 396 (2012) (explaining that the idea of separate spheres involves taking a compartmentalized view of the world).

78. *See generally id.* (arguing separate spheres create identifiable areas with distinct logics).

79. Emanuel, *supra* note 30, at 726.

80. Ballantyne, *supra* note 68, at 487–88 (highlighting other health benefits like the improvements in the general health care facilities during the research).

81. Ballantyne, *supra* note 68, at 487–88 (discussing investing in health infrastructure).

82. *Id.* at 487–88.

83. Participants 2004, *supra* note 24, at 18.

84. Ballantyne, *supra* note 68, at 487–88 (discussing other benefits available to research in lower-income countries, such as education and counseling about the disease in question).

reimbursed for their efforts.[85] At the same time, no one thinks that clinic nurses must receive study- related benefits. Nurses typically are happy to be paid a fair wage.[86] In the same way, no one argues that those who work in factories to manufacture sneakers must be compensated with sneakers.[87] Are there any reasons to think that what is required to ensure a fair deal for research participants is fundamentally different?

Critics might be assuming that clinical trials should be understood in terms of providing treatment and research participants should be understood as patients who are being treated.[88] Certainly it would be unusual to pay patients for their participation in the health care system.[89] And it would be odd to offer to build them a school. Yet, research participants are not patients, and how we should treat research participants does not depend on what constitutes appropriate treatment of patients.[90] We conclude that this criticism is mistaken.

D. Defines Fairness Procedurally Results In a Race To the Bottom

Perhaps the most influential criticism maintains that the Fair Benefits framework defines what constitutes a fair deal or transaction in a procedural way.[91] As one commentator argues, "Fair benefits reduces the ethics of international health research to a market like transaction, whereby what is fair is what is negotiated between international pharmaceutical multinationals and their frequently impoverished, under educated, local prospective trial participants."[92] This presumed reliance on a procedural account of fairness seems to suggest that the Fair Benefits framework may lead to market style bargaining between sponsors and host communities, resulting in a "race to the bottom."[93] Under the

85. *See* Constance Engelking, *Facilitating Clinical Trials: The Expanding Role of the Nurse*, 67 CANCER 1793, 1795 (1991) (noting that nurses are instrumental in clinical research); *see also* Benjamin Sachs, *The Exceptional Ethics of the Investigator-Subject Relationship*, 35 J. MED. & PHILOS. 64, 69 (2010) (explaining that nurses, acting as employees in the clinical trials, are offered reimbursement for their labor regardless of the intervention being studied).

86. Sachs, *supra* note 85 (explaining nurses are acting within their employer-employee relationship in which they earn a fair compensation for their labor).

87. *Id.* at 71 (arguing that just as there is no obligation to give coal miners coal to take home, there should also be no ethical obligation to provide participants with the investigational therapy tested in their trail after the study is over).

88. *Id.* at 76 (noting that there is a difference between an investigator-subject relationship where the subject is providing a treatment as opposed to a clinician-patient relationship where the patient is being treated).

89. *Id.*

90. *Id.* (discussing the ethical differences between an investigator-subject relationship and a clinician-patient relationship).

91. Ballantyne, *supra* note 47, at 241–42 (focusing on problems with relying on a procedural notion of fairness).

92. Schüklenk, *supra* note 7, at 2.

93. *See* London & Zollman, *supra* note 47, at 41 ("[E]ven some fairly restrictive and unrealistic requirements aimed at equalizing the bargaining power of researchers and host communities would be unlikely to prevent a race to the bottom.").

Fair Benefits framework, sponsors could propose a given study to a number of communities, and select the community that agrees to accept the lowest level of benefits.[94] Given that some benefits are better than no benefits, and many of these communities may be in very desperate circumstances, it seems possible, perhaps even likely, that this process will lead to provision of a minimal level of benefits to whichever community wins the "Fair" benefits auction with the lowest bid.[95] Is this an accurate characterization of how supporters propose to implement the Fair Benefits framework?

The first paper to describe the Fair Benefits framework stated that the host community must "determine" what constitutes a fair level of benefits.[96] Advocates of the present criticism read this statement as maintaining that the community determines what constitutes a fair level of benefits in the sense that whatever level of benefits the community happens to agree to is, according to the Fair Benefits framework, necessarily fair.[97] As noted by the critics, this is problematic because host communities may not realize what constitutes a fair deal or they may not have sufficient power to insist on a fair deal.[98] As a result, host communities may end up agreeing to what in fact is not a fair deal, but which is defined as fair by the Fair Benefits framework.[99]

This is certainly one way to read the claim that the community 'determines' what constitutes a fair deal.[100] And since the passage in which this sentence is embedded does not clarify it, the immediate text provides no reason to think that this reading is mistaken.[101] At the same time, there is another possible way to read this sentence. Consider the claim, made in the context of a criminal trial, that the jury *determines* whether the suspect is guilty. Clearly, this claim does not mean: A unanimous guilty verdict makes it the case that the individual is guilty. Instead, to claim that the jury 'determines' whether the defendant is guilty is to claim that the members of the jury use their judgment to assess whether the evidence provides sufficient reason to conclude that the individual is guilty, all

94. *See id.* at 35 (noting that host communities are more attractive research venues to researchers if they are willing to accept a lower share of the surplus value).

