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The ethics of health systems research in low and middle-income countries: A call to action

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Abstract

The increasing conduct of health systems research in low and middle-income countries (LMICs) has not been matched by concurrent work to clarify the field's ethical dimensions. To begin to address this gap, a two-day workshop on the ethics of health systems research in LMICs was convened at Johns Hopkins University in June 2013. Participants included health systems researchers, philosophers, lawyers, bioethicists, and institutional review board members from Botswana, Uganda, the United Kingdom, USA, and Zambia. Based on discussions from the workshop, the paper affirms that, while health systems research in LMICs raises ethical issues in relation to constructs (i.e. consent, risk, equipoise) common to international clinical research, the nature of the issues that arise often differ between the two fields. Three salient features of health systems research and the ethical considerations associated with each of them in LMICs are described to demonstrate this point. Recommendations for institutional review boards' oversight of health systems research in LMICs are presented. Finally, a call is made for further action to develop thinking and guidance around the ethics of health systems research in resource-poor settings.

Keywords

Health systems research; ethics; IRB oversight; developing countries

Introduction

Externally-funded health systems research (HSR) is increasingly being conducted in low and middle-income countries (LMICs) (Bennett et al., 2008). HSR has been defined as:

...a multidisciplinary field of health research which studies governance, financial and delivery arrangements for health care and public health services,

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implementation considerations for reforming or strengthening these arrangements, and broader economic, legal, political and social contexts in which these arrangements are negotiated and operate. The purpose of health systems research is to improve the understanding and performance of health systems.

(Hoffman et al., 2012, p. 18)

It is a much broader field than health *services* research, which some suggest comprises a sub-domain of HSR (Hoffman et al., 2012). HSR focuses on all health systems components, which include but are not limited to service delivery, and their interactions.¹ Thus far, the geographical focus of HSR has primarily been LMICs, though it can and has been performed in high-income countries (Gilson, 2012; Sheikh et al., 2011).²

Renewed attention to health systems in LMICs appears to have emerged strongly between 2000 and 2005, with influential actors, including the World Bank, G8, World Health Organisation (WHO), GAVI Alliance, and Rockefeller Foundation, putting health systems strengthening on their agendas and directing resources to it (Hafner & Shiffman, 2011). These actions stemmed from concern that external actors' prolonged emphasis on vertical programmes had significantly weakened LMIC health systems, creating substantial bottlenecks in efforts to meet global health objectives (e.g. increased uptake of antiretroviral therapy and expanded immunisation coverage in LMICs) and to achieve broader targets like the Millennium Development Goals (MDGs) (Hafner & Shiffman, 2011; Travis et al., 2004; Van Olmen, Marchal, Van Damme, Kegels, & Hill, 2012).

As investment in health system strengthening increased, it became clear that a stronger evidence base was needed to inform such activities in resource-poor and conflict-prone settings. Information was scattered on what barriers existed to hinder the delivery of interventions and on what strategies were required to overcome them. Reports from the WHO and global ministerial summits, therefore, drew attention to the fact that the MDGs and better global health would not be achieved without increased investment in HSR in LMICs (Global Ministerial Forum on Research for Health, 2008; Ministerial Summit on Health Research, 2004; WHO Task Force on HSR, 2005). Repeated calls to prioritise HSR subsequently led multilateral agencies, bilateral aid agencies, and philanthropic foundations to channel a somewhat larger amount of resources to HSR in LMICs and promoted conceptual work to better define the aims, scope, and methods of the field (Bennett et al., 2008; Mills, 2011; Sheikh et al., 2011). This reflects the fact that HSR is an evolving field, whose boundaries, definitions, and characteristics are still being discussed and debated (Hoffman et al., 2012).

There has been some work done on the ethics of health *services* research in high-income countries, which focuses on the ethical issues inherent in employing qualitative methods and cluster trials (Conrad & Edwards, 2011; Edwards, Braunholtz, Lilford, & Stevens, 1999; Richards & Schwartz, 2002; Weijer et al., 2011). Scholarship has also assessed the need for informed consent in health services research projects that rely on population-based records

¹Other health system building blocks include human resources, financing, governance, information technology (Gilson, 2012).

