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Why Maximizing Quality-Adjusted Life Years, rather than Reducing HIV Incidence, Must Remain Our Objective in Addressing the HIV/AIDS Epidemic

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Abstract
With efficacious behavioral, biomedical, and structural interventions available, combination implementation strategies are being implemented to combat HIV/AIDS across settings internationally. However, priority statements from national and international bodies make it unclear whether the objective should be the reduction in HIV incidence or the maximization of health, most commonly measured with quality-adjusted life years (QALYs). Building off a model-based evaluation of HIV care interventions in British Columbia, Canada, we compare the optimal sets of interventions that would be identified using HIV infections averted, and QALYs as the primary outcome in a cost-effectiveness analysis. We found an explicit focus on averting new infections undervalues the health benefits derived from antiretroviral therapy, resulting in suboptimal and potentially harmful funding recommendations.

Keywords
HIV, economic evaluation, economic model, quality-adjusted life years

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Introduction
Since the discovery of the preventive benefits of antiretroviral treatment and other prevention strategies, a combination intervention implementation strategy has been proposed to reduce the public health burden of HIV/AIDS.¹ However, establishing an effective HIV response requires making informed decisions about how best to allocate limited public health funding. Dynamic HIV transmission models can synthesize input data on the spatiotemporal course of an HIV epidemic, as well as incorporate data on existing and emerging HIV care interventions. Model output can then provide comprehensive information to inform decisions about how best to allocate available funding on combinations of HIV treatment and prevention interventions to achieve the greatest health benefit. Modeling can often be the only way to obtain credible evidence of the relative value of combination implementation strategies,
What Do We Already Know about This Topic?

We searched PubMed for papers published in English between January 2000, and January 2017, using the terms “HIV”, “AIDS” “cost-effectiveness analysis”, “health economic evaluation”, and “combination intervention”. Our searches retrieved a myriad of economic evaluations in HIV/AIDS, with some favouring the use of incidence averted as health outcome while some favouring utility-based effectiveness measure (i.e. quality-adjusted life years (QALYs) gained or disability-adjusted life years (DALYs) averted). Many health economic evaluation guidelines have endorsed the QALY/DALY-based approach, yet none of the retrieved studies have explicitly discussed the impacts and implications of selecting one over the other as the health outcome.

How Does Your Research Contribute to the Field?

Using a previously-validated dynamic HIV transmission model, we evaluated all possible combinations of five distinct interventions that were executed in British Columbia, Canada in a cost-effectiveness analysis. This study found using infections averted as the primary outcome resulted in a different set of ‘optimal’ interventions than QALY-based approach.

What Are Your Research’s Implications toward Theory, Practice, or Policy?

Our findings suggest that focusing on averting new HIV infections can lead to sub-optimal decisions as a result of ignoring the health benefits accumulated among the HIV infected population, in particular undervaluing the full benefits of antiretroviral therapy (ART) in mitigating disease progression and mortality among this population. We justified the adoption of QALYs as the basis in assessing the relative value of combination interventions to optimize population health, which is in line economic theory and international best practice guidelines in economic evaluation.

Methods

This case study is built off a model-based evaluation of HIV care interventions presented elsewhere. The model was adapted and extended upon a previously validated dynamic transmission model previously applied to estimate the health benefits of antiretroviral therapy (ART) in mitigating disease progression and mortality among people living with HIV (PLHIV) receiving ART and sustained reductions in morbidity and mortality among individuals at risk of contracting HIV/AIDS than those infected.

We demonstrate the health and equity implications of using HIV infections averted, as opposed to QALYs gained, in judging the relative value of HIV treatment and prevention interventions using a case example from British Columbia (BC), Canada.
benefits and costs of HIV interventions in the United States, BC, and China. The model partitioned the adult population into compartments on the basis of gender, HIV risk behavior, screening status, and HIV infection status, as well as CD4 count, diagnosis, and treatment status among the infected population, and explicitly simulated disease progression, as a function of CD4 count, and the dynamics of HIV transmission through homosexual, heterosexual, and needle-sharing contacts. The model was populated with comprehensive linked health administrative and registry data and validated against 15 external targets. In a prior analysis, we evaluated 5 distinct interventions that were part of a combination implementation strategy executed in BC: HIV testing in hospital, emergency departments (EDs), and outpatient clinic settings, as well as ART initiation and ART retention initiatives. We used observed aggregate-level testing rates and individual-level ART initiation and reinitiation rates during the study period to estimate the independent effects of these interventions. A more detailed description of the model, its inputs and the interventions assessed can be found in a separate manuscript.

