'Deliverability of interventions' as a criterion in priority setting for health research: the case of H3 Africa and Gene-Based interventions

John Barugahare, Ph.D., Department of Philosophy, Makerere University, Kampala, Uganda (WIP)

> ***The criterion:*** *'All things being equal, the higher the likelihood that a proposed intervention will be delivered to those who need it, and the sooner it will be delivered, the higher the priority it should be assigned'*

Summary
This case is addressing the following issue: "How should comparative judgements be made about the social value of research (e.g., likelihood, magnitude, distribution of potential benefits)?". The claim to be demonstrated in this case is that in order to improve the likelihood of improving and optimizing health benefits from research, and improving the fairness of their distribution within and between countries, in addition to the existing criteria being used in setting priorities in global health research, the *deliverability* of the proposed interventions in target countries/societies should be taken into consideration.

Brief description of case study context
Sub-Saharan Africa is one of the global regions with some of the worst health opportunities and outcomes[1] and is likely to remain so in the foreseeable future. Hence, there is a need for proposals on how the existing gap in health opportunities can be bridged through priority setting in health research. The goals of setting ethically appropriate priorities in global health research and development are among others, to optimize health impact, social value, and reduce global health inequities[2]. The essence of health equity is *reducing inequalities in health opportunities* easily accessible to individuals and social groups in space and time. With this goal in focus, progress has been made in efforts to develop and implement criteria for ethical priority setting in health research. So far existing evidence indicates that among research funders, the following criteria are used in setting priorities in research funding: The magnitude of the health problem; equity (priority to the sickest, and socially disadvantaged groups); likelihood of meeting scientific aims; reasonableness of research costs; and other benefits or harms[3]. At present, the scope of priority setting in research spans geographical distribution of research opportunities, topics (such as disease categories and disciplines), institutional or individual, sector, among others[4]. However, in the existing categories of considerations, there is no explicit mention or direct implication of the deliverability of the proposed interventions as a criterion.

The Deliverability criterion: This criterion is based on the claim that the social value of research is better realized the easier it is to deliver the researched and developed interventions to those who need them in a timely manner. Precisely, this criterion posits that: *'All things being equal, the higher the likelihood that a proposed intervention will be delivered to those who need it, and the sooner it will be delivered, the higher the priority it should be assigned'.* That is, in assigning priority to the nature of interventions to be developed, we should take into account the factors that will influence the feasibility and ease of wide and timely delivery of an intervention in target countries or communities. The implication of this criterion is that unless it is feasible and easy to widely deliver the developed

interventions in the short run, those interventions which are potential health opportunities for the affected populations will not provide actual health benefits to them in the short-run, and, perhaps in the long-run. Once this happens, it will be difficult to achieve the goal of reducing inequalities in health opportunities globally through health research.

The content and focus of the *deliverability* criterion can be better understood using Amartya Sen's concept of "Conversion Factors"[5]. According to Sen, the concept of conversion factors means the mediating factors between a good and the achievement of the potential utility it offers. It refers to the feasibility and degree in which a person (a society in this case) can transform or translate a resource into well-being. Hence, conversion factors refer to conditions which are necessary in order to convert (potential) opportunities into actual benefits or well-being. For example: possession of a bicycle (a good) presents potential opportunity for traveling faster to one's destination. However, in order for someone to actually travel faster to their destination with a bicycle, they need to have the riding skill, and the built environment that supports the use of bicycles. In this case, the riding skill, and the built environment which supports the use of the bicycle are the conversion factors. This means that for a person living in rugged mountainous area or otherwise without roads, and or, lacks the riding skill, the bicycle is a useless object. They cannot take advantage of the bicycle to move faster to their destination. Until these conditions are realized, the bicycle is not an actual opportunity to move faster to one's destination. What is true of the bicycle in this example, can be true of many health interventions by virtue of their attributes, which require certain conversion factors to enable their wide and immediate implementation in certain geographical contexts.