95. *See id.* at 41 (noting that if you have two communities that are fairly close to one another, the host community that ultimately wins the bid could expect to receive "meager" benefits).

96. *See* Participants 2004, *supra* note 24, at 23 (explaining how the population that is being asked to partake in the collaborative partnership determines whether a particular array of benefits is sufficient and fair).

97. *See* Ballantyne, *supra* note 47 at 241 (explaining that the fair distribution of the benefits of research is to be determined on a case-by-case basis by the parties involved in each study).

98. *See id.* (remarking that just because the host community is informed, consents to the research, and is involved in the research process does not mean that the deal is fair and that the host community is not subject to exploitation).

99. *See id.* (noting that if "fair" is defined as an outcome that the host community is willing to accept, it fails to recognize that exploitation may nevertheless exist, especially given "dramatic imbalances of power.").

100. *Id.*

101. *Id.*

the while recognizing that the evidence may be misleading or the jury's judgment may be faulty.[102] This alternative use of 'determines' raises the possibility that the statement in the original paper might mean that the community determines whether an offer is fair in the sense of using their judgment to confirm whether it is fair for them.[103]

This reading, but not the one endorsed by the critics, is consistent with many other aspects of the Fair Benefits framework. It is consistent with the requirement in the original paper for transparency and the development of a case law which provides examples to help the host community determine, by way of analogy, whether a given offer is fair.[104] If proponents of the Fair Benefits framework assumed that whatever deal the host community accepts is fair, why would they add this requirement?[105] This alternative reading, but not the critics' reading, is also supported by other passages in the original paper, as well as numerous passages in subsequent papers authored by proponents of the Fair Benefits framework.[106] To consider just two examples, proponents have argued that the fact the community is informed and consents "does not ensure that it is protected against exploitation. A community may be informed of and consent to a research study that is exploitative because the community is desperate and has no other options."[107] This statement is clearly inconsistent with the procedural reading. Even more clearly, one of the lead authors of the Fair Benefits framework has responded to the procedural reading as follows: "The criticisms seem to miss the fact that the fairness of agreements is not determined just by bargaining. The purpose of the transparency principle is to provide an external check."[108]

If we accept that the Fair Benefits framework does not endorse a procedural account of fairness, one might wonder why it mandates that the host community must be involved in the discussions to determine what benefits it receives. The original paper describing the Fair Benefits framework provided a brief and partial answer to this question, stating that the input of the community is critical to ensuring that the proposed benefits would be valuable for the community.[109] This suggestion has been elaborated in a more recent paper, which argues that involving host communities in the process of deciding what benefits they receive

---

102. Participants 2002 *supra* note 5, at 2134 (stating that the population participating in a research project should decide what constitutes a fair level of benefits similar to how a jury in a criminal matter may use evidence to evaluate the culpability of the defendant).

103. *Id.* at 2134.

104. *See id.* (arguing that those outside the research population are ill-equipped to determine if the offered benefits are fair); Millum, *supra* note 47, at 220 (explaining that "the population at risk of exploitation must freely decide that the level of benefits offered is sufficient").

105. Ballantyne, *supra* note 47, at 241.

106. Participants 2002, *supra* note 5, at 2134.

107. Segun Gbadegesin & David Wendler, *Protecting Communities in Health Research from Exploitation*, 20 BIOETHICS 248, 249 (2006).

108. Emanuel, *supra* note 30, at 726.

109. Participants 2002, *supra* note 5, at 2134.

is crucial, even though the agreement of the community does not make it the case that a given offer is fair.[110] Instead, involvement of the community promotes four important goals: protecting host communities, respecting host communities, promoting transparency, and enhancing social value.[111] We conclude that the original paper alone does not provide definitive reason to reject the present criticism. However, taken together, all that has been written regarding the Fair Benefits framework by its proponents makes clear that it does not endorse a procedural account of fairness.

