CME

Bridging the Efficacy–Effectiveness Gap in HIV Programs: Lessons From Economics

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Background: Bridging the efficacy–effectiveness gap in HIV prevention and treatment requires policies that account for human behavior.

Setting: Worldwide.

Methods: We conducted a narrative review of the literature on HIV in the field of economics, identified common themes within the literature, and identified lessons for implementation science.

Results: The reviewed studies illustrate how behaviors are shaped by perceived costs and benefits across a wide range of health and nonhealth domains, how structural constraints shape decision-making, how information interventions can still be effective in the epidemic's fourth decade, and how lessons from behavioral economics can be used to improve intervention effectiveness.

Conclusion: Economics provides theoretical insights and empirical methods that can guide HIV implementation science.

Key Words: HIV/AIDS, economics, behavioral economics, implementation science

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Biomedical advances such as HIV treatment-as-prevention (TasP) and pre-exposure prophylaxis have placed the "End of AIDS" on the global agenda.[1] However, clinical efficacy does not always translate to real-world effectiveness when programs are implemented at scale. For example, despite scientific consensus that a person on antiretroviral therapy (ART) cannot transmit HIV if virally suppressed,[2–4] population trials of Universal Test and Treat (UTT) have had mixed results.[5,6]

Gaps between efficacy and effectiveness reflect not only failures of implementation, the primary target for implementation science,[7,8] but also failures of policy to adequately account for human behavior and structural context in the first place. Economics offers useful, well-established theoretical frameworks for thinking about how people make decisions and the contexts in which people make those decisions. Economic theory—starting, but not ending with rational choice—has been shown to have wide applicability and predictive power, and therefore, it can point toward effective policies and interventions. Economics also offers rigorous empirical approaches to test theoretical predictions using experimental or quasi-experimental designs.

In the past decade, a robust literature in economics has applied these frameworks to understand HIV risk and care-seeking behaviors. Our review highlights several important themes that have emerged from this literature. Perhaps owing to disciplinary boundaries, some of this work has not featured as prominently in global HIV policy debates as one might expect. Our goal is to elevate some of the key insights. As a disclaimer, this review is not intended to be comprehensive. Health economists have made substantial—and well-cited—contributions to debates on cost-effectiveness and priority setting.[9,10] A separate literature has focused on macroeconomic and fiscal aspects of the HIV response.[11] This review rather focuses on studies economists would describe as "empirical microeconomics"—studies that combine tests of behavioral theory with rigorous causal study designs. Because much of the extant economics research on HIV predates the UTT era, we close by highlighting some areas of current work in HIV implementation science that would benefit from an economics perspective.

PEOPLE ARE UTILITY MAXIMIZERS, NOT HEALTH MAXIMIZERS

Many behavior change models outside economics emphasize the process of adopting specific clinically recommended health behaviors.[12–15] Economics shifts the paradigm from convincing a patient to adopt a particular behavior to asking how people actually do behave. Health is but one dimension of many that influence people's decisions. In addition to good health, there are other things that give people satisfaction, or "utility," and obtaining those other things often requires making tradeoffs. In economic theory, people are utility maximizers, not health maximizers.

A foundational principal of economics is that people's behavior reveals their underlying preferences, given the constraints (time and income) and the prices or opportunity costs they face. Because people are assumed to make decisions maximizing their utility, how people do behave is

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how they should behave. This is of course just a starting point: research in "behavioral economics" integrates theory from psychology to explore cases where behavior deviates from what one would expect in the rational model.[16] Still, until revealed otherwise, economists tend to assume that people know what is best for them and are best positioned to choose the optimal course of action. Sometimes an individual's best course of action conflicts with what is best for society, for example, because their behavior has "externalities," that is, positive or negative impacts on the welfare of others, offering a compelling rationale for intervention.

The fact that people trade off health against other sources of utility sometimes results in consequences clinicians do not like. For example, a person may choose to defer starting ART because they are concerned about the repercussions of disclosing their status to their spouse[17] or because transport costs to the clinic are high.[18] A person who is not yet HIV-infected may decide to have more condomless sex, which he enjoys, now that life-prolonging treatment is available.[19,20] A sex worker may choose to have riskier sex because the extra money she earns enables her to buy medicines for a sick child.[21] A person taking ART may choose to take a "drug holiday" because side effects make work difficult.[22] Although their choices run counter to clinical advice, each of these individuals is arguably making the best decisions they can for themselves, given the information they have and the contexts that shape the costs and benefits of their decisions.

Economic research on HIV has been critiqued for a reductionist focus on individual decision-making.[23] Yet it is easy to see in each of these examples how the economic model quickly shifts attention from the individual to the structural factors that shape the contexts and constraints in which individuals make decisions—from gender norms to economic opportunity to drug toxicities. By seeking to understand behavior in context, economics provides a useful counter-weight to more prescriptive models of "behavioral change" common in the clinical and behavioral sciences.[18]

Economic theory provides clear mechanisms for behavior change and offers clear targets for intervention (Table 1). In the classical economic model, health behaviors are influenced by 3 factors: the prices people face; their budget constraint (typically defined by their income or wealth); and their preferences (influenced by the information available to them). In this review (Sections "Costs and benefits: 'it's the

