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Cost analyses of HIV treatment should be standardized and report cost drivers

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The article by Tran *et al.* [1] entitled 'Global estimates for the lifetime cost of managing HIV: a systematic review' describes the lifetime costs of HIV care and treatment, by country income levels, perspective of the cost analysis, and modeling methods. Given the preventive effects of treatment, estimates of the lifetime cost of HIV treatment can be compared with potential investments in both primary prevention and maintaining viral suppression to reduce onward transmission, to determine whether and how those investments may reduce future medical and other costs. This study makes a much-needed contribution to the literature. It provides information that can be used as part of the decision-making process for allocating resources and motivate future investments. Moreover, this systematic review highlights many issues to address in future research.

First, studies of the lifetime costs of HIV treatment should provide more details on major cost components to allow for comparisons across studies. We commend the authors' attempt to present these details in their supplementary table. Yet, the data are sparse, the categories are not consistent between studies and no indication of personnel costs is given. These labor costs will likely vary by country and country income level, and details are needed to transpose costs from one setting to another. It would also enable comparisons to treatment cost studies which do not estimate lifetime costs.

In sub-Saharan Africa, which bears a significant portion of the global HIV burden, total spending on HIV, in 2019, was estimated at \$11.3 billion, of which 40% was funded from domestic public and private sources, whereas the remaining 60% HIV funding came from PEPFAR (39%), the Global Fund (12%), and other international sources (9%) [2]. Large multi-lateral and bilateral donors have programmatic priorities and directives on the use of their funds. Countries whose response to the HIV epidemic is primarily dependent on donor funds are not easily able to steer donated funds toward their own local priorities [3]. Therefore, in providing costs breakdowns, economic analyses in the literature can help

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these countries estimate resource needs and provide them with evidence to align donor funds toward meeting those needs.

Also, providing lifetime cost to treatment may help donors consider how to balance investments in prevention and treatment, especially as new preventive interventions become available, such as long-acting injectable pre-exposure prophylaxis. Also, understanding cost breakdowns can help large donors put pressure on various industries where they influence costs (e.g., drug or assay prices). For example, in 2017, the Bill and Melinda Gates Foundation (BMGF) made a \$20 million investment in OraSure Technologies, Inc., Bethlehem, Pennsylvania, USA, the manufacturer of OraQuick HIV Self-Test to accelerate access to affordable pricing for the HIV self-test. Through this charitable support agreement, BMGF negotiated a unit price of \$2.00 per HIV self-test kit available to 50 countries with high HIV prevalence, for 4 years [4].

Of the 75 studies included in this systematic review, 14 reported some cost components. Where reported, antiretroviral treatment accounted for more than half the lifetime cost. The introduction of additional generic medication can lead to decreasing costs for antiretroviral drugs over time, and budgetary savings to payers [5]. Conversely, we may see innovations in antiretroviral drugs. For example, clinical trials are currently evaluating long-acting injectable anti-retroviral therapy for HIV, which is likely to be more convenient for patients, especially those who face challenges in medication adherence and retention in care [6]. However, these novel therapies are expected to be more expensive than currently available treatments, yet they will likely require fewer visits to healthcare facilities. Even a rough understanding of the major cost drivers in current HIV treatment would allow for forecasting of the cost and cost-effectiveness of new therapies and cheaper generic medications. In addition, it would be helpful to identify if and how studies considered any potential changes to costs in the future.

In addition, the majority of the studies cited in this review are presented from the perspective of the healthcare payer. This perspective does not include relevant non-medical costs, notably patient time and travel costs to seek treatment. Understanding these costs will help guide innovations of HIV programs and improvements in client-centered care. Further, of the studies that took a societal perspective, the authors note 'we expect those who use a societal perspective to include productivity loss but only 50% (6/12) of these studies explicitly mentioned collecting costs related to productivity loss'.

The above gaps strongly call for standardizing costing components of HIV prevention and treatment programs to increase the applicability of economic evaluation for real-life decision-making. We appreciate and echo the author's proposal for the development and use of a standardized checklist of cost items, and the disclosure on cost items included and how they were derived.

Lastly, this article makes an important contribution by providing a comparison of lifetime cost of HIV care and treatment according to the type of decision model (cohort, microsimulation, and other). In spite of the different mathematical approaches underlying these types of models, this analysis indicates that the outcomes (i.e., lifetime treatment

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costs) were not significantly different between types of models. This is a useful finding for modelers and decision-makers who may gauge the validity and comparability of economic analyses based on the approach employed.

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