E. Lacks Theoretical Account of Fairness/Principle to Determine Which Deals Are Fair

The conclusion that the previous two criticisms are mistaken was based on the fact that the Fair Benefits framework does not endorse a procedural account of fairness. This conclusion leads naturally to the question: What theory or account of fairness does the Fair Benefits framework endorse?[112] The extant papers describing and supporting the Fair Benefits framework follow Wertheimer's account of exploitation, determining the fairness of individual transactions based on the distribution of benefits and burdens that result from the transaction.[113] On this account, the more one party to a transaction bears the burdens and risks, the more it should benefit.[114] Similarly, the greater the extent to which others benefit from a given party's contributions to the transaction, the more that party should benefit to ensure a fair deal.[115] Notice, however, that this account does not provide a general theory of fairness.[116] It does not, for example, offer an analysis of why a particular distribution of benefits and burdens is fair, whereas a different distribution would not be fair.[117] The Fair Benefits framework also does not provide a principle or principles for determining which offers are fair in practice.[118] Instead, it endorses the principle of transparency in

110. David Wendler & Seema Shah, *Involving Communities in Deciding What Benefits They Receive in Multinational Research*, 40 J. MED. PHILOS 584 (2015).

111. *Id.* at 584.

112. *See* discussion *supra* Part III.4 (addressing the criticism that the Fair Benefits framework relies on procedural fairness, which relates to a second criticism that research sponsors will choose the community which will accept the lowest level of benefits).

113. Alan Wertheimer, EXPLOITATION 207–246 (Princeton Univ. Press 1999) (using an example of rescuing stranded motorists during a snowstorm to demonstrate how to assess whether transactions are exploitative based on the distribution of burdens and benefits).

114. *See id.* at 226–277 (citing several examples in which one party bears the risk and so charges a higher fee for services to increase benefits).

115. *See id.* at 227 (using student athletes and the Marxian proletariat as examples of exploited parties because their contributions to the transaction are greater than the benefits they receive).

116. *See id.* at 216 (arguing that there is a difference between distributing social resources fairly and transacting fairly and that fair transactions account for moral factors, "such as justifying aid or redistribution.").

117. *Id.* at Ch. 7.

118. Ballantyne, *supra* note 47, at 241.

the development of a repository of deals that have been endorsed previously and against which future offers can be evaluated.[119] Some critics have argued that this approach provides reason to reject the Fair Benefits framework in favor of an alternative approach.[120]

The Fair Benefits framework certainly does not offer a definitive theory of fairness and the identification of one would be a welcome development for more than just the ethics of multinational research.[121] The absence of such an account increases the possibility that implementation of the Fair Benefits framework will result in deals that in fact are not fair.[122] Granting this possibility, no one has developed a theory of fairness which has received universal endorsement.[123] It follows that this concern applies to all approaches that attempt to address the potential for exploitation in multinational research; hence, it does not provide a reason to endorse one approach over another. For example, absent a final theory of fairness, one could equally argue that it is unclear whether making proven interventions reasonably available in host communities is sufficient to ensure a fair trial.

Finally, it seems implausible to argue that, until a final theory of fairness has been identified, no substantive frameworks should be proposed, and no attempts should be made to address the potential for exploitation in multinational research.[124] We conclude that this criticism does indeed point to a shortcoming of the Fair Benefits framework, a shortcoming that is shares with all accounts that seek to address the potential for exploitation. Absent a final account of fairness, then, or some reason to think that the Fair Benefits framework is more likely to be inconsistent with such an account than other approaches, this criticism does not provide a reason to reject the Fair Benefits framework in favor of some other approach, or no approach at all.

---

119. Participants 2002, *supra* note 5, at 2134.

120. Millum, *supra* note 47, at 220.

121. Participants 2004, *supra* note 24, at 23; *see* Participants 2002, *supra* note 5, at 2134 (noting that the lack of an international standard of fairness may impact a community's decision-making); see Ballantyne, *supra* note 47, at 244 ("A key limitation of the current debate about whether international research is exploitative has been the lack of a suitable concept of 'fair distribution'…"); *see id.* (emphasizing the need for further development of international standards of fairness).

122. *See* London & Zollman, *supra* note 47, at 34–35 (arguing that the ambiguities in the Fair Benefits approach make implementing the model fairly a difficult, if not impossible, task).

123. *See* Angela J. Ballantyne, *How To Do Research Fairly in an Unjust World*, 10 AM. J. BIOETHICS 26, 28 (2010) (noting that a lack of a "normative account of fair distribution" hinders fair transactions in international research).

124. *See* London & Zollman, *supra* note 47, at 34–35 (criticizing the Fair Benefits approach for its lack of a definitive process without proposing an alternative).