In the context of health research and the resulting interventions, some of these conversion factors include: medical technological infrastructure and related facilities; the cost of the interventions; the type, quality and spread of skills needed to deliver certain health interventions. Consequently, it is possible to develop interventions which are scientifically efficacious and safe, for diseases and conditions that account for the biggest proportion of mortality and morbidity among the most deserving populations, but at the same time fail to significantly improve their health opportunities, and hence fail to positively impact global health equity. This is especially the case in the short run and it is likely to perpetually remain so even in the long run, unless the criterion of *deliverability of researched and developed interventions* is taken seriously. This possibility is demonstrated using the case of H3Africa and the implementation of the GeneXpert machine in Uganda.

The Case: H3Africa Consortium and Gene-Based Interventions

The Human Heredity and Health in Africa (H3Africa) consortium is part of a global health research effort to apply genomic science and associated technologies to further the understanding of health and disease in diverse populations[6]. Although the consortium is a purely research enterprise, ultimately the data being generated will potentially be used to develop interventions aimed at transforming the health of African populations. The amount of financial resources that have been invested in this consortium suggest that genetics and genomic research is among the priority health research areas, and so are the potential gene-based intervention to be developed from the data being generated. So far in many LMICs, most, and arguably all gene-based interventions, can be categorized as hi-tech interventions. However, it has been indicated that because of their estimated costs, hi-tech interventions such as those which are gene-based are likely to remain difficult to deliver widely among people in LIMCs[7] including those in SSA, at least in the short run. Apart from cost, there is potentially going to be a problem of the technological infrastructure, and the lack of skill-sets requisite for their immediate and timely delivery of those interventions. These three factors and potentially more are what represent the necessary conversion factors for gene-based and other hi-tech interventions in order to increase the health opportunities from such interventions for the SSA populations.

Illustration: Implementation of the GeneXpert Machine/Technology in Uganda: Uganda is one of the countries with a high burden of TB. In 2013, the World Health Organization (WHO) reported that UNITAID invested US$ 25.9 million to purchase over 220 GeneXpert machines, and related supplies

for 21 countries including Uganda. This intervention was estimated to save an additional 62,000 lives per year[8]. The GeneXpert technology is described as being cost-effective at diagnosing TB including at early stage. It also detects genetic traits for resistance to rifampicin, a commonly used TB drug in Uganda. It is also said that the use of the GeneXpert requires minimal laboratory equipment, space technician time, and its users require minimal training and results are available to health workers within two hours[8]. Given its description, the GeneXpert machine is, in principle, an ideal intervention against TB in low resource settings like Uganda because it seems to meet the deliverability criterion in low resource settings. At present in Uganda, there is at least one machine at each of the health Centre IV (County-level health facility) – about 15 Kilometers radius for the farthest individuals who need it.

However, despite the seeming ease of implementing the use of GeneXpert machine/technology, following 10 years of its implementation in Uganda, studies indicate that its wide use has faced a number of challenges. Some of the challenges that have constrained the use of the GeneXpert machine/technology in Uganda include lack of reliable refrigeration services, limited power connectivity and frequent load shedding[9,10]. Generally, access to electricity in Uganda is currently estimated at 67% in urban areas, and 11% in rural areas[11]. In yet another study it was reported that, whereas scientifically the GeneXpert technology is effective, there were certain actions which needed to be taken into consideration to facilitate its wide implementation in Uganda. According to this study, actions that required more funding included the installation of power backups such as solar panels, installation of air conditioners, and procurement of result printers, among others. The study added that installation of facilities which required a lot of funding was not done in the short run, and this affected the performance and routine effectiveness of the GeneXpert laboratories[12].