²We recognise that health services research has long been conducted in high-income countries, though HSR, with its broader scope, is only starting to be.

(Cassell & Young, 2002; Meslin, 2006). However, despite the growth of interest in HSR in LMICs, there has been less concurrent effort to clarify the field's ethical dimensions (Mills, 2011). More importantly, there has been limited consideration of the ethics of externally-funded HSR in LMICs by the field of bioethics. At most, there has been discussion in the bioethics literature related to ethics of cluster trials in LMICs and the use of financial incentives as interventions in LMICs. Ethical issues relevant to research in high-income countries and LMICs (informed consent, risk-benefit ratios) and ethical issues that arise primarily in LMIC settings (standard of care, ancillary care, post-trial benefits) were raised and shown to have a differing application in HSR (London, Borasky, & Bhan, 2012; Orsin et al., 2009; Weijer et al., 2011).

The small amount of scholarship on the ethics of HSR in LMICs, perhaps reflects the fact that large controversies have tended to arise in relation to specific *clinical* trials in LMICs such as the AZT trials, Nonoxynol-9 trial, and Trovan trial, prompting considerable discussion around ethical issues in international clinical research (rather than HSR in LMICs). In addition, ethical frameworks for international research and international research ethics guidelines focus on biomedical research with human subjects (CIOMS, 2002; Emanuel, Wendler, Killen, & Grady, 2004; National Bioethics Advisory Commission, 2001; UNAIDS, 2007; World Medical Association, 2013). As such, IRBs typically apply guidelines for international biomedical research to HSR projects being done in LMICs that come under their review. It has been suggested that this may not be appropriate (Hyder, Rattani, Krubiner, Bachani, & Tran, 2013), but, at this stage the ethical issues that arise in HSR in LMICs have yet to be comprehensively described and formal ethical guidance for HSR performed in LMICs has not been developed for use by IRBs.

In recognition of this gap at the intersection of the HSR and ethics discourses, we convened an international workshop of health systems researchers, philosophers, lawyers, bioethicists, and IRB members. The workshop aimed to highlight the ethical issues that are particularly common to HSR in LMICs and to assess their implications for IRB oversight. It was held over two days in June 2013 at Johns Hopkins University's Berman Institute of Bioethics and Bloomberg School of Public Health, in Baltimore, Maryland (USA). Speakers and participants at the workshop spanned three continents and five countries: Botswana, Uganda, United Kingdom, USA, and Zambia. The structure of the workshop was a mix of formal presentations and extensive group interactions, with emphasis falling on the latter. A total of nine sessions were held that encompassed an overview of HSR in LMICs; a discussion of HSR ethics; IRB oversight of HSR; ethics of different HSR methods in resource-poor settings; and the benefits of HSR to participants and host communities in LMICs. These sessions generated rich dialogue that was captured in detailed notes taken by AH, BP, and NK. Thematic analysis of these notes resulted in the identification of the following themes (amongst others): need for HSR ethics, features of HSR give rise to distinctive ethical issues, and IRB review of HSR. Given the findings of this analysis, the paper first articulates why we believe that HSR in LMICs generates ethical considerations that are distinct from those arising in international clinical research. It then identifies ethical constructs associated with three specific features of HSR that were identified in workshop discussions and

describes how they might be applied in LMIC settings. Suggestions are made for how IRBs might deal with these issues and HSR in LMICs more broadly.

In doing so, the paper is intended to add to the rich literature on public health ethics. Some public health research can be considered HSR. Hoffman (2012, p. 13) states that

[t]he overlap [of HSR] with population health research... likely includes research on the public health system and the delivery of non-personal public health programs and interventions. Excluded from health systems research would be population health research's focus on measuring or describing health, examining the determinants of health status and outcomes, and assessing the effects of specific health promotion interventions.

Recognition that the characteristics differentiating clinical and public health practice lead to different ethical challenges resulted in the development of ethical frameworks for public health practice (Lee, 2012). This paper contributes to a similar process for research by looking at how certain features of HSR in LMICs give rise to ethical issues not typically generated by international clinical research. These considerations may apply to public health research that focuses on the public health system (i.e. public health research that is HSR).