F. Fails to Specify Procedures

Critics point out that the Fair Benefits framework does not specify what type of process should be used to satisfy its requirements in practice.[125] Given that the Fair Benefits framework does not offer a theory of fairness, and lacks a specific principle for determining which deals are fair, the challenge of specifying the process that should be used to implement it is especially important.[126]

We believe this is the most important challenge for the Fair Benefits framework. Future research will be needed to address this challenge and also to address a number of substantive questions regarding what a final process should look like.[127] For example, the conclusion that the Fair Benefits framework does not endorse a process account of fairness raises the question of what should be done when a host community insists on accepting what seems an insufficient level of benefits.[128] Respect for the community would suggest that perhaps the community should be allowed to accept unfair offers; emphasis on fairness as an ethical requirement suggests that these trials should not be approved.[129]

A related question concerns whether there should be an appeals process. Imagine that a sponsor proposes a package of benefits to a host community. The community regards the offer as sufficient, but the ethics review committee find it inadequate. Should there be some process for appeal to a different body? Alternatively, should the sponsor be allowed to approach other review committees and host communities to determine whether they regard the proposed offer as fair?

Describing an appropriate process or processes, and answering these substantive questions, represents the greatest challenge for the Fair Benefits framework. Yet, absent some reason to think that it will not be possible to describe an appropriate and feasible process, this challenge does not suggest that another approach is preferable to the Fair Benefits framework. Moreover, the argument that ensuring fair benefits requires a significant exercise of judgment on the part of ethics committees or those overseeing benefit-sharing

---

125. *See id.* at 34–35 (arguing that important components of the theory have not been "described in operationally useful detail.").

126. *See* Ballantyne, *supra* note 123 at 28 (noting that little progress has been made in clarifying a process for implementation, and describing a lack of specific principles as a "key limitation").

127. *See* London & Zollman, *supra* note 47, at 37 (posing questions about what the process should look like, including how the bargaining process should be shaped to meet the goals of the fair benefits framework, how priorities in the framework should be handled in the process, and how unfair proposals that are accepted by host countries should be addressed).

128. *See* Ballantyne, *supra* note 123, at 27–28 (noting it may be "rational" for host nations to agree to transactions that are exploitative because they might represent the "best available option").

129. *See* Danielle M. Wenner, *Against Permitted Exploitation in Developing World Research Agreements*, BIOETHICS 2, 2–3 (2015) (noting that some scholars feel interfering with these transactions would violate the autonomy and self-determination of the local community while others, including the author, feel that such interference would lead to better deals for the host country).

arrangements does not make fair benefits unworkable in practice.[130] There are many conditions on ethical research for which we lack a principle to determine when they are satisfied and, hence, for which judgment is required.

To consider just one example, it is widely agreed that research participants should provide voluntary consent.[131] They should not be coerced or manipulated into enrolling in a study.[132] In practice, it is extremely difficult to determine whether a given decision is voluntary and no principle exists that allows investigators to determine whether the decision of a particular individual is in fact sufficiently voluntary.[133] Yet, no one would argue that we should reject voluntary consent as a necessary ethical condition on the grounds that judgment is needed to ensure that it is realized in practice.[134] This comparison is especially apt given evidence to think that our judgment regarding which deals are acceptable is likely to be easier with respect to fairness than it is with respect to voluntariness.[135] In particular, there is compelling evidence that a sense of fairness and judgments of whether individual offers are fair or unfair is common across most, if not all human beings.[136] In contrast, we know of no evidence to suggest that individuals have a common sense for when decisions are voluntary. We conclude that the present claim represents a criticism of the Fair Benefits framework only to the extent of establishing that the framework is not complete and there is more work to do.

---

130. *See* Millum, *supra* note 47, at 221 (arguing that even in developing countries where judgment in the oversight process might be compromised due to lack of training pressure from various institutions, or insufficient funding, the fair benefits framework could still be modified to accommodate the situation).

131. *See* Paul S. Appelbaum et al., *Voluntariness of Consent to Research: A Conceptual Model*, 39 HASTINGS CTR. REP., 30, 30 (2009) (defining voluntary participation as a key component of informed consent).

132. *See id.* at 32 (recounting the widely accepted definition of voluntariness adopted in the Nuremberg decision that participants "should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion.").

133. *See* Amulya Mandava & Joseph Millum, *Manipulation in the Enrollment of Research Participant*, 43 HASTINGS CTR. REP. 38, 38 (2013) (placing the burden on researchers to consider subtle factors that might influence participants' decision to enroll, such as the participants' respect for the physician running the study); *see also* Appelbaum et al., *supra* note 131, at 30 (establishing that voluntary informed consent is a necessary requirement for ethical research participation).

