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Methodology

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## Adapting Economic Evaluation Methods to Shifting Global Health Priorities: Assessing the Value of Health System Inputs



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## ABSTRACT

*Objectives*: We highlight the importance of undertaking value assessments for health system inputs if allocative efficiency is to be achieve with health sector resources, with a focus on low- and middle-income countries. However, methodological challenges complicated the application of current economic evaluation techniques to health system input investments.

*Methods:* We undertake a review of the literature to examine how assessments of investments in health system inputs have been considered to date, highlighting several studies that have suggested ways to address the methodological issues. Additionally, we surveyed how empirical economic evaluations of health system inputs have approached these issues. Finally, we highlight the steps required to move toward a comprehensive standardized framework for undertaking economic evaluations to make value assessments for investments in health systems.

*Results:* Although the methodological challenges have been illustrated, a comprehensive framework for value assessments of health system inputs, guiding the evidence required, does not exist. The applied literature of economic evaluations of health system inputs has largely ignored the issues, likely resulting in inaccurate assessments of cost-effectiveness.

*Conclusions:* A majority of health sector budgets are spent on health system inputs, facilitating the provision of healthcare interventions. Although economic evaluation methods are a key component in priority setting for healthcare interventions, such methods are less commonly applied to decision making for investments in health system inputs. Given the growing agenda for investments in health systems, a framework will be increasingly required to guide governments and development partners in prioritizing investments in scarce health sector budgets.

Keywords: allocative efficiency, economic evaluation, health systems inputs, methodological challenges, value assessment.

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## Introduction

Global health expenditure reached US \$7.8 trillion in 2013 and is expected to increase above US \$18 trillion by 2040 (2010 purchasing power parity-adjusted dollars) (Dieleman et al<sup>1</sup>). Although the country-level composition of health expenditure varies significantly, the majority of health expenditure is on "Health System Inputs" (HSI), the factors of production serving the broad purpose of facilitating the provision of healthcare interventions and services. For example, expenditure on health workforces often constitute over a third of public health expenditure.<sup>2,3</sup> At the same time, it has long been acknowledged that health system weaknesses in low- and middle-income countries (LMICs) prevent health expenditure from translating into the provision of services and ultimately health improvements (Filmer et al,<sup>4</sup> 2000). Consequently, there is a growing agenda in global health for investments in strengthening health systems (World Health Organization [WHO] and The World Bank, 2017<sup>5</sup>). One manifestation of this agenda is the shifting away from vertical programs and toward financing system-wide investments. In the same way governments and development partners must make prioritization decisions on which healthcare interventions to finance, choices and trade-offs must be made about where to invest scarce health sector budgets in HSI. The magnitude and growth of health expenditure, in addition to the shifting priorities toward investing in strengthening health systems, increases the importance of making informed investment choices for HSI.

Economic evaluation (EE) methods—such as cost-effectiveness analysis (CEA)—are widely used in priority setting for healthcare interventions (the principles of CEA are based on constrained optimization, with the primary objective of maximizing population health gains given a budget constraint. In global health, these gains are frequently measured in disability-adjusted life-years [DALYs] averted, a generic measure of health reflecting both quantity and quality of life. For a comprehensive overview see Drummond et al<sup>6</sup>). Given the severe funding constraints faced by

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many LMICs healthcare systems, these methods provide a useful standardized framework to assess the value of planning and expenditure decisions. The growing popularity and perceived value of these methods has led to international initiatives such as the Disease Control Priorities project—among others—to address the need for evidence by reviewing, generating, and disseminating information on EEs across a wide range of healthcare interventions. EEs have been primarily implemented to inform decisions around the incremental addition (or removal) of healthcare interventions.<sup>6</sup> In LMICs, especially, they have also been used to rank healthcare interventions by their cost-effectiveness to assist in defining health benefits packages<sup>7</sup> (see also Ochalek et al,<sup>8</sup> 2018).

However, such methods have been less readily applied in informing investment and prioritization decisions for HSI, upon which the delivery of healthcare interventions depends. Several studies have undertaken reviews on the impacts of investments in HSI.9,10 However, impact evaluations alone are not sufficient to inform investment decisions, as they provide only a partial assessment of benefit and do not generally facilitate comparison with health opportunity costs.<sup>11</sup> To fully inform decision making for health system investments requires an assessment of value using similar principles to those applied to healthcare interventions (Kreif et al,<sup>12</sup> 2020), that is, comparing health gains with health opportunity costs. Applying the principals of value assessments to HSI is beneficial in the context of a number of decision problems. It could guide expenditure decisions at the aggregate budget level by informing whether committing resources toward HSI should be prioritized over expenditures on healthcare interventions. It could also inform decisions about incremental investments in specific HSI and the allocatively efficient configuration of expenditure from within a given budget for health systems inputs (or subcategories of).

Several obstacles complicate the straightforward application of current EE techniques to this domain. These have, to date, prevented the level of methodological rigor in evidence generation that is increasingly applied to value assessments and decision making for healthcare interventions, being expanded to wider health system investment.<sup>13</sup> In this article, we highlighted the methodological and data-related issues of undertaking EEs/CEAs, which prevent the straightforward application of current methods used for healthcare interventions to enable value assessments for HSI. We argue that this is an area in which far more active research is required. Health economists and system planners are fundamentally concerned with efficiency and improving resource allocation decisions; yet, current EE methods-one of the principal tools used to achieve these goals-are ill-equipped to undertake accurate value assessments for HSI, the largest expenditure items within healthcare systems. Until more authoritative evaluation frameworks provide guidance in undertaking such value

assessments, investment decisions in this critical area will continue to be underinformed.

We present results from a pragmatic rapid review of the literature to examine how assessments of the value of investments in HSI have been considered to date. The review examines both the (limited) theoretical literature, which has proposed early-stage approaches to undertaking value assessments for HSI and empirical studies of EEs of investments in HSI. To the best of our knowledge, this represents the first review of EE for priority setting and resource allocation of HSI and their application in LMICs from a methodological perspective. We conclude by making a case for the importance of the development of protocols for undertaking EEs of HSI. However, we start by briefly clarifying what is meant when we refer to HSI.