We acknowledge that certain ethical concepts (e.g. informed consent) discussed in the paper and their application may be relevant to HSR in high-income countries. There is not necessarily a clear boundary between the considerations that arise in HSR in high-income country versus LMIC settings in relation to shared ethical concepts. Some overlap between the ethical issues that arise is likely, and lessons from HSR in high-income countries may be relevant to such research in LMICs (and vice versa). Bioethics research is needed to characterise the considerations that are pertinent in *both* settings to make the boundary clearer. This paper, we hope, contributes to such an evolving process by describing some of the considerations that are relevant in LMICs.

Need for health systems research ethics

Consensus emerged amongst workshop participants that HSR in LMICs raises ethical considerations that, though related to familiar constructs in (international) research ethics like the need to balance risks and benefits and the need to be responsive to host countries' health needs and priorities, must be operationalised differently from international *clinical* research. How ethics commitments should be interpreted and put into place in HSR in LMICs arise as a result of HSR's particular characteristics, which differ to varying degrees from other types of health research. Workshop speakers emphasised that the field of HSR is still evolving, with debate continuing over its precise boundaries relative to clinical research, public health research, quality improvement research, operations research, and health services research. Current definitions of HSR reflect the development in health systems thinking spurred on by renewed attention to health systems strengthening (van Olmen et al., 2012). These definitions demonstrate recognition that health systems are composed of both *hardware* (human resources, service, governance, information technology) and *software* (norms, values) elements, as health systems are embedded in their context and emanate the prevailing values of their societies. They further reflect awareness that dynamic *complexity*

is a feature of health systems (i.e. there are complex interactions between health system elements such as feedback loops).

Although the HSR terrain is still being mapped out, consensus is emerging that the field is delimited, not by its methods but by the topics and scope of its research questions (Gilson, 2012; Mills, 2011; Sheikh et al., 2011). HSR research questions can be descriptive, explanatory, or evaluative and encompass the follow topics: describing health system hardware and software elements and the complex relationships and interactions between them; evaluating how and why health systems do not meet their goals; and identifying what to do to improve health system functioning to meet those goals (Gilson, 2012). HSR methods are determined by the nature of the research question under study and can encompass a wide range of quantitative and qualitative methods such as observational studies, cluster trials, economic evaluations, case studies, and participatory action research.

Workshop speakers highlighted that HSR differs from clinical research in a number of morally relevant ways, including not only its aims and the methods it uses but also the nature of interventions under evaluation and the research participants targeted by studies. For example, HSR will often target interventions at the systems level rather than individual level, testing the efficacy of interventions such as novel health delivery mechanisms for existing services of known efficacy, new methods of creating demand for existing efficacious services, or new human resource management strategies for clinics and hospitals. Unlike clinical research, which typically develops medical interventions for single diseases, HSR is often not disease-specific. In some instances, systems level interventions may have a particular disease focus, but they frequently address aspects of the health system like human resources or financing that generate impacts across a broad range of diseases, yielding public health improvements. HSR can also be exploratory and descriptive, which means no intervention is actually assessed as part of the research (Gilson, 2012).

The research participants of HSR are often not individuals but groups of people. Interventions are frequently targeted to entire households, clinics, schools, neighbourhoods, or communities. It is not uncommon for the unit of intervention to be different from the unit from which data are collected in HSR. For example, in a study evaluating a conditional cash transfer intervention to improve the uptake of maternal and child health services, the intervention is randomised at the municipality level but evidence on the use of maternal and child health services is collected from individuals (i.e. pregnant women and new mothers within those municipalities) (Morris, Flores, Olinto, & Medina, 2004). This raises the question of whether research participants encompass all members of participating municipalities or the pregnant women and new mothers from whom data is collected (Weijer et al., 2011). In clinical research, the units of intervention allocation and data collection are generally the same: individual human research participants.