134. *See* Appelbaum, *supra* note 131, at 39–40 (exploring the spectrum from legitimate methods of influence, which are consistent with participants voluntarily participating, to other methods that disrespect the participants' autonomy and make their involvement involuntary, such as unacceptable manipulation).

135. Appelbaum et al., *supra* note 131, at 45 (examining scenarios where the same behavior in different contexts changes whether a participant's involvement is voluntary or not, underscoring the difficulty of recognizing truly voluntary action).

136. *See* Sarah F. Brosnan & Frans B.M. de Waal, *Evolution of Responses to (Un)fairness*, 346 SCI. 1251776–1, (2014) (describing how human understanding of fairness revolves around judging how appropriate outcomes impact everyone in the community, not just the individual making the judgment); *see also*, Christopher T. Dawes, et al., *Egalitarian Motives in Humans*, 446 NATURE, 794, 796 (2007) (noting that humans are "strongly influenced by egalitarian preferences" that cause people to react negatively when faced with a socially unequal situation).

G. Responsiveness is More Practical

As we have seen, the Fair Benefits framework does not provide a theory or principle against which specific deals can be evaluated to ensure they are fair. This is concerning given that, in many cases, it will be difficult to determine what constitutes a fair deal. What offer of benefits would be fair for a phase 1 study that enrolls 10 participants and gives them a single dose of a new drug? Given this complexity, it has been argued that the combination of the responsiveness requirement and reasonable availability is more likely to yield fair deals than permitting the provisions of other types of benefits, as the Fair Benefits framework allows.[137]

This criticism is based on the fact that ethics review committees or institutional review boards need to evaluate the risks and burdens of clinical trials to ensure that their social value justifies the risks and burdens they pose.[138] Given that this process is already in place, it may be easier to rely on these judgments rather than requiring research ethics committees to make additional judgments regarding the value of other types of benefits.[139] Not only will the Fair Benefits approach require more work but, according to this critique, it requires that review committees make judgements regarding questions for which they lack expertise, such as the value to a community of building a school or staffing a health clinic.[140]

As we have noted, many studies turn out to have negative results.[141] In these cases, reliance on responsiveness and reasonable availability to address the potential for exploitation is inadequate. Or it implies that sponsors and researchers can discharge their obligations merely by providing the community with the information that the study drug is not effective against a condition of interest to the community.[142] In contrast, reliance on Fair Benefits might result in the community receiving a school or a health clinic. In these cases at least, it seems that communities are more likely to receive a fair level of benefits under the Fair Benefits framework.

---

137. *See* Millum, *supra* note 47, at 221 (arguing in favor of the responsiveness requirement and reasonable availability over the Fair Benefits framework on this basis).

138. Nancy King, Larry Churchill, *Assessing and Comparing Potential Benefits and Risks of Harm*, *in* THE OXFORD TEXTBOOK OF CLINICAL RESEARCH ETHICS 514, 514 (2008) (Ezekiel J. Emanuel et al. eds., 2008).

139. *See* Millum, *supra* note 47, at 220–22 (noting that under the responsiveness requirement, "a research project that involved testing an experimental hepatitis A vaccine on rural inhabitants of Tanzania if the only benefits that accrued to the local population were that the research team built a clinic and a school" would be prohibited).

140. Millum, *supra* note 47, at 221.

141. Rafael Dal-Ré et al., *Protections for Clinical Trials in Low and Middle Income Countries Need Strengthening not Weakening*, 349 BRIT. MED. J. 1, 2 (2014).

142. London, *supra* note 18, at 739 (noting that in cases that have negative results, the benefits from a study that was responsive to a community's needs can vary).

What about successful trials? Is reliance on responsiveness and reasonable availability better in these cases? The present criticism is based on the fact that review committees already make risk-benefit evaluations for these trials. It follows that reliance on the Fair Benefits framework will result in review committees having to make an additional determination. Whether this fact suggests that the Fair Benefits approach is less likely to address the potential for exploitation depends on more than just the number of determinations that need to be made. It depends on the extent to which review committees' judgement is accurate in each case. The fact that research ethics committees are required to evaluate the risks and burdens of a given study in comparison to the social value of the information to be gained does not imply that committees' judgements in this regard are accurate, nor that these determinations are easier to make than the determinations called for by the Fair Benefits framework.[143]