Table 1. Economic Theory and HIV Risk and Care-seeking Behavior

Construct	Definition	Examples in Economics of HIV
Prices	Market value of a good or service, which is what a consumer must pay to purchase it or what a producer can expect to receive for it. In a competitive market, individuals have little control over prices. Taxes and incentives (subsidies) are common approaches to change prices. In addition to the "sticker price" of a good or service, other nonmonetary costs are often conceptualized as affecting prices, eg, the opportunity cost of time spent seeking care instead of working, or productivity losses from side effects.	Condom purchases are responsive to prices, implying a rationale for subsidy given the positive externalities of condom use. Individuals reduce their sexual risk-taking when incentivized to stay STI-free. Sex workers can charge higher prices for riskier sex and the premium for risky sex is often related to underlying HIV prevalence in a region. People experiencing side effects may not adhere to ART, implying that drugs with similar efficacy but fewer toxicities are valuable. Reducing clinic wait times reduces the price of care-seeking, although reductions in price are greater for higher-income people with greater opportunity costs of time.
Budget constraint	Typically conceived as a person's income or wealth, which can be allocated to different goods and services. People cannot consume beyond their budget constraint (except by borrowing against future consumption), and consuming more of one thing means consuming less of something else. Income is determined by a person's education and health, as well as by structural factors such as policy, legal environments, and historical disadvantage.	Unconditional cash transfers reduce reliance on transactional sex for income, leading to lower HIV infection and pregnancy rates. Structural factors such as education policy and legal protections for women's property rights shape HIV risk.
Preferences	The "utility" or satisfaction that people get from different goods and services, in the present and in the future. A person's preferences are encoded in their utility function, which determines the relative utility that people get from different goods and services. People's preferences are based on their beliefs and in turn on the information they have about a good or service. In general, there is diminishing marginal utility the more one consumes, which is the basis of economic arguments for redistribution and insurance.	Preferences may shape behavior with respect to sexual risk-taking and care-seeking. Information on the higher HIV prevalence among older vs. younger men shifted preferences of young women towards younger partners. Beliefs about current HIV status and the likelihood of future HIV infection may shape risk taking, as the benefits of protective action fall if infection is perceived to be inevitable. Information gaps persist, with low knowledge of current biobehavioral approaches to prevention.
Choice architecture	The context in which a choice is made, including the number of options, framing of options as defaults, whether choices are framed as losses or gains, and other factors that lead to deviations from rational behavior.	Making HIV testing opt-out rather than opt-in at health facilities increased testing participation. There is growing recognition that many traditional interventions targeting price, income, and information also affect behaviors through choice architecture.

prices, stupid'," "Constraints on choice," "Preferences, beliefs, and information gaps"), we discuss how these 3 features shape HIV risk and care-seeking behaviors and how different interventions have targeted these elements. We then (Section "Behavioral economics and choice architecture") review lessons from behavioral economics, which focuses on aspects of "choice architecture" (the context in which a decision is made) that lead to predictable deviations from rational behavior. We note that in many cases, interventions combine different theoretical elements. For example, a cash incentive for ART adherence has both price effects (changing the price of the behavior) as well as income effects (increasing the budget constraint) and may also affect behavior by signaling an official endorsement of adherence and encouraging habit formation. We close our review with a discussion (Section "Rigorous evaluation of real-world effectiveness") of empirical methods from economics with implications for implementation science and outline an agenda for economic research on HIV in the UTT era (Section "An agenda for future work on the economics of HIV").

COSTS AND BENEFITS: "IT'S THE PRICES, STUPID"

If there is one generalizable finding from economics, it is that prices influence behavior. Demand for a consumer product, for example, depends on the price of the product. A number of economics studies have shown how prices influence HIV-related behaviors. Evidence from randomized trials has shown that in low-income settings, people's likelihood of using health products and services is highly sensitive to prices—even at very low prices. As is the case for prevention technologies such as bed nets and water filtration products,[24] a recent study shows that prices strongly influence demand for HIV self-tests in Zimbabwe.[25] An important implication of this finding is that particularly when usage of a health product has positive effects on the welfare of others—a positive externality—there is a strong rationale for price subsidies that lower the prices faced by consumers. Indeed, for many HIV prevention and treatment services in sub-Saharan Africa (SSA), prices or user fees are not charged in public sector clinics.

Importantly, it is not only the prices for HIV services that affect demand but also the costs associated with using HIV services such as transportation costs and even the opportunity costs of time taken to seek services.[26] Beyond subsidizing HIV services to the extent that there are user fees, it may thus be necessary to offer incentives to adequately offset these additional costs.[27] When there are positive externalities associated with certain behaviors, economic theory provides a compelling explanation for why subsidies and incentives are warranted. Economic incentives have also increasingly been used to motivate health-seeking behaviors along the HIV care cascade, including circumcision,[28] HIV testing,[29] linkage to care,[30] ART adherence,[31] viral suppression,[32] and retention in care for prevention of mother-to-child transmission.[33] Although these interventions have had mixed success, it is clear that incentives have entered the mainstream of HIV implementation science strategies.[34]

Non-monetary features of health products may also operate as prices. Brennan et al[46] found that Zambian HIV patients who started an ART regimen with Tenofovir were more likely to be retained in care than patients who started on D4T (a more toxic regimen), and Kluberg et al[47] found that shifting from multiple-pill ART regimens to a single-pill fixed-dose combination regimen led to greater patient retention in South Africa.

A separate strand of the economics literature studied the role of prices in the supply of risky sexual behavior. Studies conducted with female sex workers (FSW) in Mexico, Zimbabwe, and Kenya show that the one reason FSW engage in unprotected sex with some partners is that they are compensated more in sexual encounters without condoms than with condoms.[35–37] Because sex workers who insist on safer sex may lose clients; coordinated market-level interventions such as Thailand's 100% condom use campaign may be necessary to reduce HIV spread in markets for sex.

Some studies have sought to intervene directly to change the price of risky sex through financial incentives for not acquiring sexually-transmitted infections (STIs). In Lesotho, Björkman-Nyqvist et al (2018) randomly assigned study participants to a lottery with a large cash payout if they later tested negative an STI. Relative to control participants, the intervention reduced HIV incidence by 21.4% over 2 years. The lottery had greater effects for participants willing to take risks, suggesting such a strategy may be well targeted.[38] In Tanzania, De Walque et al[39] randomized incentives to stay STI-free and found similarly sized reductions in STI prevalence at follow-up among intervention participants. And in Mexico, a pilot trial by Galárraga et al[40] found increased condom-use among male sex workers in Mexico City with an incentive to stay STI-free, although effects did not persist after incentives were removed. Although the scalability of these initiatives is debatable, these studies show clearly that decisions to engage in risky sex are responsive to prices.