## **Defining HSI**

The delivery of healthcare interventions is dependent on a whole range of HSI.<sup>14,15</sup> However, a lack of conceptual clarity has been identified as causing confusion between a number of commonly used terms.<sup>16</sup> This partly stems from the development of several influential yet distinct conceptual health system frameworks.<sup>14,15,17–21</sup>

Two of the most prominent taxonomies come from the World Health Report 2000, which outlines 4 health system functions that determine health system performance: financing, provision of health services, stewardship, and resource generation<sup>20</sup> (Fig. 1). These functions match those highlighted by Murray and Frenk<sup>17</sup> and Papanicolas et al, (2022)<sup>22</sup> in their health system frameworks. An updated framework introduced 6 health system building blocks: leadership and governance, healthcare financing, health workforce, medical products and technologies, information and research, and service delivery<sup>15</sup> (Fig. 2). Spending on these functions or building blocks should constitute 100% of spending in the health sector. Despite differences in terminology, there is a large degree of overlap in the organizational components outlined in both frameworks. Both include components capturing financing and governance. The physical and human inputs required to deliver healthcare interventions are captured by resource generation in the 2000 framework, whereas these are separated into distinct components in the 2007 framework (health workforce, medical products and technologies, information and research, and aspects of service delivery as this component includes health infrastructure).

According to Papanicolas et al, (2022),<sup>22</sup> resource generation "ensures that a health system has all the inputs it needs to function. These inputs take many forms: health workers, medical devices, medical equipment, infrastructure, pharmaceuticals, vaccines, consumables, medical supplies, etc. The role of the

#### BOX 1. Common defining characteristics and features of HSIs.

- HSIs do not directly translate into health benefits.
- HSIs are often defined by their multifunctionality in that they frequently influence the delivery (quantity and quality) of multiple healthcare interventions.
- HSIs must often be generated and/or maintained, ie, they have stock levels and measures of functionality.

• HSIs require capital investments and/or recurrent expenditure.

HSI indicates Health System Inputs.

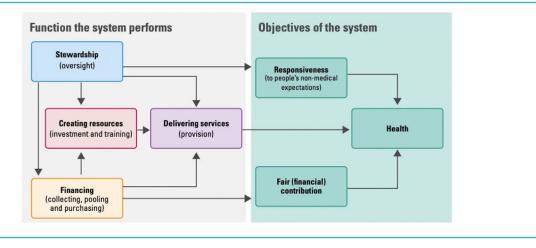
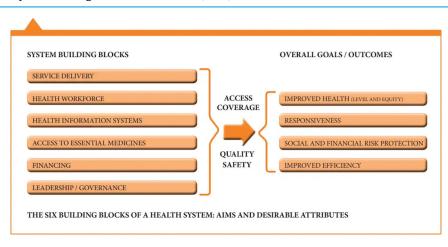


Figure 1. WHO health system functions. Source: Papanicolas et al. (2022).<sup>22</sup>

resource generation function is to ensure that these inputs are produced, procured, made available, or maintained at the place and time they are needed...resource generation [is] a function that brings together all of the health system inputs." The resource generation function has 3 sub-functions: (1) health workforce, (2) infrastructure and medical equipment (it should be noted that the definition of health infrastructure includes all physical structures and supporting systems that operate within the health system, that is, buildings, power and water supply, waste management systems, Information and Communication Technology infrastructure and systems, transport and logistic systems, etc), (3) and pharmaceuticals and other consumables.<sup>20,22</sup> It is the former 2 sub-functions of the resource generation function that we refer to as HSI. As such HSI might be conceptualized as the factors of production that facilitate the delivery of pharmaceuticals and consumables and provision of healthcare interventions (healthcare interventions are defined as "any act performed for, with or on behalf of a person or population whose purpose is to assess, improve, maintain, promote, or modify health, functioning, or health conditions"<sup>23</sup>). The health effect of investments in HSI are mediated through impacts on the delivery of healthcare interventions. For example, praziquantel for treatment of Schistosomiasis represents a specific healthcare intervention, whereas the drug supply chain facilitating its (and other drugs) delivery to health centers represents a HSI. These inputs are typically (although not always) population-based functions, best organized at the system-wide level, and affect health system capacity. Therefore, investments in HSI are primarily about alleviating input constraints to improve outcomes. Box 1 highlights characteristics of HSIs.

We also highlighted a relevant distinction between investment in HSI and investment in health system strengthening (HSS). Chee et al<sup>24</sup> distinguish between HSS and investments in HSI (they use the terminology health system support when referring to investments in health system inputs). They view the latter as "activities [that] improve the system's functionality primarily by increasing inputs," whereas HSS involves going beyond investing in inputs to reforming how health systems operate. They provide examples of investments in HSI such as buying generators for health facilities or improving training of health workers. Whereas HSS would involve creating mechanisms for periodic equipment or skills assessment surveys, complemented with budgets for

Figure 2. WHO Health system building blocks. Source: WHO (2007).<sup>20</sup>



regular equipment maintenance and replacement and training budgets, and so on. Similarly, Kutzin and Sparks<sup>16</sup> view HSS as going investing in inputs, "meaning reforming how the health system actually operates."

Although many of the same issues that complicate EEs for investment in HSI also apply when attempting to undertake value assessments of investment in HSS, there are important differences in modeling complexity, the availability, and generalizability of data on the impacts of HSS required to parameterize the economic and health system models, which make this distinction nontrivial. The methodological implications of the differences between HSI and HSS and specifics of the rationale for this distinction are addressed in the discussion.

# Literature Review: Theory and Empirical Evidence

#### Methodology

Because of the lack of standardized terminology, as illustrated by the numerous distinct health system frameworks, and the overlap in terminology with the extensive program/impact evaluation literature examining the relationship between countrylevel HSI and various health-related outcomes, standard literature review search methods would have resulted in an unmanageable number of studies.