Imagine a study evaluating a new approach to developing a malaria vaccine in a community where malaria is endemic. To determine the value of the study for the community, one needs to evaluate the chances that the general approach will be successful, the chances that this success will lead to the development of a specific vaccine, that this vaccine will be effective and reasonably safe, and it will be provided to the community at a cost its members can afford.[144] These are extremely complicated judgments, and determining whether a particular study offers sufficient value for the community to compensate for the burdens it poses is difficult at best. Contrast this with the question of the extent to which the community would benefit from access to potable water, or the building and staffing of a school. These seem to be easier judgments to make. This suggests that, in practice, the Fair Benefits framework may be more likely to result in fair deals for participants and host communities compared to the combination of responsiveness and reasonable availability. Of course, there will be cases in which responsiveness and reasonable availability provide appropriate benefits for the host community.[145] However, these cases do not pose a problem for the Fair Benefits framework given that it endorses responsiveness and it allows the requirement for fair benefits to be satisfied by provision of the study drug.[146]

---

143. *See* King & Churchill, *supra* note 138, at 524 (noting that balancing the risks of harm and potential benefits takes several steps). *But see* Millum, *supra* note 47, at 221 (arguing that the responsiveness requirement is easy to apply).

144. *See* Millum, *supra* note 47, at 220 (noting the objection to the responsiveness requirement that results in a successful project should ensure that intervention is reasonably available to the host community).

145. *See id.* at 221 (exemplifying a case of malaria vaccine where a responsiveness requirement would prevent exploitation); Ezekiel J. Emanuel, *Addressing Exploitation: Reasonable Availability versus Fair Benefits, in* THE EXPLOITATION IN DEVELOPING COUNTRIES 286, 296 (Jennifer S. Hawkins & Ezekiel J. Emanuel eds., 2008) (noting that "reasonable availability" works well in successful Phase III clinical research).

146. London, *supra* note 18, at 744 (concluding that the nature of responsiveness encompasses the social value which comes from addressing the most significant health needs of the community's members).

Finally, the present proposal attempts to leverage the fact that review committees already are charged with evaluating whether the potential benefits of a study in terms of the information to be gained justify the risks it poses.[147] The thought then is that this process also provides a way to ensure individuals and host communities receive fair benefits. The problem with this suggestion is that review committees evaluate whether the potential benefits of a study justify its risks. However, the potential for exploitation is not limited to the risks and burdens to which individuals in lower-income countries are exposed.[148] It also includes the extent to which individuals in lower-income countries contribute to the benefits that result from the trial.[149] This factor is not typically evaluated by ethics review committees.[150] They do not, for instance, assess to what extent participants and host communities contribute to the profits realized by commercial sponsors and whether the benefits offered to the participants and host communities are commensurate with these contributions.[151] We conclude that the combination of responsiveness and reasonable availability is unlikely to yield fair deals across a broader range of cases than the Fair Benefits framework.[152]

H. Undermines Responsiveness

One might assume that requiring reasonable availability of study interventions makes sense only to the extent that the study satisfies the responsiveness requirement.[153] Specifically, the extent to which the host community will benefit from the reasonably availability of tested and proven intervention depends on the extent to which the testing of that intervention was responsive to the host community's health needs. At the extreme, testing and making available an intervention for a condition that is absent in the community will provide it with no benefits. This connection between the two requirements

147. S*ee* King & Churchill, *supra* note 138, at 514.

148. S*ee id.* (indicating that when evaluating the ethics of a study under Fair Benefits, benefits and risks must be considered); *see* Millum, *supra* note 47, at 219 (2012) (arguing that one party can exploit another even if both benefit from their interaction).

149. James V. Lavery, *Obligation to Ensure Access to Beneficial Treatments for Research Participants at the Conclusion of Clinical Trials*, *in* THE OXFORD TEXTBOOK OF CLINICAL RESEARCH ETHICS 697, 701 (Ezekiel J. Emanuel ET AL. eds., 2008) (indicating that there are ethical issues regarding the obligation to recognize the contribution of research participants, particularly in low- and middle-income countries).

150. *See* Millum, *supra* note 47 (suggesting that under the responsiveness approach, ethics review committees do not need to spend time talking with representatives of communities, examining data, and comparing proposed benefit arrangements with arrangements elsewhere).

151. *See* Millum, *supra* note 47, at 219 (criticizing foreign scientists who hide the true prospects for commercialization from a community that has little contact with the modern world when obtaining knowledge of a native plant's healing properties).

152. Participants 2004, *supra* note 24 (proposing that a "fair benefits" framework offers a more reliable and justifiable method to prevent exploitation).

153. *See* Millum, *supra* note 47, at 220 (noting that the responsiveness requirement should include a provision that ensures the intervention is made "reasonably available" to populations after the trial).

raises the question of whether it makes sense for the Fair Benefits framework to endorse responsiveness as a necessary requirement for ethical multinational research, but then offer an alternative to the reasonable availability requirement. Why, in other words, require responsiveness without mandating reasonable availability? If sponsors do not have to make tested interventions reasonably available to the host communities, why think that the interventions they test in lower-income countries must be relevant to the health needs of those communities?