Workshop participants felt that these additional dimensions of HSR were sufficient to give rise to a range of ethical considerations in HSR in LMICs that would not necessarily need to be addressed in international clinical research, though they recognised that some ethical issues would be shared. Indeed, numerous ethical questions were put forward by workshop attendees as being relevant to HSR in LMICs that were not as central to the ethics of

international clinical research. Furthermore, they recognised that HSR in LMICs is strongly affected by the context of research and that contexts of scarcity gives acuity to even those ethical issues that are more generally relevant.

Ethical issues associated with features of HSR

To illustrate how certain features of HSR can raise particular ethical considerations, we describe the ethical issues that can arise in HSR in LMICs when the unit of randomisation is not the individual, where the intervention under study is a delivery method, and where the intervention under study is a method of creating demand. In doing so, we do not mean to imply that these ethical issues (and their associated ethical concepts) are *only* relevant when those particular HSR features are present. Other features of HSR (that we do not consider) may generate such issues as well.

Unit of randomisation

Unlike clinical research, HSR is population-focused and, as a result, interventions are often tested by being randomised at the level of the district, community, or health institution rather than the individual level. In instances where the unit of randomisation is not the individual, ethical issues relating to informed consent are raised for HSR that are less straightforward than those arising in clinical studies. Where HSR interventions are allocated to households in particular districts or to health clinics and hospitals across a country, should researchers inform individuals that the study is going on? Should researchers be required to give individual patients or household members a choice to participate in the study? And when is individual informed consent necessary if ‘gatekeepers’ such as government officials, community leaders, school directors, or hospital administrators have already agreed for the intervention to be implemented in their environment or jurisdiction?

In clinical research, the general norm is for research to proceed in most cases with individual informed consent. However, workshop participants pointed out that, for certain systems level interventions, individual consent may be rendered meaningless where it is impossible or extremely difficult to avoid exposure to the intervention such as where a hospital is randomised to a study arm that involves a different type of staffing arrangement for emergency care. They also noted that many HSR studies might meet the criteria for a waiver of consent under the Code of Federal Regulations (CFR) in the USA, but the appropriateness of those criteria for HSR would need to be analysed. Weijer et al. (2011) have previously argued that informed consent may not be required for cluster trials that do not randomise interventions amongst individuals and/or meet CFR waiver requirements. They point out that informed consent requirements only apply to research participants. When an intervention is targeted at a cluster, if patients or community members are only indirectly impacted by the study intervention and if no identifiable private information is collected from them, then they may not meet US regulations’ definition of research participants. As a result, informed consent is not required (Weijer et al., 2011). Meeting CFR waiver requirements means a study poses no more than minimal risk; the rights and welfare of subjects are not adversely affected; the research could not be carried out practicably otherwise; and, when appropriate, subjects will be debriefed. In such instances, informed consent is not seen to be necessary given the low level of risk involved (Weijer et al., 2011).

Beyond relying on existing regulations to determine when informed consent is required, a distinction between informing individuals of study interventions and gaining informed consent was put forward by workshop participants. This distinction is based on an understanding of informed consent as having two components: 1) providing information about a study and the intervention it is testing (where applicable), and 2) obtaining agreement from prospective participants that they will voluntarily enter a study based on that information. Where HSR interventions are not randomised at the individual level, while seeking *consent* from individuals may not be feasible, researchers may still be able to *inform* patients or community members that the study is taking place. By informing patients or community members that a study is going on, these individuals then, in many cases, may have the option *not* to participate and can make the choice to opt-out by, for example, seeking medical care for their illness at a hospital in a non-participating district. (Here, we recognise that, in some cases, opting out may be quite difficult even with prior knowledge of the study, especially for vulnerable groups who cannot afford to alter their behaviours in order to do so. We return to this point later in the section.)