The perceived costs and benefits of risky sex are also directly affected by the prevalence of HIV, risk of infection, and the costs of HIV acquisition, which have fallen with increasing access to ART. Economists have found evidence of behavioral disinhibition among HIV-uninfected persons with the introduction of ART in the United States[19] and in Kenya.[20] The presence of competing mortality risks may also shape HIV-related risk behaviors. Oster[43] finds that behavior change in response to rising HIV prevalence was greater in places with lower competing mortality risks. Although HIV treatment may lead to disinhibition, it also directly increases the benefits of care-seeking. In an analysis of nationally representative data from Zambia, Wilson[44] finds that HIV treatment scale-up led to substantial increases in HIV testing. Similarly, in a regression discontinuity design (RDD), Moscoe et al show that when one household member starts HIV treatment because of an eligible CD4 count, other members of the household are more likely to learn their HIV status.[45] Although these may seem like obvious points, the joint scale-up of ART and HIV testing in SSA has made it difficult to disentangle association from impact without rigorous designs.

It bears noting that "price effects" can be complex. An important result regards social tolerance. A naïve model might presume that stigma increases the price of HIV infection and thereby reduces risk behavior. Yet evidence from Malawi suggests that in fact social tolerance for people with HIV is associated with lower risk behavior, including fewer partners and lower likelihood of having extra-marital sex.[41] In the United States, greater tolerance for homosexuals led lower-risk men to enter the pool of potential partners and led sexually active men to substitute away from underground, anonymous sex encounters.[42]

CONSTRAINTS ON CHOICE

Although choices are sensitive to changes in prices, people are also constrained in their decision-making. Several studies of transactional sex in SSA underscore the importance of the budget constraint—or one's economic circumstances—in influencing decisions. Female sex workers in Kenya engaged in more risky sex work when a child was ill, to cover medical expenses.[21] It is not only FSWs who respond to prices and economic conditions but also women in the general population. De Walque et al[48] find higher STI incidence among women experiencing economic shocks—that is, unanticipated income losses—in Tanzania relative to women not experiencing shocks in the same period, with a three-fold increase in transactional sex. While not the sole determinant of women's engagement in transactional sex, economic circumstances do play an important role. Improving access to credit and insurance could buffer the impact of economic shocks and reduce reliance on transactional sex in these settings.

One policy response to this problem is to offer people cash grants that alleviate the budget constraint that influences their decision-making. In a cluster-randomized trial in Zomba, Malawi, Baird et al (2011, 2012) randomized adolescent girls to unconditional cash transfers, to transfers conditional on school attendance, and to control. The girls in the cash transfer arms had lower pregnancy rates, lower HIV and STI prevalence at follow-up, and were less likely to engage in transactional sex.[49,50] The 3-arm study enabled the authors to disentangle the effects of the income transfer from the effects of the condition and found that the effects on HIV prevalence seemed to be driven by income support. The role of income is further supported by a quasi-experimental study of rainfall-related income shocks over 19 African countries. Burke et al[51] find that infection rates for both women and men increased significantly with exposure to droughts, with results among women driven by those engaged in agriculture.

Effects of income are ambiguous, however, and depend on preferences and on who "supplies" and who "demands" risky sex. Although income may reduce risk exposure for women, some studies have found cash transfers increase exposure among men. Kohler and Thornton[52] report that men in Malawi had more condomless sex in the wake of a one-time income transfer, whereas women had less condomless sex. Similarly, Wagner et al[53] found that men had more partners and more unprotected sex with nonprimary partners in response to winning a randomized income lottery.

Beyond direct income transfers, policies targeting deeper structural factors that determine access to resources can shape HIV-related decision-making and provide enabling environments for implementation of HIV interventions.[54] Early in the epidemic, HIV spread most among people with higher education.[55] Yet as information on HIV diffused, condom use increased more rapidly among the better-educated,[56] and the epidemic profile has shifted. Quasi-experimental evaluations have shown that policies to expand secondary schooling reduced HIV risk behaviors in Uganda[57] and incident infections in Botswana,[58] as well as increasing women's labor force participation and reducing early childbearing. Women's legal rights also shape access to resources and constrain choice. Comparing residents of African countries with different marital property rights for women, Andersen (2018) found that being exposed to a common-law legal system (former British colonies) led to lower bargaining power for women, lower rates of condom use, and higher HIV prevalence. To construct a valid control group, the study compared members of the same ethnic group living on either side of national boundaries with different colonial legal regimes in a RDD.[59] These constraints shape patterns of HIV risk and may affect care-seeking behavior as well and should be considered in the design and implementation of HIV programs.

PREFERENCES, BELIEFS, AND INFORMATION GAPS

Preferences are the third key determinant of individuals' decision-making. Understanding people's preferences is critical to design interventions and policies that may bring about desired changes in HIV-related behavior, from uptake of prevention and treatment to engagement in risky sexual behavior. Preferences include one's attitudes toward risk and present-future tradeoffs, as well as one's likes and dislikes. Economists typically think of the latter as being influenced in part by the information one is exposed to. Traditionally, economists like informational interventions because, in a rational choice framework, providing information enables people to form well-informed preferences and to make the best decisions they can, based on those preferences.

It is widely believed in the public health community that information about HIV has fully disseminated. The persistence of risk behaviors—in the context of high reported awareness—is therefore interpreted as evidence that informational interventions do not work. Yet it matters specifically what information is conveyed. HIV education campaigns have often relied on simplistic slogans—AIDS Kills, Abstain-Be Faithful-Condomize, etc—that may not provide the decision-relevant, actionable information needed for people to make informed choices and reduce exposure to risk.

Given the above evidence that "prices matter," it should not be surprising that information on prices can matter too. For example, in a randomized trial in Kenya, Dupas (2013)

provided information to adolescent girls on the relative risks of HIV infection among older vs. younger male partners. In contrast to the traditional ABC messages, which proved difficult for many people to operationalize in their lives, information on relative risks of prevalence led adolescent girls to choose younger partners in lieu of older partners, ostensibly reducing their exposure to HIV. Godlonton et al[60] find evidence of reduced sexual risk-taking among uncircumcised men in Malawi when presented with information that circumcision halves infection risk.