To answer this question, more research will be needed on whether responsiveness is an independent ethical requirement on research in lower-income countries. As noted previously, the responsiveness and reasonable availability requirements can be understood as addressing different ethical concerns.[154] Responsiveness provides a justification for why a trial is conducted in a particular place and addresses concerns regarding fair subject selection, while reasonable availability attempts to ensure that the risk-benefit profile of the study is ethically appropriate when conducted in that place.[155]

Put in these terms, the present challenge is the following: Does a study that is not subject to the reasonable availability requirement need to be responsive to the heath needs of the local community in order to ensure that is satisfies the requirement for fair subject selection? The answer depends on whether studies that are not responsive, but which nonetheless provide participants and host communities with sufficient benefits, are ethical.[156] However, the answer to this question does not seem clear, at least to us. It is not clear that unresponsive studies exploit participants who receive a fair share of the benefits. This suggests that enrolling specific individuals or targeting a specific community might be justified on the grounds that they will benefit from their participation in the trial. In these cases, the responsiveness requirement is not needed to address the potential exploitation. Whether it is needed at all then depends on whether there is other normative work for it to do in these cases.

One possibility would be to argue that requiring responsiveness in addition to fair benefits provides a way to maximize the use of scarce resources. If there are several studies competing for a limited number of sites or participants, it might make sense for lower-income countries to prioritize the studies that offer the greatest value for the community or the country. This goal might be realized by focusing on studies that are responsive to the community's health priorities.[157]

This analysis suggests that the present argument would offer a challenge to the Fair Benefits framework if responsiveness *is* an independent ethical

154. *See infra* text accompanying note 47; *see infra* text accompanying note 157

155. *See* Millum, *supra* note 47, at 220 (explaining that a responsiveness requirement means that research is justified only if it is responsive to the health needs or priorities of the host community).

156. Lavery, *supra* note 149, at 697, 699.

157. Seema K. Shah, Rebecca Wolitz, & Ezekiel Emanuel, *Refocusing the responsiveness Requirement*. 27 BIOETHICS 151, at 158 (2013).

requirement on research in lower-income countries and it must be combined with reasonable availability to address the potential for exploitation. We have argued that this is not the case; a requirement for fair benefits addresses the potential for exploitation better than a requirement for reasonable availability. Alternatively, it might turn out that the provision of fair benefits is sufficient to ensure ethical trials, in which case responsiveness is *not* ethically necessary. This conclusion would not provide a reason to reject the Fair Benefits framework. Instead, it would provide a reason to endorse a revised version, one which continues to insist on the provision of a fair level of benefits but which dispenses with the requirement for responsiveness. We leave for future analysis the question of whether this revised version represents a better Fair Benefits framework.

IV. SUMMARY

It is widely agreed that research conducted in lower-income countries by investigators and sponsors from higher-income countries should not exploit participants and host communities.[158] Most commentators also agree that, in order to address the potential for exploitation, participants and host communities should receive adequate benefits.[159] Debate now focuses on how the requirement for adequate benefits should be realized in practice.[160] For this purpose, the Fair Benefits framework was proposed as an alternative to the reasonable availability requirement. It is intended to ensure an appropriate distribution of the risks and benefits that result from a given trial.[161] To realize this goal, the framework specifies that the host community and participants should be provided with a fair level of benefits, given the risks and burdens they face, and the extent to which others benefit from their contributions to the trial.[162]

The preceding discussion has evaluated what we take to be the 8 most prominent criticisms of this proposal. This analysis suggests that the prominent criticisms can be placed in three categories. First, a number of the criticisms are in fact not criticisms of the Fair Benefits framework itself, but concern related issues. These issues are important, but they do not provide a reason to reject fair benefits. For example, some have argued that the Fair Benefits framework does not require that individual trials are approved only when they represent the best

158. Participants 2004, *supra* note 24, at 17–18 (noting Fair Benefits Framework has been developed in an effort to prevent exploitation of research participants).

159. *Id*. at 22.

160. *Id.* at 18 (describing how some commentators argue that unless a host community receives the fruits of clinical research, the trial is exploitative).

161. *Id.* at 22.