In determining when individual level consent still ought to be required, workshop attendees proposed that researchers might consider whether a study intervention alters the local environment in a way that patients or citizens would normally be consulted about prior to implementation.³ Many decisions are made by government and health authorities that citizens or patients have no say in, or are typically not informed about such as where hospitals alter the management system for their personnel. A continuum of health decision-making was suggested, where decisions fell into the following categories: 1) decisions that are made without government authorities and health administrators informing their citizens or patients (such as biosafety laws), 2) decisions that are made by government authorities and health administrators, where citizens and patients are subsequently informed (such as legislation around health behaviours), 3) decisions that are made with input from citizens and patients (such as health information decisions), and 4) decisions that are made solely on the basis of what citizens and patients say they want (such as health incentive decisions).

Workshop participants felt that, where HSR interventions altered the environment in ways that individuals would not have a say outside of the research environment (i.e. categories 1 and 2), informing people through broad-based disclosure methods, without seeking individual consent, may be ethically appropriate. This would apply even to interventions that alter circumstances in ways that individuals might not normally be told about by government or health officials (category 1). It is necessary to inform individuals about such interventions in order to ensure that they can opt-out if they feel very strongly against an intervention.

Such a strategy, nonetheless, raises further ethical questions that bear consideration like what information should be disclosed to the citizens of particular districts or attendees at a particular hospital where a study takes place? Should people be told simply what the aims of a study are and what kind of intervention is being tested or should they also be fully

³In LMIC contexts, the choice of consent strategy must be informed not only by professional, institutional and environmental norms but also by social and political influences (negative and positive) and by the degree of trust in social/health systems and institutions. This is to reduce the potential for the consent strategy to further legitimise and entrench norms that relate to a lack of transparency in some contexts (Molyneux et al., 2005; Rosenthal, 2006; Upvall & Hashwani, 2001).

informed about the risks and benefits associated with the intervention under evaluation? Should steps be taken to ensure that people, especially members of vulnerable groups, have an available means of opting-out? What features of a study must be in place in instances where people will not be able to easily opt-out? These issues need further discussion in order for appropriate guidance to be developed for governments, researchers, sponsors, and IRBs.

A further consideration that might bear on the decision to inform people rather than to seek individual consent is where, from a cultural standpoint or as a matter of tradition, community members prefer or let the 'community' to make decisions for them. This type of norm may have implications for consent when interventions are applied at a community level in contexts where such tradition is both strong and involves fair process.

Nature of the intervention: Novel delivery methods

Where HSR assesses the efficacy of new delivery methods for particular health services, nuanced ethical issues related to equipoise and the standard of care provided to control/ comparison groups are especially prominent. There was debate amongst workshop participants over when conditions of equipoise actually exist in HSR. The question was raised: if the health care being delivered has been proven effective and the delivery method has been shown efficacious for other medical interventions, are conditions of equipoise met? It was argued that, when there was more than a 50-50 chance that the intervention would work, rather than doing research, the delivery strategy should simply be rolled out by the Ministry of Health and evaluated at baseline and at time points afterwards. Such a comment highlights that the distinction between HSR and programme development and evaluation can get quite blurry. In certain instances, it may not be clear which option is called for. For example, is an efficacy trial or a feasibility evaluation needed when a delivery mechanism has been shown to work multiple times but local policymakers want further evidence that it works in their specific setting?

Here, workshop participants highlight that HSR (where delivery methods are tested) can be associated with equipoise in relation to the delivery method but a lack of equipoise in relation to the health services being delivered. They purported that this has implications for what control groups are owed during HSR. Debate ensued on the matter of whether it is ethical to refrain from providing control groups with access to the health care or services being provided to the comparison (or control) group through the novel delivery mechanism.

On this issue, there was significant division between workshop attendees, with most taking one of two opposing viewpoints—namely, that care is owed or care is not owed. One group felt that control villages, for example, should be provided with health care (through existing delivery mechanisms) if proven medical interventions exist for the condition being researched. This position was grounded in the duty of rescue (Singer, 1972), with workshop participants arguing that if researchers have knowledge that people in the control group will become sick or even die, it is unethical for researchers not to take steps to prevent it, where doing so is not hugely burdensome for them. Those with an opposing view raised two reasons for their position. First, it was asserted that delivering health care to the control group fell beyond the scope of researchers' obligations, suggesting it was the responsibility of the Ministry of Health and local health system. Second, the moral distinction between