In this case study, we take this analysis one step further to assess the impact of all possible combinations of the interventions considered (excluding ART retention interventions, shown to be ineffective in our prior analysis), to compare the optimal sets of HIV care interventions that would be identified using: (a) HIV infections averted, and (b) QALYs as the

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**Figure 1.** Health production functions to select the optimal combination of HIV care interventions in British Columbia, Canada (2011-2038). A, Selection on the basis of infections averted. B, Selection on the basis of QALYs gained. QALY indicates quality-adjusted life years.
primary outcomes in a cost-effectiveness analysis. We con-
considered a total of 15 combinations of interventions, plotting
them according to their incremental cost and benefit, com-
pared to a status-quo scenario with no additional public health
investment. We then plotted health production functions showing the highest valued combinations of strategies for a
range of incremental public health investment over the
28-year study period (3-year intervention implementation
period + 25-year time horizon). Combinations falling under
the production function generated lower health benefits for a
given investment level and were thus weakly dominated
strategies.\(^23\) We plotted the health production functions with
both HIV infections averted and QALYs in the y-axes to
illustrate differences in valuation using these 2 outcome mea-
sures. These results were drawn from the same set of analyses,
focusing on one outcome measure as opposed to the other. A
third-party payer perspective was applied, accounting for
all direct medical and program costs, and we presented all
costs in 2015 CDN at an annual discount rate of 3% for both
costs and QALYs.

According to best practices guidelines, combinations of stra-
tegies lying along the health production function were com-
pared to the next-most resource intensive strategy. The ICERs,
represented by the slope of the lines along the production func-
tion, can be used in combination with the estimated budgetary
impact, communicated in the x-axis, to determine how much a
given jurisdiction is willing and able to commit to HIV care
strategies. The WHO recommends ICERs <1 times gross
domestic product (GDP) per capita per QALY gained to be
considered “highly cost-effective,” and <3 times GDP per
capita per QALY gained to be considered “cost-effective”\(^24\)
(BC GDP per capita: $55,405). In contrast, it has been proposed that the lifetime treatment cost for a person living with HIV/
AIDS (an estimated $420,000 in 2015 CDN)\(^25\) should be the
“cost-saving” threshold for HIV infections averted. A jurisdic-
tion’s budget constraint, however, may force selection of a
strategy below the recommended threshold.

Results

With HIV infections averted in the y-axis, ED testing, ED +
hospital-based testing, all primary care testing and the
combined interventions lie on the health production function
(Figure 1A). In contrast, with QALYs in the y-axis (Figure 1B),
ED testing, ED testing + ART initiation, ED + hospital-based
testing + ART initiation, and the combination of all the inter-
ventions assessed lie on the health production function. If the
funding decision is made without regard for total budgetary
impact, the ICERs comparing increasingly resource-intensive
strategies along the health production functions indicate the
combination strategy would be chosen in both cases, as ICERs
compared to less-intensive strategies are below threshold val-
ues in both cases. An estimated 516 HIV infections would be
averred, including 116 observed in the first 10 years of the
study period, 223 observed in the next 10 years, and 177
observed in the final 8 years. However, if the total available

Discussion

Using HIV infections averted in the denominator of ICER
calculations to assess the relative value of a set of HIV care
interventions resulted in a different set of “optimal” interven-
tions identified, as opposed to the evidence-based standard
QALY. It should be clear from this exercise that using HIV
infections averted in the denominator of the ICER undervalues
the full benefits of ART, fully ignoring the direct, individual-
level health benefits to PLHIV through delaying or reversing
disease progression and thus extending life. We note that while
HIV testing in and of itself provides no immediate health ben-
efit to the individual; diagnosis reduces sexual risk beha-
vior\(^26\) and provides the basis for subsequent linkage to
care, and thus onward transmission. On the other hand, ART
initiation immediately slows disease progression and extends
life, in addition to its secondary preventive benefits.