Discussion: The above case is intended to alert stakeholders in research including those in H3Africa to the need for taking into consideration the needed conversion factors for the interventions that will potentially be developed from the data being generated, especially if such interventions will be intended primarily for sub-Saharan Africa. The illustration with the Uganda case of GeneXpert machine is not intended to advance a claim that the use of the GeneXpert machine in Uganda is sufficiently wide or not, or that the 10 years it has taken to reach its current geographical coverage is short enough to be regarded as timely or too long. The case is also not intended to indicate that GeneXpert is either a low-tech or hi-tech intervention, although its description above suggests that it can be categorized as a low-tech intervention. Rather, the purpose of the case is to illustrate the critical importance of taking into consideration the criterion of *deliverability* of interventions proposed to be researched by bearing in mind the required conditions for their implementation and the degree to which those conditions exist among populations affected by the disease for which such interventions are targeted. This case provides additional evidence to the view that certain interventions are likely to be difficult to deliver widely among many people in LMICs, including poor populations in SSA by virtue of some of the attributes of those interventions which make them difficult to deliver[7,13], at least in the short run. If it has been difficult to implement an arguably low-tech intervention in Uganda, then it can be worse for most hi-tech interventions in many low resource settings.

Apart from the cost of these interventions, there is potentially going to be a problem of technological infrastructure requisite for their implementation. There is yet the lack of the necessary skills to implement such interventions. These three factors – cost, technology and skill-sets – and potentially more are the necessary conversion factors for hi-tech interventions in order to increase the health opportunities of Ugandans and other low resource settings in the short run.

One potential argument in favour of prioritizing hi-tech interventions despite the current economic, technological and skill-set gaps among many LMICs could be based on the optimism that later these interventions will be accessible to the affected populations as their economies, technology and skill-sets improve. The problem with this view is that from the point of view of equity, the relative period each society or social class waits before they can access benefits from certain interventions while others are already accessing them, matters. In discussions of equity in health, the issue is not simply

who should get what, and who should lose out completely. The concept of *equality of opportunity* takes into account who benefits first, and who waits and for how long to benefit from the same opportunity. That is, the longer one society or social class waits to access the needed health interventions while other societies or social classes are accessing it, the deeper the health inequity between those groups. Hence, due to technological constraints and absence of other conversion factors, hi-tech interventions will remain largely inaccessible to most citizens in LMICs who need them in the short run, while such interventions are being accessed in places where the needed conversion factors exist. Hence, if the *deliverability* of interventions is not taken seriously in setting health research priorities, then it means that global health inequity will perpetually stay with us.

Ethical Issues: The outcome of the discussion above is that in order to meet the goal of reducing global health inequities through research, during health research priority setting it is important to take into account the *deliverability criterion*, by ensuring that there are favorable conditions that allow wide timely delivery of the prioritized interventions to be researched. However, there may be some questions which may need to be answered in order to implement the deliverability criterion.

1. What is a reasonable timeframe for the results of research to lead to interventions that can be delivered to those who need them?
2. On whom do obligations to ensure deliverability fall?
3. Should research sponsors or researchers in low-resource settings always prioritize interventions that are deliverable?
4. From the point of view of equity, does the relative time of waiting to access an approved intervention between two societies matter?
5. What potential challenges may be encountered in applying the criterion of deliverability of interventions at the time of reviewing research grants, and how can these be mitigated?

Conclusion and recommendation

Even though interventions which are initially difficult to implement in some settings eventually become easy to implement, on the basis of what equity requires this case illustrates a need to take seriously the *deliverability* criterion in priority setting in global health research. The value of reflecting on this criterion and its related concept of the concept of conversion factors is to alert the stakeholders in priority setting for research to always bear in mind the distinction between actual and merely potential health opportunities, or health opportunities in principle and health opportunities in practice for certain populations. The deliverability criterion leads to an additional consideration to the criteria for priority setting for health research. That is, it suggests a need to complement the questions such as, 'what interventions are safe and efficacious?'; 'what populations deserve priority?; 'what disease categories …'?; among others, with the question of 'what interventions are *deliverable* among which populations?' By way of recommendation, the *deliverability criterion* and its related concept of conversion factors as its enabler should be adopted as a complementary consideration, especially for health research targeting low resource settings. Secondly, there is a need for more empirical evidence on the degree/extent to which attributes of interventions usually constrain their deliverability in low resource settings.

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