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Serosorting and the evaluation of HIV testing and counseling for HIV prevention in generalized epidemics

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Introduction

UNAIDS and the WHO recognize the importance of HIV Testing and Counseling (HTC) as a gateway to both treatment and prevention (1). Many studies aimed at identifying behavioral changes following HTC have, however, registered only modest reductions in risk behaviors: change –if any– is most commonly reported by women, HIV positives, and in serodiscordant couples. This is also the gist of the review of early studies from predominantly Europe and North America (2–4), and a review of seven studies set in developing countries (5). More recent studies from sub-Saharan Africa, summarized in Table 1, largely corroborate these conclusions. The most ambitious HTC impact evaluation studies target reductions in HIV incidence, but none have been detected so far (6–8). In serodiscordant couples, however, HTC is associated with a reduction in HIV transmission (9).

Skeptics argue that the meager benefits of HTC for HIV prevention will dilute further as efforts are mounted to increase HTC uptake. First, it is argued that the tested population will become less self-selective, and therefore less inclined to behavioral change (10). Second, some observers anticipate that the scaling up of HTC will affect the quality of counseling sessions, thereby reducing opportunities to promote behavioral change (11). We argue that this pessimistic outlook on the role of HTC in fostering behavioral change is premature. Existing studies may have under-estimated the preventative effects of HTC because they conceptualize behavioral change largely in terms of the ABC behaviors (abstinence, faithfulness and condom use), and because they almost exclusively measure the effects of HTC at the individual level (Table 1).

There is ample evidence that individuals in sub-Saharan African countries are not confined to the ABCs when developing strategies to lower their exposure to HIV: some divorce an infected or unfaithful spouse (12–14), some discuss prevention measures with their primary partners (15, 16), and others deploy –sometimes elaborate– rules to choose new partners they deem safe(r) (12, 13, 17). One such strategy that has garnered less attention is *serosorting*; a practice whereby individuals seek partners of the same HIV serostatus and that was first described in men who have sex with men (MSM) in concentrated epidemics (18–21). Despite possible drawbacks –serosorting is not a foolproof preventative strategy (22–25) and HIV positives are at risk of infection with multiple strains of the virus (26)– serosorting and its associated changes in sexual networks could mitigate the spread of HIV (27–30). Serosorting has hardly been studied in generalized heterosexual epidemics, and we use it as a case in point to argue that new study designs are needed to evaluate the impact of HTC on (risky) sexual behaviors and the spread of HIV.

Serosorting in generalized epidemics

To date, the evidence for serosorting in populations with generalized epidemics is anecdotal or restricted to in-depth studies of small samples. Examples of match-making agencies or events for HIV positives have been reported in the popular press for Ethiopia, India, Kenya, South Africa and Zimbabwe (31–35). In northern Nigeria and eastern Uganda HIV/AIDS support groups have been described as partnership markets for HIV positives (36, 37). Whereas these examples and initiatives serve the niche markets of HIV positives, premarital screening for HIV is likely to increase seroconcordant unions of both negatives and positives. In Kenya, personal advertisements in newspapers and magazines now often make reference to the HIV status of the seeker and desired partner (38). More formal efforts at premarital testing are usually driven by faith-based organizations. Some churches in the Democratic Republic of Congo, Nigeria and Rwanda have made HIV testing prior to marriage mandatory (39–41).

Among MSM, the key motives for serosorting include a need for intimacy and comfort in sexual partnerships, and a desire to engage in unprotected sex (42). The rationale for serosorting in populations with generalized heterosexual epidemics is probably similar. Condom use is undesirable in stable heterosexual relationships because it questions the trust between partners, and even in casual encounters condoms are often perceived as an obstacle to sexual pleasure (13, 43, 44). Other advantages of serosorting depend on the serostatus of the partners practicing it. Through serosorting, HIV negatives can maximize their long-term health outcomes without compromising their reproductive ambitions. HIV positives, on the other hand, may seek seroconcordant partners out of altruistic considerations, or, because it removes the uncertain consequences (including rejection, divorce and violence (14, 37, 45)) of disclosing HIV positive status to a partner of unknown or HIV negative status. The companionship of a partner with the shared experience of living with HIV/AIDS is also an important motivation to form seroconcordant HIV positive partnerships (37).