Decision-making on the basis of cost-effectiveness analyses
estimated with QALYs is not a panacea. Considerable debate rages
on the threshold value of the ICER, or the cutoff we should use to
determine whether interventions should be considered “cost-
effective” or not. A jurisdiction’s “ability to pay,” our selected
approach, is one such possibility,\(^27\) though willingness to pay
and the opportunity cost of displacing existing health services
are other considerations. The debate on the threshold ICER value
will no doubt continue; however, the methodology and theoretical
underpinnings of the QALY-based approach nonetheless have
widespread support in the scientific literature.\(^8,30\)

Although the use of HIV infections averted may hold some
intuitive appeal, the relative value of interventions focused on
HIV, compared to other disease areas, cannot be compared.
Further, while it may be tempting to use the lifetime cost of
medical care for PLHIV as a threshold for HIV infections
averred, this is not technically correct. Via second- and third-
order transmission, incident cases may be averted long after an
intervention is initiated, with costs attributable to HIV infection
only incurred after diagnosis. Therefore, the majority of these
costs may fall outside study time horizons in model-based anal-
yses. Even so, the costs (and benefits) of averted HIV cases are
captured explicitly in a dynamic HIV transmission model, so
considering an intervention “cost saving” if the ICER is below
$420,000/infection averted is patently false. A positive number
in the numerator of the ICER necessarily means higher incre-
mental costs for the intervention compared to the status quo.

Whether used in the denominator of an ICER or otherwise
set as the focal end point of a modeling study, an explicit focus
on reducing HIV incidence is potentially misleading and anti-
thetic to the central principle of health economic evaluation
that resource allocation decisions should be made toward


optimizing the health of the population. Despite the intuitive appeal and apparent momentum of incidence reduction as the primary objective of public health campaigns to address HIV/AIDS, we argue maximizing QALY gains should form the basis for selecting combination implementation strategies to reduce HIV-related morbidity, mortality, and transmission, and thus maximize population health.

**Authors’ Note**
The Localized HIV Modeling Study Group is comprised of Czarina N. Behrends, MPH, PhD, Department of Healthcare Policy and Research, Weill Cornell Medical College; Carlos Del Rio, MD, Hubert Department of Global Health, Emory Center for AIDS Research, Rollins School of Public Health of Emory University; Julia Dombrowski, MD, Department of Epidemiology, University of Washington; Daniel J Feaster, PhD, Center for Family Studies, Department of Epidemiology and Public Health, Leonard M. Miller School of Medicine, University of Miami; Kelly Gebo, PhD, Bloomberg School of Public Health, Johns Hopkins University; Matthew Golden, MD, Division of Allergy and Infectious Diseases, University of Washington; Reuben Granich, MD, International Association of Providers of AIDS Care; Thomas Kerr, PhD, BC Centre for Excellence in HIV/AIDS, Faculty of Medicine, University of British Columbia; Gregory Kirk, PhD, Bloomberg School of Public Health, Johns Hopkins University; Brandon DL Marshall, PhD, Department of Epidemiology, Brown University School of Public Health, Rhode Island, United States; Shruti H Mehta, PhD, Bloomberg School of Public Health, Johns Hopkins University; Lisa Metsch, PhD, Department of Sociomedical Sciences, Mailman School of Public Health, Columbia University; Julio SG Montaner, MD, BC Centre for Excellence in HIV/AIDS, Faculty of Medicine, University of British Columbia; Bohdan Nosyk, PhD, BC Centre for Excellence in HIV/AIDS, Faculty of Health Sciences, Simon Fraser University; Bruce R Schackman, PhD, Department of Healthcare Policy and Research, Weill Cornell Medical College; Steven Shoertaw, PhD, Centre for HIV Identification, Prevention and Treatment Services, School of Medicine, University of California Los Angeles; William Small, PhD, BC Centre for Excellence in HIV/AIDS, Faculty of Health Sciences, Simon Fraser University; Steffanie Strathdee, PhD, School of Medicine, University of California. The funders had no direct role in the conduct of the analysis or the decision to submit the manuscript for publication. British Columbia Ministry of Health; National Institutes of Health/National Institute on Drug Abuse. Comment on The Cost-Effectiveness of Human Immunodeficiency Virus Testing and Treatment Engagement Initiatives in British Columbia, Canada: 2011-2013. Nosyk B, Min JE, Krebs E, Zang X, Compton M, Gustafson R, Barrios R, Montaner JSG; STOP HIV/AIDS Study Group. Clin Infect Dis. 2018 Feb 10;66(5):765-777. The University of British Columbia/Providence Health Care’s research ethics board waived the need for ethics approval and the need to obtain consent for the analysis and publication of the retrospectively obtained and anonymized data for this noninterventional, quality improvement initiative study.

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**Declaration of Conflicting Interests**
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