acts and omissions—causing harm versus seeing suffering and not doing anything to address it—was also put forward as being applicable here. In effect, some proposed that researchers should only have an ethical obligation to provide care to control villages if they were the primary agents responsible for the people not having access to such care. In making these arguments, workshop participants applied ideas drawn from cosmopolitan approaches to justice from political philosophy. The principle of rescue is a feature of Singer's consequentialist cosmopolitanism and Pogge's human rights cosmopolitanism argues that agents have obligations of rectification where they cause harm to individuals by creating deficits in their human rights (e.g. health) (Caney, 2001; Pogge, 2008; Singer, 1972; Singer, 2009).

To address conditions where equipoise exists for the delivery method but not for the health services being delivered in HSR, a stepped wedge design may be used. Such a design entails progressively rolling out the study intervention (and, in effect, the health care provided with it) to participating villages so that even control villages receive the intervention by the end of a study. Although the study intervention would have been randomised, all villages in a study would have received it in the end. With stepped-wedge designs, however, individuals can still have negative health effects even with delayed provision if there is a time-window for individual benefit. As such, some people in villages that received the study intervention later may still suffer due to a lack of health care, but it may be a lower number than if a stepped-wedge design was not used (assuming the delivery method under study was efficacious). However, by analogy, were the Ministry of Health to take on the responsibility of improving access to health care, any initiative it implemented would likely be progressively rolled out too, and disability or deaths would result in that scenario as well during the roll out.

Aside from issues of equipoise, HSR studies also raised ethical concerns about relying on various types of human resources as a delivery mechanism. For example, workshop participants queried whether it was ethical to use community health workers as a delivery mechanism so frequently in LMIC settings. They suggested that doing so may be an 'escapist approach' that may weaken the local health care system. By encouraging individuals to seek treatment at home, health authorities can avoid having to make improvements at clinics or hospitals. Where new delivery mechanisms rely on health workers, workshop attendees also affirmed that an ethical consideration should be determining what adding new responsibilities to health workers repertoire means for their other responsibilities. Is there an opportunity cost for employing health workers to provide an additional service to community members on top of what they are already doing? This can be assessed by informally talking to people, including current health workers, in the host community or by carrying out exploratory HSR to answer the question. (Conducting exploratory HSR prior to intervention-focused HSR is very much within the field's remit.) If a significant opportunity cost exists, using health workers as a means of delivering a treatment may not be the best option in a particular setting. Under such circumstances, it may not be appropriate to test the intervention in that setting.

Nature of the intervention: Creating demand for existing services

Where HSR assesses the efficacy of interventions that are designed to create population demand, distinctive ethical considerations related to fairness and justice, risk, and autonomy may arise. Being responsive to the particular conditions of host communities or districts means that HSR should develop and test methods to improve access to health services that reflect the specific barriers to access experienced in those settings. Where the study intervention is a financial incentive to promote the use of certain health services, financial barriers to accessing those services should be strongly prevalent in host communities or districts. For example, to ensure the responsiveness of voucher schemes (which are often the focus of demand-oriented HSR), researchers should verify that financial constraints constitute a significant barrier to accessing health services for individuals in host communities or districts. If people are failing to access health services primarily due to other reasons, then a conditional cash transfer intervention may not be appropriate for that context. Exploratory HSR on barriers to health care access may be needed prior to evaluation studies in many settings to determine whether demand-side interventions are indeed responsive to local needs.

Sustainability considerations may also be involved in determining if a financial incentive intervention is appropriate for host communities. Workshop participants queried whether it was sustainable to pay people to access health services over the long-term, particularly in settings with very limited resources. Where would the money come from once external research funding ended? How could governments afford to pay for the programme in the long-term? Introducing and then removing a material incentive for an activity can generate negative consequences if people have changed their behaviours due to the incentive. As a result, if the incentive is not sustainable in a given community, it may be more harmful than beneficial to test it there. In response, it was suggested that the cost of paying people to access services might be less than the costs associated with people not accessing those same services. In the case of a maternal and child voucher programme, for example, a LMIC government might be able to afford to keep the programme running based on the savings generated from not having to address more serious maternal and child health conditions and their associated social and economic costs. To assess the potential sustainability of a demand-side intervention in particular host communities, costing studies could be conducted to provide relevant information for ethical analysis as part of exploratory HSR conducted prior to intervention-focused HSR.