Perhaps one of the most heavily researched questions in economics of HIV is the impact of learning HIV status through HIV testing—a powerful informational intervention—on sexual risk taking. A purely self-interested agent would be predicted to have more unprotected sex upon learning that they were HIV-infected because there is no longer a risk of becoming newly HIV infected. Here, the evidence is mixed. Some studies have found higher STI incidence in people receiving HIV-positive test results.[61,62] However, these studies were conducted before[61] and during the initial stages[62] of ART rollout. Other studies find that people with HIV respond to an HIV-positive test result by having less (rather than more) risky sex.[63,64] One explanation of this behavior is that people have altruistic preferences, valuing the wellbeing of their sex partners.[65] In a pooled analysis of DHS data from 25 countries, Wilson[66] finds that people who are HIV positive and have tested for HIV report lower HIV risk behaviors than people who are HIV negative and have tested for HIV, with the largest effects among married respondents.

Informational interventions do not always change beliefs as intended. For example, Thornton[67] finds in a study in Malawi that although HIV testing affected subjective beliefs about HIV infection in the short term, these differences did not persist at 2 years. Similarly, in a study of young adults in rural South Africa, Bor et al[68] found that a substantial share of respondents who reported they previously tested positive for HIV did not believe that they were HIV infected. Clinical and public health information are only one piece of the broader information set that people consider in forming their beliefs.

Informational interventions can also backfire. The preponderance of "fear appeals," eg, the ubiquitous message that "it only takes one unprotected sex act to become HIV infected," has led to widespread overestimation of transmission risks. Economists have pioneered careful measurement of subjective probabilities—that is, quantitative beliefs about the likelihood of events occurring—which is valuable in understanding what respondents really means by "likely."[69] Although people in rural South Africa perceive the single-act transmission probability to be over 80%,[68] the best estimate from meta-analyses of large cohorts is 0.3%.[70] This may also explain why people believe it is highly improbable that a couple can be serodiscordant. If one partner in a married couple is HIV positive, men in rural Ugandan communities believed it is unlikely that the other partner is HIV negative.[71]

These misperceptions may have behavioral implications. Overestimating transmission risk can lead to fatalism about infection risk and in turn may demotivate behavior change. If infection is perceived to be inevitable, why to take steps to avoid it? Kerwin (2016) randomized people to receive information on the true per-act risk of HIV transmission in Malawi, emphasizing that HIV is harder to transmit than people might otherwise believe. Consistent with fatalism, respondents with high *ex ante* perceived risk of infection reduced their risk behavior in response to this information.[72] In a dangerous feedback loop, fatalism in high-risk populations can lead to very high infection rates.[73,74] Public health authorities have been skittish about disseminating information that HIV transmission rates are low. However, the scale-up of HIV TasP may offers an opportunity to correct misperceptions and reduce fatalistic behavior. Wilson et al[75] found that information on lower transmission risks with circumcision actually reduced sexual risk behavior, contrary to the prediction from a risk compensation model, and suggests that a reduction in fatalism may have made risky behavior seem more costly.

Most economics research makes inferences on people's underlying preferences based on their observed behaviors. However, increasingly, economists have sought to measure preferences directly using discrete choice experiments (DCE). In DCEs, respondents are asked to choose between 2 (or more) interventions that differ across a set of key domains, for example, price, quality, and convenience. By randomly varying intervention attributes and asking respondents to make a series of choices, it is possible to determine preferences for different attributes and which factors are most important in shaping demand. For example, in a DCE on biobehavioral HIV-prevention methods, Quaife et al[76] found that different population groups had different preferences: Men valued prevention methods with low side effects; women valued prevention methods that also protected against pregnancy; and FSW valued methods that also prevented STIs. Although DCEs have been critiqued for relying on hypotheticals, they can be valuable in guiding intervention design.

BEHAVIORAL ECONOMICS AND CHOICE ARCHITECTURE

The standard economic model of individuals as rational decision makers can go a long way toward understanding HIV-related behaviors and identifying effective behavior change interventions. However, some HIV behaviors have required explanations that go beyond the rational model. The contributions of behavioral economics for HIV treatment and prevention has been reviewed in depth elsewhere, including in this journal,[16,77,78] and a full discussion is beyond the scope of this review. Here, we summarize some key insights from behavioral economics with implications for HIV implementation science.

Before proceeding, it is important to recognize that the term "behavioral economics" has been used in the HIV research community as a general descriptor for research on behavior that uses insights from economics, including models of rational decision-making. As our overview above of the

vast literature on the economics of HIV reveals, many facets of behavior can be explained (and modified) using predictions from rational decision-making models. However, others cannot. Within the economics discipline itself, "behavioral economics" typically refers to research that extends beyond rational choice theory, integrating insights from psychology to model predictable deviations from rational behavior.

One recurring theme in behavioral economics is that small changes in clinical practice can have large impacts—much larger than one would typically if one conceived these changes as changes in "price." For example, changing the default option for HIV testing from opt-in to opt-out at health facilities increased testing uptake from 38% to 66%.[79] This intervention may be characterized as a behavioral "nudge," defined as an "aspect of the choice architecture that alters people's behavior in a predictable way without forbidding any options or significantly changing their economic incentives."[80] Many recent HIV guideline changes have had large impacts on behavior by shifting the way choices are framed, while only modestly changing incentives. Offering ART to patients on the same day as diagnosis, rather than after several counseling visits, increased ART uptake from 72% to 97%.[81] Similarly, immediate ART eligibility increased 12-month retention by 18 percentage points relative to deferred eligibility and referral to pre-ART monitoring.[82] By encouraging people to test for HIV or start ART, these interventions may help patients to realize their preferred long-run care-seeking outcomes.