To address this issue, a targeted rapid review approach was employed. The review aimed to capture both methodological articles, outlining the key challenges in conducting EEs for investments in HSI and potentially offer ways of addressing these, and applied articles using EEs to HSI. The purpose of examining applied articles was to identify if any studies had applied any of the methodologies suggested and to further understand the practical challenges of doing so.

The targeted review was conducted, first prior knowledge was used to identify several key known studies examining EEs for investments in HSI. Furthermore, experts in the field were approached and asked to identify any relevant research that addressed this topic. The reference lists for articles identified through these means were reviewed and a snow-balling approach was applied to identify further relevant publications. Additionally, an unstructured search of PubMed was undertaken. Finally, the references collated were shared with experts to identify any known sources that may have been missed to be added to the review. See Appendix A in Supplemental Materials found at https://doi.org/10.1 016/j.vhri.2023.08.005 for typology of articles identified.

It should be noted that because of the search techniques employed, and despite efforts to consult experts, we do not claim to have captured an exhaustive list of all relevant literature. Despite this, we believe the review captures a representative overview that accurately reflects the state of the literature on methods and applications of EEs for investments in HSI.

### **Theoretical Literature**

Recognition of the need to consider HSI and related bottlenecks in resource allocation decisions is not new. Several comparable early nonlinear optimization models were developed to guide health sector resource allocation considering multiple health system constraints.<sup>25–30</sup> These models acknowledge that healthcare interventions often compete for the same limited HSI, such that financial resources are not always the primary delivery constraint. Therefore, they implicitly allow for a calculation of the value of a marginal relaxation of constraints via HSI investments through comparison of the costs and outcomes achievable with the health system constraint imposed with one in which the constraint is relaxed. However, although these models allowed calculation of the value of the marginal relaxation of health system constraints, they were not specific CEAs of HSI investments, thereby not enabling strategic comparisons between expenditures on HSI and healthcare interventions. Building on this approach, Murray et al<sup>31</sup> created a model whereby instead of allocating a fixed proportion of HSI costs to each intervention, interventions are assigned to consume a mix of HSI. Therefore, in addition to healthcare interventions, this optimization model considers investments in HSI directed toward relaxing service constraints as individual investment choices.

Although the above represent wider models of resource allocation, recent literature has incorporated health system constraints into individual EEs of healthcare interventions. Mills et al<sup>32</sup> highlight that an intervention's cost-effectiveness calculated without consideration of constraints should be considered as reflecting the potential cost-effectiveness of what can be achieved in well-functioning health systems. Vassall et al<sup>33</sup> emphasize the importance of considering both demand and supply constraints in evaluating the cost-effectiveness of healthcare interventions, proposing 2 approaches. The first entails calculating the intervention's cost-effectiveness and the cost-effectiveness of activities required to remove implementation constraints separately. They give an example of the introduction of a new malaria diagnostic test with an associated cost-effectiveness, which may or may not be implemented with an enhanced training affecting the cost, benefits and therefore the cost-effectiveness of the diagnostic test. The difference in benefits from implementing health interventions alone or with investments removing HSI constraints is analogous to the difference between intervention "effectiveness" and "efficacy."<sup>34</sup> The second proposes incorporating the cost of removing implementation constraints directly into the costeffectiveness of the intervention. Both obtain the value of investing in health systems relevant to the intervention assessed. Bozzani et al<sup>35</sup> apply the second approach to assessing the costeffectiveness of tuberculosis interventions, whereas Stoppard et al<sup>36</sup> and Hontelez et al<sup>37</sup> model the removal of health system capacity constraints for HIV interventions. There have been calls to incorporate health system constraints as standard practice in future evaluations.<sup>38</sup> Hauck et al<sup>39</sup> provide a typology of constraints that should be considered for incorporation into EEs. Adang<sup>40</sup> suggests including a short- and long-run perspective in CEAs of interventions, with investments in HSI being one potential factor behind differences between them. Similarly, Faria et al<sup>41</sup> propose a framework to value activities to improve implementation of cost-effective interventions accounting for how constraints may change over time. Building on the concept of disaggregated HSI constraints, Revill et al<sup>42</sup> recognize that intervention's costeffectiveness may depend on the use of HSI that are saved or reallocated. These studies, therefore, suggest removing the standard implicit assumption that there is limitless elasticity in the health system to accommodate the introduction of new interventions, explicitly acknowledging that there may be capacity constraints that require addressing and should be incorporated into cost-effectiveness calculations.

However, the above approaches remain healthcare intervention-centric. Although technically allowing for the assessment of the value of investments in HSI, this is done from the perspective of algorithms that attempt to optimize packages of healthcare interventions or from the effect investments inputs have on the implementation and cost-effectiveness of single interventions or intervention packages within disease programs. Assessment of the value of HSI investments is a secondary, often implicit, outcome from the perspective of resource allocation among competing healthcare interventions. Recently, a number of studies have outlined frameworks for undertaking EEs of HSI investments from the same perspective from which one might begin when commissioning an EE of individual healthcare interventions. These frameworks put investments in HSI at the center of the value assessment, instead of being considered and incorporated as part of an evaluation on a healthcare intervention. Studies taking this approach have looked into addressing the unique analytical problems faced in the explicit evaluation of the value of investments in HSI.43-45 In contrast to the above interventioncentric approaches, these have been referred to as the "platform approach."<sup>46</sup> All acknowledge the issue that, unlike healthcare interventions, the health benefits of investments in HSI do not materialize directly. Instead, health benefits are mediated through impacts on the delivery of, often multiple, healthcare interventions. This introduces a key attribution problem in the evaluation of these investments utilizing standard EE frameworks.