An important risk to consider in studies testing demand-side interventions is their potential to negatively impact the supply-side. Workshop participants questioned the ethics of introducing a demand-side intervention when it was clear that the supply-side would not be able to cope with its effects. They further suggested that, where it is known that increased demand will substantially burden or overwhelm local health services, there is an obligation to strengthen the supply-side as part of the intervention. For these particular contexts, workshop participants recommended redesigning studies, contending that the intervention under study may include a package to strengthen both households' demand for services and the local health care facilities' capacity to supply them. In other contexts, where the risk is

lower, it may be sufficient to include monitoring for supply-side burdens as part of the study design.

Finally, workshop participants considered whether a financial incentive intervention like a voucher programme was autonomy-reducing or autonomy-promoting. In clinical trials, concerns have been raised that offering financial incentives to participate can undermine individual autonomy. People are swayed to behave in ways that they otherwise wouldn't were it not for the monetary inducement. In a recent article, however, London et al. (2012) asserted that, when financial incentives encouraging specific health-promoting behaviours are tested in research, they have the potential to *enhance* individual autonomy. In accordance with this view, workshop participants felt that voucher schemes can strengthen recipients' autonomy if they increase the range of opportunities available to them. Voucher schemes generally afford participants a greater chance to do things that they want to do and that they otherwise would not have been able to achieve such as accessing maternal and child health services.

Additionally, the *intent* behind a financial incentive was identified as being a morally relevant consideration in determining whether the incentive is autonomy-reducing or autonomy-promoting. Where financial incentives serve to entice people to face risks that they otherwise would not, they are more likely to undermine autonomy. Where financial incentives serve to expand individuals' opportunity range and help them achieve goals/benefits that they desire, such incentives can enhance autonomy. Nonetheless, other factors bear consideration such as the motivations of the recipient. A range of motivational states lie between strong aversion and strong commitment to an activity and individuals are often motivationally ambivalent (London et al., 2012). In cases where recipients have a more ambiguous attitude toward an activity being incentivised, it may become less clear if their autonomy is being enhanced or undermined.

Ethical oversight of HSR

Workshop participants raised the concern that, by relying on ethical guidelines for international biomedical research, IRBs may fail to consider how ethical constructs should best be applied to HSR. Suggestions were made to improve IRB oversight of HSR. First, it was recommended that a practical decision guide be developed for IRBs to guide their review of HSR projects in LMICs. Since HSR is a very broad field, there is a lot of variation amongst projects in terms of their features such as, the nature of the intervention being tested, the level of randomisation, and the level of data collection. To perform a comprehensive assessment, IRBs might classify HSR projects according to their features and then consider the ethical constructs associated with each feature. A decision tool containing targeted questions can possibly further guide IRBs on the ethical issues that arise in relation to each construct (Table 1). As different features of HSR may give rise to ethical issues associated with the same constructs, consideration of a single HSR feature cannot be relied upon by IRBs to reach a conclusion on, for example, appropriate consent or the level of risk/benefit in a study. It may also be important for IRBs to consider the interconnectedness of ethical issues raised by different features of HSR.

Second, workshop attendees noted that oversight should be limited to aspects of studies that investigators have control over. Two contrasting scenarios were presented to demonstrate what this might mean in practice. In scenario 1, external researchers are brought in to evaluate a systems level intervention after it has been implemented in a LMIC. The researchers had no control over what the intervention was or which communities were selected to participate in the study; and they are not responsible for delivering the intervention. In scenario 2, external researchers have played a significant role in designing and bringing an intervention into host communities. They have trained local health workers to deliver the intervention and to explain it to the community; and they have been involved in the project at every stage. In this scenario, the IRB has considerable potential for oversight because researchers are in control of all phases of the project. In contrast, in scenario 1, the IRB's ability to require alterations to aspects of the intervention project that are ethically troubling is much weaker. At the workshop, it was suggested that IRBs may limit their analysis to those aspects of studies that researchers are in a position to influence.