Given the relatively low HTC coverage rates in countries with generalized epidemics, serosorting may not have played an important role in the early development of the HIV epidemic, but a few Demographic and Health Surveys (46–48) suggest that this may be changing rapidly, particularly in high HIV prevalence settings. The percentage of women ever tested (including receipt of test results) and tested within the last 12 months were 54.8% and 28.6%, 40.7% and 21.9%, and 35.3% and 18.5% for Namibia (2006), Swaziland (2006–07) and Zambia (2007), respectively (46–48). Because provider initiated HTC is now often integrated with antenatal care, the testing coverage rates are usually higher for women than for men, but these statistics suggest nonetheless that the conditions for the large scale application of serosorting are increasingly being met. The scale-up of ART also extends the (healthy) life expectancy of HIV positives, thus leading to increased numbers of HIV positives on partnership markets.

Serosorting and the flaws of existing study designs

There is currently no quantitative evidence for either the prevalence of serosorting or the effects of serosorting in generalized epidemics because the sexual behavior surveys in these settings are not appropriately designed to detect those. Among MSM in concentrated epidemics, studies of serosorting have been based on information provided by survey respondents on their partner(s)' HIV status at the time of last sex or at the time of relationship formation (19, 20). More rigorous investigations have used contact tracing designs in which partners of an index case were located and enrolled in the study (49). A comparable sensitivity for partner characteristics has not been sufficiently incorporated in studies of generalized heterosexual epidemics in developing countries. A step in the right

direction has been made by the HTC efficacy studies with a focus on couples and couple counseling. Not surprisingly, these studies have consistently identified higher ABC type behavioral changes (e.g., condom use) in serodiscordant couples (9, 50, 51). These studies usually limit the analysis to existing partners, however, and do not incorporate the characteristics of new partners that are acquired following HTC.

The omission of serosorting (and of partner characteristics more generally) from HTC impact evaluation studies in generalized epidemics may lead to bias in HTC efficacy estimates for two reasons. The first is equivalent to an omitted variable bias: individuals who are aware of their own and their partners' serostatus may not find it useful to take precautionary measures if their HIV status is concordant, but are more likely to make behavioral adjustments if they are serodiscordant. The omission of this interaction with partner's HIV status will bias estimates of HTC efficacy towards zero. A similar observation has been made in the context of condom effectiveness studies (52).

Second, HTC efficacy studies have narrowly focused on the detection of differences in individual behaviors and differences in HIV incidence between testers and non-testers. The total effects of HTC, however, unfold at the level of *sexual networks and populations*. For example, a man who tests positive during HTC may deliberately seek an HIV positive partner. By taking two HIV-infected individuals "off the market", this serosorted relationship will reduce the likelihood that a susceptible person forms a serodiscordant partnerships and will thus lead to declines in HIV incidence. Similarly, if a man who tests negative purposefully seeks (and finds) a seroconcordant partner, then there will be fewer susceptibles available for mixing with HIV-infected individuals. Serosorting thus leads to what economists label *externalities*, i.e., a situation in which the behavior of one person not only affects the person practicing this behavior, but also others to whom he may or may not be directly connected (see (53) for a related argument).

The presence of such externalities violates the assumption of non-interference between study units; a central assumption of experimental designs (54). Through induced changes in sexual partnership networks, individuals in the non-tested or control arm of such studies are (likely positively) affected by HTC. Whereas experimental designs with random assignment of individuals to HTC have been presented as the gold standard of research on HTC efficacy, they are particularly vulnerable to this design flaw. Interference between study units generally leads to under-estimates of the efficacy of an intervention.

Concluding remarks

In this review we argued that the effects of HTC on risk behaviors and exposure to HIV could be significantly larger or at least more complex than previously thought. The example of serosorting has allowed us to highlight a number of important flaws in study designs commonly used to investigate the association between HTC and risk behaviors in generalized epidemics. Not accounting for serosorting implies that we miss a potentially important preventative effect of HTC in its own right, and possibly that we misjudge the effects of HTC on ABC-type markers of behavioral change. The source of many of these problems is the failure to recognize that the effects of HTC may extend beyond the person who underwent testing. In other words, studies of behavioral adjustments following HTC cannot be disaggregated to the individual or even couple level, but should in principle take communities as the unit of analysis (see (55) for an example). In addition, these studies should be longitudinal with sufficiently long follow-up periods because the effects of some of the seroadaptive behaviors will unfold over the course of months, possibly years.