162. Participants 2002, *supra* note 5, at 2133–34 (explaining that under the Fair Benefits framework, research must address a health concern of the tested population, research objectives must justify testing in that population, and research must pose a favorable risk/benefit ratio).

use of resources for host communities.[163] This might be an important requirement; however, it also seems like an independent one. Even when a trial represents the best possible use of the available resources of a given community, it will still be important to ensure that the trial does not exploit host communities; the Fair Benefits framework is intended for this purpose.[164]

Second, we have argued that a number of the criticisms of the Fair Benefits framework are mistaken. This is true of one of the most prominent criticisms of the Fair Benefits framework—the claim that it assumes a procedural account of fairness and, in practice, would lead to a race to the bottom. A few isolated statements in the original paper endorsing the Fair Benefits framework are consistent with this view.[165] However, a reading that takes into account the entirety of the original paper and the subsequent papers authored by its proponents makes clear that this reading is mistaken.

Third, some criticisms are accurate, such as the criticism that the Fair Benefits framework does not provide a definitive theory of fairness.[166] While it would be preferable to have such a theory, this criticism does not provide a reason to reject the Fair Benefits framework. The absence of a definitive theory is a concern for any proposal to address the potential for exploitation in multinational research. However, we do not think that this fact provides a reason to abandon the attempt to do the best we can to ensure fairness for research participants and host communities in lower-income countries. Many of the widely-accepted requirements on ethical research lack the support of a complete theory.[167] The example we considered in this regard is the requirement that informed consent must be voluntary.[168]

The present analysis suggests that the most important criticism points out that the Fair Benefits framework does not provide a complete description of the procedures that should be used to implement it in practice.[169] This criticism highlights the need for future research to describe and refine the Fair Benefits

163. Lie, *supra* note 47, at 3 (describing the Thai Havrix case, where the research was the most prudent use of in-country resources to build research capacity, despite the drug not being particularly useful for the native population).

164. Participants 2002, *supra* note 5, at 2133–34 (describing how the Fair Benefits Framework avoids exploitation of the host community).

165. Lie, *supra* note 47, at 3.

166. Participants 2002, *supra* note 5, at 2133–34 (explaining that the Fair Benefits framework still lacks total agreement within the research community and that there is no consensus on a theory of fairness).

167. Ballantyne, *supra* note 47, at 244 (noting there is not one standard for what constitutes a fair distribution of benefits).

168. Mandava & Millum, *supra* note 133, at 38–47, 44 (discussing how disclosure, understanding, and voluntariness can affect consent to such a degree that it is invalidated).

169. *See* London & Zollman, *supra* note 47, at 34–35 (arguing the Fair Benefits Framework suffers from fundamental ambiguities at a "conceptual and operational level.").

framework to make clear exactly what procedures would best implement it.[170] While this is an important challenge, we believe that it can be addressed.

Finally, we pointed out that provision of fair benefits to host communities raises the question of whether research must also be responsive to their health needs.[171] While this is an important question, it is more a challenge for proponents of the responsiveness requirement. Why should we think that a study needs to be responsive in addition to providing a fair level of benefits? Is responsiveness nonetheless needed to satisfy the requirement for fair subject selection? A finding that there is a reason to require responsiveness in addition to fair benefits would validate the Framework's original endorsement of this requirement. A finding that the provision of fair benefits is sufficient, and responsiveness is not ethically necessary, would provide a reason to endorse a revised version of the framework, one which continues to insist on the provision of a fair level of benefits but which dispenses with the requirement for responsiveness.

In sum, the present analysis suggests that the extant criticisms provide no reason to reject the Fair Benefits framework. We conclude that the Fair Benefits framework represents the best approach for addressing the potential exploitation of research participants and host communities in lower-income countries.

Funding: This work was funded by intramural funds of the U.S. NIH Clinical Center.

Disclaimer: The views expressed are the authors' own. They do not represent the position or policy of the NIH, DHHS, or United States government.

170. *See id.* at 35 (describing an economic model as a potential method to consistently implement the Fair Benefits framework).

171. London, *supra* note 18, at 737 (discussing the issue of responsiveness to the health needs and concerns of a host community).

Assessment of the Major Criticisms of the Fair Benefits (FBs) Framework

Criticism	Comments	Assessment
Ignores background injustice	FBs addresses trial specific duties	Distinct Issue
Does not require best use resources	FBs determines which trials fair, not which trials best	Distinct Issue
Benefits should be study/health related	Fairness is about the level, not type, of benefits	False
Defines fairness procedurally	Inconsistent with transparency requirement and many statements	False
Lacks a theory or principle of fairness	Challenge for any attempt to address exploitation	True
Lacks details on procedures	Not a reason to reject FBs; need further research	True
Responsiveness more practical	Untrue in many cases	Likely False
Undermines responsiveness	Challenge for responsiveness, not FBs	Possibly True