Behavioral economics provides insights as to why these small changes have big impact. Although the benefits of HIV testing and treatment are long term, people disproportionately weigh the immediate costs and benefits they face, leading to procrastination (often described as present-biased decision-making). Although a full accounting of the prices faced by individuals or the beliefs they hold can help explain suboptimal uptake of HIV services, present bias can raise the significance of immediate hassle costs that may seem insignificant in the long run relative to life-saving therapy. These costs can take many forms. Individuals may not seek HIV services that are inconvenient to use or require taking time off from work. People may stop taking ART due to the hassle of adhering to complex regimens.[47] Relatedly, people may avoid HIV testing, status disclosure, and ART initiation because they do not wish to know, and to be reminded daily, that they are living with HIV.[83]

A second theme is that predictable nonrationalities can be built into an intervention design. For example, setting adherence goals that are less than clinically recommended adherence targets but which are perceived to be more achievable can be an impetus to initial behavior change and to positive behavioral feedback cycles.[84] In another example, incentives can be used to support learning and formation of self-perpetuating habits. For example, a time-limited cash transfer to support food security during the first 6 months of ART increased longer-run retention in care and increased intrinsic motivations for adherence.[85,86]

Finally, new research shows that poverty causes stress and consumes mental resources, reducing cognitive bandwidth to make good decisions and leading to less future-oriented decision-making. Bringing people out of poverty—through cash transfers—can reduce stress, enable people to make the best decisions for themselves, and lead to forward-looking behaviors.[87–89] This can be an added rationale for the cash transfer interventions that were discussed earlier. Poverty, therefore, can affect decision-making by constraining choices (as in the rational model of decision making) and psychologically by changing preferences and limiting cognitive bandwidth.

RIGOROUS EVALUATION OF REAL-WORLD EFFECTIVENESS

Finally, one of the strengths of the economics literature on HIV is the use of rigorous quasi-experimental designs and pragmatic trials. If the goal is real-world effectiveness, then it is important to measure it. Although clinical trials are well-suited to demonstration of clinical efficacy, they are not always the best choice for showing real-world impact of programs implemented at scale. For example, although START, HPTN-052, and TEMPRANO showed clinical benefits to immediate ART, the control patients were retained at >97% in each trial, which did not reflect true standard of care. Using a regression-discontinuity design, Bor et al (2017) show that immediate eligibility increased 12-month retention from 21% among patients who deferred ART because they were not yet eligible to 91% among patients induced to start because they had an eligible CD4 count. This real-world behavioral impact of immediate eligibility was not captured by the trials and suggests the benefits of UTT are greater than previously believed. Many of the articles reviewed previously were large-scale policy evaluations using population-representative data and rigorous quasi-experimental designs. The increased availability of programmatic and administrative data and population-representative household surveys will yield even more opportunities for rigorous evaluation of real-world impact.

AN AGENDA FOR FUTURE WORK ON THE ECONOMICS OF HIV

Most work on the economics of HIV has focused on sexual behaviors related to HIV transmission. However, in the current global HIV landscape, questions about sexual behavior have been eclipsed by behavioral questions underpinning the real-world effectiveness of HIV TasP, namely uptake of HIV testing, linkage to care, and long-run adherence retention in and adherence to ART and pre-exposure prophylaxis. The success of HIV TasP hinges on 2 classic behavioral problems: (1) long-run therapeutic management of chronic diseases and (2) control of infectious diseases with positive externalities. Economics has much to contribute on both accounts.

Chronic disease management is challenging because the costs are borne in the present—in the form of daily ART adherence—while the health and nonhealth benefits extend far into the future. The economics literature has provided several conceptual building blocks for further study. With respect to prices, incentives could be used to increase desired behaviors at high leverage points in the care cascade and to

support habit formation. Interventions that reduce the time and transport costs of care-seeking could also increase demand for ART.[18] Income transfers may relieve constraints and increase forward-looking behavior. In addition, qualitative research suggests scope for informational interventions on the lower toxicity of current regimens and the myriad nonhealth benefits of ART.[90–92] Interventions informed by behavioral economics, such as commitment devices and optimal goal-setting could increase present investments in future health. With unmanaged chronic illness leading the global burden of disease,[93] lessons from chronic HIV management could have important implications for other conditions.

The second challenge is that the costs of daily adherence are borne by private actors (people living with HIV), yet substantial benefits accrue to society through reduced transmission risk—a positive externality. For some individuals, particularly those still early in HIV infection, the private benefits may not exceed the private costs, leading to suboptimal uptake of therapy. In economics, the classic approach to solving this problem is to subsidize the socially desired behavior and thereby change the price of adherence. In most countries, governments and donors already heavily subsidize the costs of treatment. Yet, further subsidies (including incentives) may be warranted. Despite concerns about equity and sustainability, there is some evidence for this approach, particularly when integrated with behavioral insights to support habit formation.[31,86] Another approach—as yet untested—would be to focus on preferences and to encourage ART uptake and adherence early in HIV infection by appealing to existing altruistic motivations to avoid transmission.[66]

A third approach would be to focus on information. Oddly, UTT has been implemented without widespread education on the prevention benefits of ART—the primary rationale for the policy. Young adults in rural South Africa grossly underestimate the efficacy of ART in reducing transmission risk.[68] It is only now, more than 5 years after the HPTN-052 trial results were published, that countries are beginning to embrace messaging around TASP, such as "undetectable = untransmittable" or "U = U".[94] A recent community-randomized trial suggests that providing information on U = U could be beneficial due to the role of stigma in "markets" for sex partners. In Tanzania, providing information to communities on the reduction in transmission risk with ART led to lower stigma and increases in HIV testing.[95] Stigma is a rational response to fear of infection. Qualitative research affirms that many people choose not to start ART because they do not wish to signal to potential partners that they are HIV positive.[18] In fact, because U = U, ART should be a signal of low transmission risk. If disseminating U = U information can shift community perceptions, then existing market incentives (to find a safe sex partner) may encourage greater demand for HIV testing, ART uptake, and viral suppression. Moreover, behavior change is likely to be efficient from a targeting perspective because the signaling benefit of ART is greater if a person has a higher previous probability of being HIV infected.

Our review uncovered several lessons from the pre-UTT era which are likely to continue to be important. First, people respond to changes in prices associated with HIV services and behaviors. Mitigating the costs and enhancing the benefits associated with these services and behaviors is an important avenue of intervention. Second, people consider HIV behaviors alongside other competing interests and are not driven purely by the desire to improve their health. These competing interests are shaped by structural factors such an income, education, and legal rights that constrain choice and may need to be addressed independently. Third, there remain significant gaps in knowledge that—if addressed—could translate into behavior change. Fourth, integrating economics with lessons from psychology offers a compelling way forward to support effective implementation of HIV programs.