Finally, it was recommended that HSR projects involving human subjects be subject to careful IRB oversight, particularly where it is unclear if the project constitutes research or practice. The boundaries between HSR and programme development and evaluation are often not well-defined. Where work is deemed practice-based rather than research-based, it is typically not subject to ethical review, making the distinction seemingly important. However, we take the position that ethical discussions can be helpful, regardless of whether activities are classified as research or practice. This is in accordance with comments made recently by Kass et al. (2013) and MacQueen and Buehler (2004, p. 931) that call for 'developing methods of oversight for public health investigations that are less dependent on the research versus practice distinction and more geared to assessing the level of risk and ensuring ethical conduct.'

A call to action

The workshop described in this paper constituted an effort to *start* a broader discourse on the ethics of HSR in LMICs amongst bioethicists, health system researchers, IRB members, lawyers, and philosophers across countries. A case was made as to why ethical considerations for HSR in LMICs may be particularly nuanced relative to international *clinical* research. A number of specific ethical issues were identified as corresponding to particular features of HSR such as the type of intervention being tested and the level of randomisation. Nonetheless, considerable work remains to be done to further describe the ethically relevant and distinctive features of HSR in LMICs, to identify the ethical issues to which they give rise, and to determine how these issues should be addressed. The features of HSR that we consider in this article do not constitute all the points of divergence between it and clinical research. More investigation of the ethical issues associated with different types of systems level interventions, types of research participants, and methods in HSR is needed. In determining how identified ethical issues might be addressed, we further emphasise that guidance from existing public health ethics frameworks (Kass, 2001; Upshur, 2002; Lee, 2012) may be particularly useful because they are population-based rather than individual-focused. We call for conceptual and empirical work by bioethicists that is informed by HSR practice; additional workshops on HSR ethics that emphasise interaction and discussion and

involve research funders and policymakers; sessions on HSR ethics at conferences on public health, global health, and bioethics; the development of training modules on HSR for IRBs; IRB training on HSR ethics; and the development of ethical guidelines for HSR in LMICs. Each of these activities is needed to fully explore this area of study and to ensure that ethical oversight is appropriate for HSR. We hope this call to action will stimulate an active global discourse on ethics of HSR in LMICs.

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Table 1

Example of key ethical questions pertinent to health systems research in low and middle-income countries

Feature	Potential Questions for Ethical Consideration
Level of randomisation is not the individual	<p>Informed consent</p> <ul style="list-style-type: none"> Does the project meet the requirements for a waiver of consent? <ul style="list-style-type: none"> If yes, would informing individuals of the study be ethically appropriate? If no, should individuals be informed or should consent be sought?
Intervention is a delivery mechanism	<p>Equipoise</p> <ul style="list-style-type: none"> Does equipoise exist for the delivery mechanism? <p>Standard of care for control group</p> <ul style="list-style-type: none"> Will participants in the control group receive the health care or services provided to the intervention group without researchers' intervention? What will happen to participants in the control group if they do not receive the care or services? Should the health care or services provided to the intervention group be provided to the control group? Would a stepped wedge design reduce the risk to the control group? Could it be employed in this study? <p>Risk</p> <ul style="list-style-type: none"> Are community-based personnel being used as a delivery mechanism in the study? What are the opportunity costs of doing so?
Intervention is a financial incentive	<p>Autonomy</p> <ul style="list-style-type: none"> Does the intervention promote autonomy? <p>Risk</p> <ul style="list-style-type: none"> What are the implications of the intervention for the supply-side? Can host communities health systems handle the increased demand caused by the study intervention? How can burdens to the supply-side be minimised? <p>Justice and fairness</p> <ul style="list-style-type: none"> Is a lack of financial resources a significant barrier to performance of the sought after behaviour? How sustainable is the intervention post-study? Who will pay for it and what is the likelihood that it can be sustained long-term?

Source: Workshop participants and authors