Studies taking the "platform approach" depart from treating value assessments of investments in HSI through a diseasespecific or programmatic lens. Because multiple healthcare interventions rely on a common set of HSI, any changes to these inputs will have wide-ranging implications on the total costs, benefits, and, therefore, the cost-effectiveness of numerous interventions. Therefore, these studies recognize the interdependencies between interventions that rely on common HSI and the potential for new interventions to crowd out preexisting services. Subsequently, an important step in all these approaches is identifying healthcare interventions that rely on a common set of HSI and clustering these into groups. Any investment in such HSI could affect all identified grouped interventions. This broader characterization of the links between HSI and sets of healthcare interventions allow for the assessment of the full value of such investments. These articles provide a useful bridge for how we might consider assessing value of investments in HSI adhering to the fundamental principles of EE through the utilization of more general constrained optimization methods, such as those outlined in Crown et al.47

Although the "platform approach" represents a step-forward for how to undertake value assessments for investments in HSI, there remain a number of further issues that require guidance before they can be considered comprehensive theoretic frameworks. Several technical issues introduced, are only briefly considered. For instance, no guidance is provided on how to identify and group healthcare interventions relying on common HSI. Similarly, it is unclear what should represent best practices in the calculation of production functions between HSI and healthcare interventions, which represents key information in the proposed approaches. The complexity of such production functions increases the further HSI are from the delivery of healthcare interventions. These issues represent important considerations that need to be addressed, ideally with a set of standardized best practices.

Recognizing the additional challenges in undertaking value assessments for HSI, Verguet et al<sup>48</sup> propose the development of new analytic models of health systems to enable better value assessments of HSI. They propose priority research areas, which require attention to fill current evidence gaps. Identifying and quantifying the dynamic interactions between HSI will be required to incorporate feedback loops and synergies between HSI, as well as incorporating system-specific constraints affecting the delivery of health services. Once this information is collected, dynamic mathematical models could be used to predict systemwide health impacts and provide estimates of value assessments for input investments (we do not discuss it here, but Madan et al (2020)<sup>49</sup> take an alternative approach, which is based on assessing the value of HSI investments using a "realist evaluation" approach that is much less data intensive).

## **Empirical Literature**

No studies were identified that have operationalized the "platform approach" in empirical EEs of investments in HSI. Empirical EEs of investments in HSI have all taken disease- or program-specific perspective.<sup>50</sup> Impact evaluations of HSI/HSS have largely faced the same issue, potentially leading to the misestimation of the actual impacts by not acknowledging broader affects.<sup>51</sup>

Cleary<sup>50</sup> undertook a review of EEs of investments in HSI identifying 33 studies (in the study, Cleary<sup>50</sup> actually refers to these interventions as HSS). However, 13 were cost or budget impact analysis without any calculation of benefits, whereas 8 reported benefits in natural units (eg, facility deliveries and device uptake) restricting comparability and proper value assessments from taking place. The evaluations presenting results in generic health outcomes (DALYs/quality-adjusted life-years) include 2 voucher schemes incentivizing maternal, child, and delivery services,<sup>52,53</sup> the implementation of guidelines, trainings, and feedback for health workers,<sup>54</sup> the scale up of mental health services,<sup>55,56</sup> a state health insurance program,<sup>57</sup> training for commercial drug retailers,<sup>58</sup> integration of a package of maternal and newborn care,<sup>59</sup> and expansion of health systems toward provision of surgical services.<sup>60</sup> None of the cited studies made attempts to identify the set of healthcare interventions that might be affected. Therefore, cost-effectiveness estimates were based on the narrow disease- or program-specific set of outcomes identified as priorities for the evaluations. Similarly, Hendrix et al<sup>61</sup> undertook a review but only included studies for which an incremental cost-effectiveness ratio was calculable, identifying 27 studies.

Similarly, Vaughan et al<sup>62</sup> undertook a review of EEs of community healthcare workers (CHWs), but all studies identified took the perspective of a single intervention or disease area. Vaughan et al<sup>62</sup> indicate that CHWs in the studies included addressed a number of health areas, including reproductive, maternal and child health, tuberculosis, malaria, malnutrition, and so on. Despite this, none acknowledged or attempted to incorporate the potential impacts on the wider set of healthcare interventions delivered by CHWs. A similar issue is faced with the evaluation of a quality improvement intervention for CHWs in Kenya.<sup>63</sup> Mcpake et al<sup>64</sup> estimate the cost-effectiveness of the introduction of CHWs in 3 countries. Although they include a portfolio of services provided by CHWs in their calculations, they did not attempt to incorporate the wider health system impacts of introducing a new healthcare cadre. The evaluation of CHWs by Escribano Ferrer et al<sup>65</sup> faces a similar limitation.

Several studies have estimated the cost-effectiveness of performance-based financing (PBF) schemes (sometimes referred to as results-based financing or pay for performance schemes) in LMICs<sup>66</sup>; although, using the categories of Chee et al,<sup>24</sup> these are an example of HSS rather than investments in HSI. Borghi et al<sup>67</sup> evaluate a scheme in Tanzania but only consider additional facility births to estimate health benefits, although the scheme incentivized a wider group of interventions. Zeng et al<sup>68</sup> and Salehi et al<sup>69</sup> are more aligned with the "platform approach," through acknowledging the impact of PBF schemes on multiple healthcare interventions and calculating the total benefit as the aggregation of the quality-adjusted life-years. However, both studies acknowledge the schemes incentivized and likely affected several additional healthcare interventions and services not included in their calculations. Recent literature has also

highlighted an important consideration in PBF schemes has been the impact on nonincentivized services.<sup>70</sup> This, again, is an acknowledgment that such schemes affect the service delivery platforms that many different healthcare interventions rely on. As such, although a number of assessments of the value of PBFs have been undertaken using the EE principles, a full value assessment cannot be made without considering the impact on all services that share the common HSI, a principle outlined by the "platforms approach."

LeFevre et al<sup>71</sup> assessed the value of a mobile messaging service by examining changes in utilization of antenatal care visits and childhood immunizations without consideration of the impact on other interventions that utilize these delivery platforms or changes in quality. This method of calculating cost-effectiveness through changes in utilization rates, undertaken by a substantive number of studies, is frequently a result of utilizing the Lives Saved Tool. This results in particularly restrictive assumptions being made about how utilization changes for a subset of interventions translate into generic measures of health benefit. A study that highlights the issues of this approach is Witter et al.<sup>72</sup> They evaluate the cost-effectiveness of a health-system-wide reform based around the removal of user fees for maternal and child services. However, although this likely had system-wide impacts, cost-effectiveness was only calculated using coverage changes of the key maternal and child healthcare interventions made free under the program.