In summary, economics has theoretical constructs and empirical tools that are of value for implementation science. Theory is valuable for predicting behavioral responses to interventions and suggesting where and how to intervene. Empirical tools, such as quasi-experimental designs, can generate causal evidence in real-world settings. Finally, recognizing that people have goals other than maximizing their health can help guide design of interventions that are more likely to improve wellbeing.

REFERENCES

1. UNAIDS. Fast-Track: *Ending the AIDS Epidemic by 2030*. Geneva, Switzerland: The Joint United Nations Programme on HIV/AIDS; 2014.
2. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med*. 2011;365:493–505.
3. Rodger AJ, Cambiano V, Bruun T, et al. Sexual activity without condoms and risk of HIV transmission in serodifferent couples when the HIV-positive partner is using suppressive antiretroviral therapy. *JAMA*. 2016;316:171–181.
4. Eisinger RW, Dieffenbach CW, Fauci AS. HIV viral load and transmissibility of HIV infection. *JAMA*. 2019;321:451.
5. Iwuji CC, Orne-Gliemann J, Larmarange J, et al. Universal test and treat and the HIV epidemic in rural South Africa: a phase 4, open-label, community cluster randomised trial. *Lancet HIV*. 2018;5:e116–e125.
6. Hayes RJ, Donnell DJ, Floyd S, et al. *Impact of Universal Testing and Treatment in Zambia and South Africa: HPTN071 (PopART)*. Seattle, WA: CROI; 2019:92. Available at: http://www.croiconference.org/sessions/impact-universal-testing-and-treatment-zambia-and-south-africa-hptn071popart. Accessed October 19, 2019.
7. Kitson AL, Rycroft-Malone J, Harvey G, et al. Evaluating the successful implementation of evidence into practice using the PARiHS framework: theoretical and practical challenges. *Implement Sci.* 2008;3:1.
8. Michie S, van Stralen MM, West R. The behaviour change wheel: a new method for characterising and designing behaviour change interventions. *Implement Sci.* 2011;6:42.
9. Eaton JW, Menzies NA, Stover J, et al. Health benefits, costs, and cost-effectiveness of earlier eligibility for adult antiretroviral therapy and expanded treatment coverage: a combined analysis of 12 mathematical models. *Lancet Glob Health*. 2014;2:23–24.
10. Galárraga O, Colchero MA, Wamai RG, et al. HIV prevention cost-effectiveness: a systematic review. *BMC Public Health*. 2009; 9(suppl 1):S5.
11. Haacker M. *The Economics of the Global Response to HIV/AIDS [Internet]*. Oxford, United Kingdom: Oxford University Press; 2016. doi:10.1093/acprof:oso/9780198718048.001.0001.
12. Rosenstock IM. Historical origins of the health belief model. *Heal Educ Behav*. 1974;2:328–335.
13. Ajzen I. From intentions to actions: a theory of planned behavior. *Action Control*. 1985:11–39. doi:10.1007/978-3-642-69746-3_2.
14. Prochaska JO, Velicer WF. The transtheoretical model of health behavior change. *Am J Heal Promot*. 1997;12:38–48.