Ochalek et al<sup>8</sup> (2018) allows for the calculation of the value of investing in the removal of constraints that prevent full implementation of healthcare interventions without specifying what type of HSI investments are required. Mohan et al,<sup>73</sup> using the principles of the "platform approach," utilize a linear constrained optimization approach to consider the value of investing in additional health workers to relieve human resource constraints in the delivery of healthcare interventions.

### **Discussion**

There has been a general impetus in the development and adaptation of EEs methods to ensure that they are fit for purpose and the problems faced in global health.<sup>74</sup> Overcoming these methodological challenges is particularly important with the move away from vertical- and disease-specific programming. In fact, limiting the scope of EEs to healthcare interventions may have contributed toward the proliferation of the vertical disease-specific and programmatic approach many health systems adopted in the first place.

This review demonstrates increasing interest, and persistent challenges faced, in undertaking EE to guide investments in health systems inputs. We identify 2 principal factors that complicate calculating estimates of cost-per-DALY-averted for investments in HSI compared with healthcare interventions. It is ultimately the receipt of healthcare interventions that result in health improvements. As such, healthcare interventions are proximal to and directly related to the outcome of interest, health gains. Conversely, the health benefits from HSI are realized only through effects on the delivery of healthcare interventions. Therefore, the distal nature of HSI to the ultimate health gains complicates accurately identifying gains realized from investments. There is a continuum of difficulty in linking investments in HSI with outcomes related to the proximity of the input to health service delivery. For example, an investment to overcome a bottleneck in service delivery, such as in specific transport infrastructure to take HIV diagnostic samples collected at facilities to central laboratories for analyses, with the results returned in a timely manner to

facilities, are relatively straightforward to link to estimates of subsequent health gains. However, many investments in HSI, such as in laboratories themselves that are used by many disease programs, in outbreak surveillance programs or in the health workforce training, involve increasing system-wide capabilities. This introduces problems of interdependencies between services that utilize the same inputs. These factors create an "attribution problem," which prevents the straightforward application of EE methods used for healthcare interventions to enable value assessments for HSI (there is an additional potential issue that investments in HSI may more frequently have a large budget impact. Health opportunity costs are likely to change with investments with nonmarginal budget impacts, which can be problematic for value assessments when using EE methods providing empirical estimates of health opportunity costs based on the marginal productivity of expenditure.<sup>75</sup> This creates another potential issue when applying EE principals and methods to assess investments in HSI. However, this concern is beyond the scope of this article).

The intensification of focus on HSI requires an accompanying improvement in the evidence used to inform and justify investments choices. There is increasing recognition of the importance of undertaking EEs for investments in HSI to guide resource allocation decisions. However, unlike healthcare interventions, there is not currently a well-developed framework and consensus on how to undertake value assessments for such investments. This article presented the case for the importance of undertaking value assessments for investments in HSI, as well as highlighting the additional conceptual and analytical challenges of doing so. Early attempts have been made to outline theoretical approaches and frameworks when considering EEs of investments in HSI; however, a comprehensive framework, comparable with the one guiding EEs of healthcare interventions, is yet to be developed.

Early frameworks continued to revolve around evaluations of individual or packages of healthcare interventions while enabling evaluations of system inputs. Morton et al,<sup>43</sup> Van Baal et al,<sup>44</sup> and Hauck et al<sup>47</sup> provide a starting point for the development of a comprehensive conceptual frameworks for assessing the value of investments in HSI following the principles of EEs. However, work is required to link HSI with service delivery to identify the realization of health gains from investments. This necessitates outlining production functions relating HSI with healthcare interventions. Given this evidence gap, existing empirical evaluations typically report on impacts on only select interventions, without consideration of wider impacts and interactions, inadvertently verticalizing investments in HSI.<sup>6</sup> Therefore, until a more comprehensive theoretic framework is developed outlining criteria and steps for undertaking EEs for HSI (similar to that for healthcare interventions), empirical EEs of HSI investments will likely continue to significantly underestimate the benefits and cost-effectiveness of such investments. Health systems modeling, which could capture dynamic interactions between the availability and quality of HSI and delivery of healthcare intervention, offer particular promise.48

The potential benefits of such modeling go beyond just appropriately valuing the health benefits of investments in HSI. Often modeling these production functions can make efficient use of preexisting evidence. Instead of undertaking resource intensive impact evaluations examining the health impacts of specific investments in HSI, in which large sample sizes and long time horizons are needed to detect effects on rare events (infections avoided, mortality, etc), pragmatic use of preexisting evidence from large-scale randomized controlled trials on the health effects of healthcare interventions can be made. Modeling can link pathways between HSI and healthcare interventions. For many types of HSI, evidence of their relationship with the delivery of healthcare interventions may commonly exist, for example, health worker time in motion studies or impacts of opening healthcare facilities improving access. This still requires that pathways between HSI and all downstream healthcare interventions influenced are modeled, which may, for certain HSI, continue to necessitate the implementation of real-world evaluations to identify the full spectrum of healthcare interventions influenced.

However, when data permit, modeling production functions relating HSI with health benefits although their relationship with healthcare interventions allows for the generation of evidence to inform investment and resource allocation decisions without the need for pilot studies to generate estimates of the health effects of investments in HSI. This movement from "ex-post" evidence generation to "ex-ante" is more compatible with dynamic health system planning. Additionally, such a modeling approach allows for simultaneous consideration of many relevant comparators, enabling comparison of many possible competing investments in HSI (and non-HSI), as opposed to the alternatives considered being limited by the number of pilot studies and impact evaluations that can practically be implemented. The use of secondary data and model-based CEA, as opposed to trial-based analysis, is already well established and provide many benefits for value assessments of healthcare interventions. These methods also offer potential solutions to the idiosyncratic methodological challenges of evaluating investments in HSI.

Although similar methodological issues affect value assessments for both investment in HSI and HSS, the proposed modeling solutions offer greater efficiency gains in terms of leveraging existing data far more readily for the former. Modeling linkages between HSI (ie, physical and human inputs) and the delivery of healthcare interventions is arguably easier, given existing data availability, than modeling how changes in the organizational structure of healthcare systems (ie, HSS), for example, related to governance or financing, affects intervention delivery. As noted by Chee et al,<sup>15</sup> HSS is often a much more holistic and tailored country/system-specific activity "accomplished by more comprehensive changes to policies and regulations, organizational structures, and relationships across the health system building blocks that motivate changes in behaviour." Because HSS will often involve unique and nuanced combinations of activities and reforms, it is unlikely data that might inform how such a reform impacts service delivery are readily available. This would necessitate undertaking impact evaluations for each distinct HSS activity to fully elucidate the breadth of impact and parameterize specific impacts on interventions. Because the scope of impacts from HSS are likely even wider and pathways more complex than HSI, in undertaking evaluations, it may ultimately be easier to directly examine changes in health outcomes, rather than capturing the various effects on HSI and subsequent healthcare service delivery (however, an impact evaluation on the healthcare service delivery effect of investments in HSS activities and reforms should still apply the principle of capturing the effect of HSS on all the healthcare interventions impacted). As such, the type of health system and economic modeling proposed is potentially less immediately beneficial when applied to investments in HSSbecause of this modeling complexity and lower external validity of preexisting data-as it is for decision making regarding investments in HSI. The above provides a rationale for distinguishing between HSI and HSS. The further development of a framework and guidelines clarifying data requirements and modeling approaches will shed light on the circumstances and types of health system investments in which value assessments might feasibly be undertaken.

Until a comprehensive framework is developed, guiding the evidence required and thereby stimulating the generation and collation of such evidence, the same methodological rigor as seen with value assessments and priority setting for healthcare interventions will not be applied to value-for-money assessments for HSI investments. This will continue to act as a significant constraint for improving the allocative efficiency of healthcare budgets globally.

## **Supplemental Material**

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.vhri.2023.08.005.

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## REFERENCES

- Dieleman J, Templin T, Sadat N, et al. National spending on health by source for 184 countries between 2013 and 2040. *Lancet*. 2016;387(10037):2521– 2535.
- Hernandez-Peña P, Poullier J, Van Mosseveld C, et al. Health worker remuneration in WHO Member States. Bull World Health Organ. 2013;91(11):808– 815.
- Hernandez P, Dräger S, Evans DB, Edejer TT, Dal Poz MR. Measuring expenditure for the health workforce: evidence and challenges. Evidence and Information for Policy. Geneva: World Health Organization; 2006.
- Filmer D, Hammer J, Prichett L. Weak links in the chain II: a prescription for health policy in poor countries. *World Bank Res Observer*. 2002;17(1):47–66.
  Healthy systems for universal health coverage – a joint vision for healthy
- Healthy systems for universal health coverage a joint vision for healthy lives. World Health Organization, The World Bank. https://www.uhc2030. org/fileadmin/uploads/uhc2030/Documents/About\_UHC2030/mgt\_arrange mts\_\_\_docs/UHC2030\_Official\_documents/UHC2030\_vision\_paper\_WEB2. pdf. Accessed November 6, 2023.

- Drummond M, Sculpher M, Claxton K, Stoddart G, Torrance G. Methods for the Economic Evaluation of Health Care Programmes. 4th ed. Oxford, United Kingdom: Oxford University Press; 2015.
- Glassman A, Giedion U, Smith P. What's In What's Out: Designing Benefits for Universal Health Coverage. Washington, DC: Brookings Institution Press and Center for Global Development; 2017.
- Ochalek J, Revill P, Manthalu G, et al. Supporting the development of a health benefits package in Malawi. BMJ Clob Health. 2018;3(2):e000607.
- Witter S, Palmer N, Balabanova D, et al. Health system strengthening—reflections on its meaning, assessment, and our state of knowledge. Int J Health Plann Manage. 2019;34(4):e1980–e1989.
- Hatt L, Johns B, Connor C, Meline M, Kukla M, Moat K. Impact of health systems strengthening on health. Health Finance & Governance Project. https://www.hfgproject.org/wp-content/uploads/2016/03/Impact-of-Health-Systems-Strengthening-on-Health-7-24-1.pdf. Accessed November 6, 2023.
- Walker S, Fox A, Altunkaya J, et al. Program evaluation of population- and system-level policies: evidence for decision making. *Med Decis Making*. 2022;42(1):17–27.
- Kreif N, Mirelman A, Love-Koh J, et al. From impact evaluation to decisionanalysis: assessing the extent and quality of evidence on 'value for money' in health impact evaluations in low- and middle-income countries. *Gates Open Res.* 2021;5(1):1.
- Li R, Ruiz F, Culyer A, Chalkidou K, Hofman K. Evidence-informed capacity building for setting health priorities in low- and middle-income countries: a framework and recommendations for further research. F1000Res 2017; 2017;6:231.
- Roberts MH, Berman W, Reich P, Getting M. Health Reform Right: a Guide to Improving Performance and Equity. Oxford, United Kingdom: Oxford University Press; 2008.
- Everybody's business: strengthening health systems to improve health outcomes. WHO's Framework for Action. World Health Organization. https://www. who.int/publications-detail-redirect/everybody-s-business—strengthening-h ealth-systems-to-improve-health-outcomes. Accessed November 6, 2023.
- **16.** Kutzin J, Sparks S. Health systems strengthening, universal health coverage, health security and resilience. *Bull World Health Organ*. 2016;94(1):2.
- Murray C, Frenk J. A framework for assessing the performance of health systems. Bull World Health Organ. 2000;78(6):717–731.
- Arah O, Klazinga N, Delnoiji D, ten Asbroek A, Custers T. Conceptual frameworks for health systems performance: a quest for effectiveness, quality, and improvement. Int J Qual Health Care. 2003;15(5):377–398.
- Atun R. Health Systems, systems thinking and innovation. *Health Policy Plan*. 2012;27(4):iv4-iv8.
- **20.** World Health Organisation. *The World Health Report 2000. Health Systems: Improving Performance.* World Health Organisation; 2000.
- Aday LA. A framework for assessing the effectiveness, efficiency and equity of behavioural healthcare. In: *American Journal for Managed Care*. CE Begley. DR Lairson. CH; 1999.
- **22.** Papanicolas I, Rajan D, Karanikolos M, Soucat A, Figueras J, eds. *Health system performance assessment: a framework for policy analysis.* Geneva: World Health Organization; 2022 (Health Policy Series, No. 57). Licence: CC BY-NC-SA 3.0 IGO.
- International Classification of Health Interventions (ICHI). World Health Organization. https://www.who.int/standards/classifications/internationalclassification-of-health-interventions. Accessed November 6, 2023.
- 24. Chee G, Pielemeier N, Lion A, Connor C. Why differentiating between health system support and health system strengthening is needed. *Int J Health Plann Manage*. 2013;28(1):85–94.
- Feldstein M, Piot M, Sundaresan T. Resource Allocation Model for Public Health Planning: a case study of tuberculosis control. *Bull World Health Or*gan. 1973;48(suppl):110.
- Forgy L. Cost-effectiveness in child health: a minimum information approach to planning and forecasting. In: Hil K, ed. *Child Health Priorities for the 1990s*. Baltimore, MD: Johns Hopkins University Institute for International Programs; 1992:309–335.
- 27. Stinnet A, Paltiel D. Mathematical programming for efficient allocation of health care resources. *J Health Econ.* 1996;15(5):641–653.
- 28. Barnum H, Barlow R. Modelling resource allocation for child survival. *Popul Dev Rev.* 1984;10:367–387.
- **29.** Torrance GT, Thomas WH, Sackett DL. A utility maximization model for evaluation of health care programs. *Health Serv Res.* 1972;7(2):118.
- **30.** Chen M, Bush J. Maximising health system output with political and administrative constraints using mathematical programming. *Inquiry*. 1976;13(3):215–227.
- **31.** Murray C, Kreuser J, Whang W. Cost-effectiveness analysis and policy choices: investing in health systems. *Bull World Health Organ*. 1994;72(4):663–674.
- Mills A, Rasheed F, Tollman S. Strengthening health systems. In: *Disease Control Priorities in Developing Countries*. 2<sup>nd</sup> ed. Washington, DC: The World Bank; 2006;87–102.
- **33.** Vassall A, Mangham-Jefferies L, Gomez G, Pitt C, Foster N. Incorporating demand and supply constraints into economic evaluations in low-income and middle-income countries. *Health Econ.* 2016;25:95–115.
- Schwartlander B, Stover J, Hallett T, et al. Towards an improved investment approach for an effective response to HIV/AIDS. *Lancet*. 2011;377(9782):2031– 2041.