15. Fisher JD, Fisher WA. The information-motivation-behavioral skills model. In: DiClemente RJ, Crosby RA, Kegler MC, eds. *Emerging Theories in Health Promotion, Practice, and Research: Strategies for Improving Public Health*. San Francisco, CA: Jossey-Bass; 2002:40–70.
16. Linnemayr S, Stecher C. Behavioral economics matters for HIV research: the impact of behavioral biases on adherence to antiretrovirals (ARVs). *AIDS Behav*. 2015;19:2069–2075.
17. Chin YM. Does HIV increase the risk of spousal violence in sub-Saharan Africa? *J Health Econ*. 2013;32:997–1006.
18. Ahmed S, Autrey J, Katz IT, et al. Why do people living with HIV not initiate treatment? A systematic review of qualitative evidence from low- and middle-income countries. *Soc Sci Med*. 2018;213:72–84.
19. Lakdawalla D, Sood N, Goldman D. HIV breakthroughs and risky sexual behavior. *Q J Econ.* 2006;121:1063–1102.
20. Friedman WH. Antiretroviral drug access and behavior change. *J Dev Econ*. 2018;135:392–411.
21. Robinson J, Yeh E. Transactional sex as a response to risk in Western Kenya. *Am Econ J Appl Econ*. 2011;3:35–64.
22. Papageorge NW. Why medical innovation is valuable: health, human capital, and the labor market. *Quant Econom*. 2016;7:671–725.
23. Johnston D. *Economics and HIV: The Sickness of Economics [Internet]*. New York, NY: Routledge; 2013. doi:10.4324/9780203768709.
24. Dupas P. Getting essential health products to their end users: subsidize, but how much? *Science*. 2014;345:1279–1281.
25. Chang W, Matambanadzo P, Takaruza A. Effect of prices, distribution strategies, and marketing on demand for HIV self-test kits in Zimbabwe: a randomized clinical trial. *JAMA Netw Open*. 2019;2:e199818.
26. Chimbindi N, Bor J, Newell ML, et al. Time and money: the true costs of health care utilization for patients receiving "free" HIV/tuberculosis care and treatment in rural KwaZulu-natal. *J Acquir Immune Defic Syndr*. 2015;70:e52–e60.
27. Galárraga O, Genberg BL, Martin RA, et al. Conditional economic incentives to improve HIV treatment adherence: literature review and theoretical considerations. *AIDS Behav*. 2013;17:2283–2292.
28. Thirumurthy H, Masters SH, Rao S, et al. Effect of providing conditional economic compensation on uptake of voluntary medical male circumcision in Kenya: a randomized clinical trial. *JAMA*. 2014;312:703.
29. Bygrave H, Mtangirwa J, Ncube K, et al. Antiretroviral therapy outcomes among adolescents and youth in rural Zimbabwe. *PLoS One*. 2012;7: e52856.
30. Maughan-Brown B, Smith P, Kuo C, et al. A conditional economic incentive fails to improve linkage to care and antiretroviral therapy initiation among HIV-positive adults in cape town, South Africa. *AIDS Patient Care STDS*. 2018;32:70–78.
31. Linnemayr S, Stecher C, Mukasa B. Behavioral economic incentives to improve adherence to antiretroviral medication. *AIDS*. 2017;31:719–726.
32. El-Sadr WM, Donnell D, Beauchamp G, et al. Financial incentives for linkage to care and viral suppression among HIV-positive patients. *JAMA Intern Med.* 2017;177:1083.
33. Yotebieng M, Thirumurthy H, Moracco KE, et al. Conditional cash transfers and uptake of and retention in prevention of mother-to-child HIV transmission care: a randomised controlled trial. *Lancet HIV*. 2016; 3:e85–e93.
34. Bassett IV, Wilson D, Taaffe J, et al. Financial incentives to improve progression through the HIV treatment cascade. *Curr Opin HIV AIDS*. 2015;10:451–463.
35. Jakubowski A, Omanga E, Agot K, et al. Large price premiums for unprotected sex among female sex workers in Kenya: a potential challenge for behavioral HIV prevention interventions: to the editors. *J Acquir Immune Defic Syndr.* 2016;72:e20–e22.
36. Elmes J, Nhongo K, Ward H, et al. The price of sex: condom use and the determinants of the price of sex among female sex workers in eastern Zimbabwe. *J Infect Dis*. 2014;210(suppl 2):S569–S578.
37. Gertler P, Shah M, Bertozzi SM. Risky business: the market for unprotected commercial sex. *J Polit Econ*. 2005;113:518–550.
38. Nyqvist MB, Corno L, de Walque D, et al. Incentivizing safer sexual behavior: evidence from a lottery experiment on HIV prevention. *Am Econ J Appl Econ*. 2018;10:287–314.
39. de Walque D, Dow WH, Nathan R, et al. Incentivising safe sex: a randomised trial of conditional cash transfers for HIV and sexually transmitted infection prevention in rural Tanzania. *BMJ Open*. 2012;2: e000747.
40. Galárraga O, Sosa-Rubí SG, Kuo C, et al. Punto seguro: a randomized controlled pilot using conditional economic incentives to reduce sexually transmitted infection risks in Mexico. *AIDS Behav*. 2017;21:3440–3456.
41. Delavande A, Sampaio M, Sood N. HIV-related social intolerance and risky sexual behavior in a high HIV prevalence environment. *Soc Sci Med*. 2014;111:84–93.
42. Francis AM, Mialon HM. Tolerance and HIV. *J Health Econ.* 2010;29: 250–267.
43. Oster E. HIV and sexual behavior change: why not Africa? *J Health Econ.* 2012;31:35–49.
44. Wilson N. Antiretroviral therapy and demand for HIV testing: evidence from Zambia. *Econ Hum Biol*. 2016;21:221–240.
45. Moscoe E, Bor J, Tanser F, et al. *Does HIV Treatment Availability Encourage People to Learn Their HIV Status?* Seattle, WA: CROI; 2017: 960.
46. Brennan AT, Bor J, Davies MA, et al. Medication side effects and retention in HIV treatment: a regression discontinuity study of Tenofovir implementation in South Africa and Zambia. *Am J Epidemiol*. 2018;187: 1990–2001.
47. Kluberg S, Fox MP, LaValley M, et al. *Single-Pill ART and Retention in Care: A Regression Discontinuity Study in S. Africa.* Boston, MA: CROI; 2018.
48. de Walque D, Dow WH, Gong E. Coping with risk: the effects of shocks on reproductive health and transactional sex in rural Tanzania. *Policy Res Work Pap*. Washington DC: The World Bank; 2014.
49. Baird SJ, Garfein RS, McIntosh CT, et al. Effect of a cash transfer programme for schooling on prevalence of HIV and herpes simplex type 2 in Malawi: a cluster randomised trial. *Lancet*. 2012;379: 1320–1329.
50. Baird S, McIntosh C, Ozler B. Cash or condition? Evidence from a cash transfer experiment. *Q J Econ*. 2011;126:1709–1753.
51. Burke M, Gong E, Jones K. Income shocks and HIV in Africa. *Econ J*. 2014;125:1157–1189.
52. Kohler H-P, Thornton RL. Conditional cash transfers and HIV/AIDS prevention: unconditonally promising? *World Bank Econ Rev*. 2012;26: 165–190.
53. Wagner Z, Gong E, de Walque D, et al. The impact of positive income shocks on risky sexual behavior: experimental evidence from Tanzania. *AIDS Behav*. 2017;21:650–654.
54. Schwartländer B, Stover J, Hallett T, et al. Towards an improved investment approach for an effective response to HIV/AIDS. *Lancet*. 2011;377:2031–2041.
55. Fortson JG. The gradient in sub-saharan Africa: socioeconomic status and HIV/AIDS. *Demography*. 2008;45:303–322.
56. de Walque D. How does the impact of an HIV/AIDS information campaign vary with educational attainment? Evidence from rural Uganda. *J Dev Econ*. 2007;82:686–714.
57. Alsan MM, Cutler DM. Girls' education and HIV risk: evidence from Uganda. *J Health Econ*. 2013;32:863–872.
58. De Neve JW, Fink G, Subramanian SV, et al. Length of secondary schooling and risk of HIV infection in Botswana: evidence from a natural experiment. *Lancet Glob Health*. 2015;3:e470–e477.
59. Anderson S. Legal origins and female HIV. *Am Econ Rev*. 2018;108: 1407–1489.
60. Godlonton S, Munthali A, Thornton R. Responding to risk: circumcision, information, and HIV prevention. *Rev Econ Stat.* 2016;98:333–349.
61. Gong E. HIV testing & risky sexual behaviour. *Econ J*. 2014;125:32–60.
62. Baird S, Gong E, McIntosh C, et al. The heterogeneous effects of HIV testing. *J Health Econ.* 2014;37:98–112.
63. De Paula A, Shapira G, Todd PE. How beliefs about HIV Status affect risky behaviors: evidence from Malawi. J Appl Econ. 2014;29:944–964.
64. Fedor TM, Kohler H-P, Behrman JR. The impact of married individuals learning HIV status in Malawi: divorce, number of sexual partners, and condom use with spouses. *Demography*. 2015;52:259–280.
65. King R, Lifshay J, Nakayiwa S, et al. The virus stops with me: HIV-infected Ugandans' motivations in preventing HIV transmission. *Soc Sci Med*. 2009;68:749–757.
66. Wilson N. Altruism in preventive health behavior: at-scale evidence from the HIV/AIDS pandemic. *Econ Hum Biol*. 2018;30:119–129.
67. Thornton RL. HIV testing, subjective beliefs and economic behavior. *J Dev Econ*. 2012;99:300–313.
68. Bor J, Barofsky J, Flanagan D, et al. *Beliefs About the Benefits of HIV Treatment in the Era of Treat All*. Population Association of America