- Bozzani FM, Sumner T, Mudzengi D, Gomez GB, White R, Vassall A. Informing balanced investment in services and health systems: a case study of priority setting for tuberculosis interventions in South Africa. *Value Health*. 2020;23(11):1462–1469.
- Stoppard I, McGillen J, Hauck K, Hallett T. The influence of constraints on the efficient allocation of resources for HIV prevention. *AIDS*. 2019;33(7):1241.
- Hontelez JA, Chang AY, Ogbuoji O, de Vlas SJ, Bärnighausen T, Atun R. Changing HIV treatment eligibility under health system constraints in sub-Saharan Africa: investment needs, population health gains, and cost-effectiveness. *AIDS*. 2016;30(15):2341–2350.
- Mikkelsen E, Hontelez J, Jansen M, et al. Evidence for scaling up HIV treatment in sub-Saharan Africa: a call for incorporating health system constraints. *PLOS Med.* 2017;14(2):1–5.
- Hauck KT, R Smith P. Departures from cost-effectiveness recommendations: the impact of health system constraints on priority setting. *Health Syst Reform*. 2016;2(1):61–70.
- **40.** Adang E. Economic evaluation of innovative technologies in health care should include a short-run perspective. *Eur J Health Econ.* 2008;9(4):381–384.
- Faria R, Walker S, Whyte S, Dixon S, Palmer S, Sculpher M. How to invest in getting cost-effective technologies into practice? A framework for value of implementation analysis applied to novel oral anticoagulants. *Med Deicision Making*, 2017;37(2):148–161.
- Revill PW, Cambiano S, Phillips V, A Sculpher M. Reflecting the real value of health care resources in modelling and cost-effectiveness studies—the example of viral load informed differentiated care. *PLoS One*. 2018;13(1):1–13.
- **43.** Morton A, Thomas R, Smith PC. Decision rules for allocation of finances to health systems strengthening. *J Health Econ.* 2016;49:97–108.
- 44. Van Baal P, Morton A, Severens JL. Health care input constraints and cost effectiveness analysis decision rules. *Soc Sci Med.* 2018;200:59–64.
- **45.** Hauck K, Morton M, Chalkidou K, et al. How can we evaluate the costeffectiveness of health system strengthening? A typology and illustrations. *Soc Sci Med*. 2019;220:141–149.
- 46. Smith P. Evaluating the cost-effectiveness of health system strengthening: a platforms perspective. OHE Seminar Briefing. Office of Health Economics. https:// ideas.repec.org/p/ohe/sembri/002245.html. Accessed November 6, 2023.
- **47.** Crown W, Buyukkaramikli N, Thokala P, et al. Constrained optimization methods in health services research—an introduction: Report 1 of the ISPOR Optimization Methods Emerging Good Practices Task Force. *Value Health*. 2017;20(3):310–319.
- Verguet S, Feldhaus I, Kwete XJ, et al. Health system modelling research: towards a whole-health-system perspective for identifying good value for money investments in health system strengthening. *BMJ Glob Health*. 2019;4(2):e001311.
- Madan J, Kumar M, Taegtmeyer M, Barasa E, Singh S. SEEP-CI: A structured economic evaluation process for complex health system interventions. *Int J Environ Res Public Health*. 2020;17(18):6780.
- Cleary S. Economic evaluation and health systems strengthening: a review of the literature. *Health Policy Plan.* 2020;35(10):1413–1423.
- Adam T, Hsu J, De Savigny D, Lavis JN, Røttingen JA, Bennett S. Evaluating health systems strengthening interventions in low-income and middleincome countries: are we asking the right questions? *Health Policy Plan*. 2012;27(suppl 4):iv9–iv19.
- Alfonso Y, Bishai D, Bua J, Mutebi A, Mayora C, Ekirapa-Kiracho E. Costeffectiveness analysis of a voucher scheme combined with obstetrical quality improvements: quasi experimental results from Uganda. *Health Policy Plan*. 2015;30(1):88–99.
- Kingkaew P, Werayingyong P, Aye SS, et al. An ex-ante economic evaluation of the Maternal and Child Health Voucher Scheme as a decision-making tool in Myanmar. *Health Policy Plan*. 2016;31(4):482–492.
- Barasa E, Ayieko P, Cleary S, English M. A multifaceted intervention to improve the quality of care of children in district hospitals in Kenya: a costeffectiveness analysis. *PLoS Med.* 2012;9(6):e1001238.
- **55.** Chisholm D, Heslin M, Docrat S, et al. Scaling-up services for psychosis, depression and epilepsy in sub-Saharan Africa and South Asia: development and application of a mental health systems planning tool (OneHealth). *Epidemiol Psychiatr Sci.* 2017;26(3):234–244.
- 56. Levin C, Chisholm D. Cost-effectiveness and affordability of interventions, policies, and platforms for the prevention and treatment of mental, neurological, and substance use disorders. In: Patel V, et al., eds. Mental, Neurological, and Substance Use Disorders: Disease Control Priorities. 3rd ed. Washington, DC: The International Bank for Reconstruction and Development/The World Bank; 2016:219–236.
- Gomez GF, Brals N, Nelissen D, et al. Improving maternal care through a state-wide health insurance program: a cost and cost-effectiveness study in rural Nigeria. *PLoS One.* 2015;10(9):e0139048.
- Goodman C, Mutemi WM, Baya EK, Willetts A, Marsh V. The costeffectiveness of improving malaria home management: shopkeeper training in rural Kenya. *Health Policy Plan.* 2006;21(4):275–288.
- **59.** Greco G, Daviaud E, Owen H, et al. Malawi three district evaluation: community-based maternal and newborn care economic analysis. *Health Policy Plan.* 2017;32(suppl 1):i64-i74.
- 60. Mock C, Donkor P, Gawande A. Essential surgery: key messages of this volume. In: Debas H, et al., eds. Essential Surgery: Disease Control Priorities. 3rd

ed. Washington, DC: The International Bank for Reconstruction and Development/The World Bank; 2015:1–19.

- **61.** Hendrix N, Kwete X, Bolongaita S, et al. Economic evaluations of health system strengthening activities in low-income and middle-income country settings: a methodological systematic review. *BMJ Glob Health*. 2022;7(3):e007392.
- Vaughan K, Kok MC, Witter S, Dieleman M. Costs and cost-effectiveness of community health workers: evidence from a literature review. *Hum Resources Health*. 2015;13(1):1–6.
- **63.** Kumar M, Madan M, Auguste P, et al. Cost-effectiveness of community health systems strengthening: quality improvement interventions at community level to realise maternal and child health gains in Kenya. *BMJ Glob Health*. 2021;6(3):e002452.
- 64. McPake B, Edoka I, Witter S, et al. Cost-effectiveness of community-based practitioner programmes in Ethiopia, Indonesia and Kenya. *Bull World Health Organ.* 2015;93:631–639.
- 65. Escribano Ferrer B, Hansen KS, Gyapong M, Bruce J, Narh Bana SA, Narh CT. Cost-effectiveness analysis of the national implementation of integrated community case management and community-based health planning and services in Ghana for the treatment of malaria, diarrhoea and pneumonia. *Malar J*. 2017;16(1):1–18.
- Chi Y-L, Gad M, Bauhoff S, et al. Mind the costs, too: towards better costeffectiveness analyses of PBF programmes. *BMJ Glob Health*. 2018;3(5):e000994.
- Borghi J, Little R, Binyaruka P, Patouillard E, Kuwawenaruwa A. In Tanzania, the many costs of pay-for-performance leave open to debate whether the strategy is cost-effective. *Health Aff*. 2015;34(3):406–414.

- Zeng W, Shepard DS, Nguyen H, et al. Cost-effectiveness of results-based financing, Zambia: a cluster randomized trial. *Bull World Health Organ*. 2018;96(11):760.
- Salehi A, Borghi J, Blanchet K, Vassall A. The cost-effectiveness of using performance-based financing to deliver the basic package of health services in Afghanistan. *BMJ Glob Health*. 2020;5(9):e002381.
- **70.** Sherry T, Bauhoff S, Mohanan M. Multitasking and heterogeneous treatment effects in pay for performance in health care: evidence from Rwanda. *Am J Health Econ.* 2017;3(2):192–226.
- **71.** LeFevre A, Cabrera-Escobar M, Mohan D, et al. Forecasting the value for money of mobile maternal health information messages on improving utilization of maternal and child health services in Gauteng, South Africa: cost-effectiveness analysis. *JMIR MHealth UHealth.* 2018;6(7):e8185.
- 72. Witter S, Brikci N, Harris T, et al. The free healthcare initiative in Sierra Leone: evaluating a health system reform, 2010-2015. *Int J Health Plann Manage*. 2018:434–448.
- **73.** Mohan S, Walker W, Sengooba F, et al. Supporting the revision of the health benefits package in Uganda: a constrained optimisation approach. *Health Econ.* 2023;32(6):1244–1255.
- Lauer JM, Culyer A, A Chalkidou K. What Counts in Economic Evaluations in Health? Benefit-Cost Analysis Compared to Other Forms of Economic Evaluations. World Health Organization. https://www.who.int/publications/i/ item/9789240008878. Accessed November 6, 2023.
- Lomas J, Claxton K, Martin S, Soares M. Resolving the "cost-effective but unaffordable" paradox: estimating the health opportunity costs of nonmarginal budget impacts. *Value Health*. 2018;21(3):266–275.