Annual Meeting; Denver, CO; 2018. Available at: https://paa.confex.com/paa/2018/meetingapp.cgi/Paper/22950. Accessed October 19, 2019.
69. Delavande A, Kohler HP. Subjective expectations in the context of HIV/AIDS in Malawi. *Demogr Res*. 2009;20:817–874.
70. Boily MC, Baggaley RF, Wang L, et al. Heterosexual risk of HIV-1 infection per sexual act: systematic review and meta-analysis of observational studies. *Lancet Infect Dis.* 2009;9:118–129.
71. Ndyabakira A, Chamie G, Emperador D, et al. Men's beliefs about the likelihood of serodiscordance in couples with an HIV-positive partner: survey evidence from rural Uganda. *AIDS Behav*. 2019. doi:10.1007/s10461-019-02531-7.
72. Kerwin J. Scared straight or scared to death? The effect of risk beliefs on risky behaviors. *SSRN*. 2016. doi:10.2139/ssrn.2797493.
73. Kremer M. Integrating behavioral choice into epidemiological models of AIDS. *Q J Econ.* 1996;111:549–573.
74. Sterck O. HIV/AIDS and fatalism: should prevention campaigns disclose the transmission rate of HIV? *J Afr Econ.* 2014;23:53–104.
75. Wilson NL, Xiong W, Mattson CL. Is sex like driving? HIV prevention and risk compensation. *J Dev Econ*. 2014;106:78–91.
76. Quaife M, Eakle R, Cabrera Escobar MA, et al. divergent preferences for HIV prevention: a discrete choice experiment for multipurpose HIV prevention products in South Africa. *Med Decis Making*. 2018;38:120–133.
77. Linnemayr S. Behavioral economics and HIV: A review of existing studies and potential future research areas. In: *Behavioral Economics and Healthy Behaviors: Key Concepts and Current Research*. Hanoch Y, Barnes A, Rice T, eds. Routledge Taylor & Francis Group; 2017. doi:10.4324/9781315637938.
78. Linnemayr S, Rice T. Insights from behavioral economics to design more effective incentives for improving chronic health behaviors, with an application to adherence to antiretrovirals. *J Acquir Immune Defic Syndr*. 2016;72:e50–e52.
79. Montoy JCC, Dow WH, Kaplan BC. Patient choice in opt-in, active choice, and opt-out HIV screening: randomized clinical trial. *BMJ*. 2016;532:h6895.
80. Thaler R, Sunstein C. *Nudge: Improving Desicions Abouth Health, Wealth and Happiness.* New York, NY: Penguin; 2008. doi:10.1007/s10602-008-9056-2.
81. Rosen S, Maskew M, Fox MP, et al. Initiating antiretroviral therapy for HIV at a patient's first clinic visit: the RapIT randomized controlled trial. *PLoS Med*. 2016;13:e1002015.
82. Bor J, Fox MP, Rosen S, et al. Treatment eligibility and retention in clinical HIV care: a regression discontinuity study in South Africa. *PLoS Med*. 2017;14:e1002463.
83. Kaler A, Watkins S. Asking God about the date you will die: HIV testing as a zone of uncertainty in rural Malawi. *Demogr Res*. 2010;23:905–932.
84. Huang H, Linnemayr S. *A Spoonful of Sugar: The Effect of Small Lottery Incentives on Medication Adherence Among HIV-Positive Youth in Uganda*. Santa Monica, CA: Pardee RAND Graduate School; 2017.
85. McCoy SI, Njau PF, Czaicki NL, et al. Rationale and design of a randomized study of short-term food and cash assistance to improve adherence to antiretroviral therapy among food insecure HIV-infected adults in Tanzania. *BMC Infect Dis*. 2015;15:490.
86. Czaicki NL, Dow WH, Njau PF, et al. Do incentives undermine intrinsic motivation? Increases in intrinsic motivation within an incentive-based intervention for people living with HIV in Tanzania. *PLoS One*. 2018;13:e0196616.
87. Haushofer J, Fehr E. On the psychology of poverty. *Science*. 2014;344:862–867.
88. Haushofer J, Shapiro J. The short-term impact of unconditional cash transfers to the poor: experimental evidence from Kenya. *Q J Econ*. 2016;131:1973–2042.
89. Mani A, Mullainathan S, Shafir E, et al. Poverty impedes cognitive function. *Science.* 2013;341:976–980.
90. Thirumurthy H, Zivin JG, Goldstein M. The economic impact of AIDS treatment: labor supply in western Kenya. *J Hum Resour*. 2008;43:511–552.
91. Baranov V, Kohler HP. The impact of AIDS treatment on savings and human capital investment in Malawi. *Am Econ J Appl Econ*. 2018;10:266–306.
92. Bor J, Tanser F, Newell ML, et al. In a study of a population cohort in South Africa, HIV patients on antiretrovirals had nearly full recovery of employment. *Health Aff*. 2012;31:1459–1469.
93. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380:2095–2128.
94. Calabrese SK, Mayer KH. Providers should discuss U=U with all patients living with HIV. *Lancet HIV*. 2019;6:e211–e213.
95. Derksen L, Van Oosterhout J. Love in the time of HIV: testing as a signal of risk [internet]. 2019. Available at: https://sites.google.com/site/lauraderksen/research. Accessed October 19, 2019.