Because existing studies probably underestimate the true impact of HTC on behavioral change, they ultimately lead us to undervalue the rationality of the actors under threat of

HIV infection. Whereas MSM in developed countries are often portrayed as assertive agents who have adopted some of the advocated protective behaviors (e.g., condom use), ignored others (e.g., abstinence and monogamy), and developed a few of their own (e.g., serosorting) (56), that same degree of agency is not usually attributed to the men and women facing HIV/AIDS in developing countries. In those settings, studies are usually designed to assess the extent to which individuals respond to the classic prevention messages of abstinence, faithfulness and condom use. This constraint and the partial results that ensue are likely to undermine the fragile policy support for HTC scale up for preventative purposes.

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Table 1
Description of selected HTC efficacy studies in sub-Saharan Africa and their main findings

Study, Year	Setting	Outcome measures	Study design	Comparison group	Main findings
Roth <i>et al.</i> (57), 2001	Kigali (Rwanda)	<ul style="list-style-type: none"> Unprotected sex with main partner Coercive sex 	<ul style="list-style-type: none"> Observational study Prospective study of women recruited at prenatal and pediatric wards whose partners were subsequently enrolled Unit of analysis: couples Non-random selection of participant, non-random assignment to HTC 	<ul style="list-style-type: none"> Before after comparison of couples where men received male-focused HTC 	<ul style="list-style-type: none"> Rates of unprotected sex decreased for all, except for seroconcordant negative couples Lower rates of coercive sex in couples with at least one HIV positive partner
Allen <i>et al.</i> (50), 2003	Lusaka (Zambia)	<ul style="list-style-type: none"> Condom use 	<ul style="list-style-type: none"> Observational study Prospective cohort of serodiscordant couples Unit of analysis: couples Non-random selection of participants, non-random assignment to HTC 	<ul style="list-style-type: none"> Seronegative couples Before-after comparison of serodiscordant couples 	<ul style="list-style-type: none"> Condom use increased following HTC Condom use increased more in serodiscordant than in seroconcordant negative couples
Matovu <i>et al.</i> (58), 2007	Rakai (Uganda)	<ul style="list-style-type: none"> Condom use Number and type of partners HIV incidence 	<ul style="list-style-type: none"> Observational study Prospective HIV-negative cohort Unit of analysis: individual Random selection of study participants, non-random assignment to HTC 	<ul style="list-style-type: none"> Comparison of first-time acceptors, repeat acceptors and those who refused HTC, all living in the same communities 	<ul style="list-style-type: none"> Higher level of condom use in HTC acceptors, no difference between first-time and repeat acceptors More inconsistent condom use in repeat acceptors than in non-acceptors of HTC First-time acceptors of HTC reported fewer multiple partnerships in the last 6 months than non-acceptors, no difference for repeat acceptors No difference between groups in terms of non-regular partners No differences between groups in HIV incidence

Study, Year	Setting	Outcome measures	Study design	Comparison group	Main findings
Mola <i>et al.</i> (59), 2006	Beira and Chimoio (Mozambique)	<ul style="list-style-type: none"> Condom use by partner type Intercourse with casual partners 	<ul style="list-style-type: none"> Observational study Prospective cohort of VCT center clients Unit of analysis: individual Non-random selection of participants, non-random assignment to HTC 	<ul style="list-style-type: none"> Visitors to general outpatient clinics (e.g., general medicine and antenatal care) 	<ul style="list-style-type: none"> Larger increases in condom use in the HTC group compared to the control group Larger increases in condom use in HIV positives than negatives No change in intercourse with casual partners
Arthur <i>et al.</i> (60), 2007	Thika and Nairobi (Kenya)	<ul style="list-style-type: none"> Number of sexual partners Condom use by partner type (primary vs. non-primary partner) Self reports of STI symptoms 	<ul style="list-style-type: none"> Observational study Prospective cohort of VCT center clients Unit of analysis: individual Non-random selection of participants, non-random assignment to HTC 	<ul style="list-style-type: none"> Before-after comparison of VCT center clients 	<ul style="list-style-type: none"> Reduction of the number of sexual partners Increased (albeit low level of) condom use Reduction in reported STI symptoms
Sherr <i>et al.</i> (8), 2007	Manicaland (Zimbabwe)	<ul style="list-style-type: none"> Age at first sex Lifetime number of partners, by partner type (regular vs. casual), Condom use, by partner type Concurrent partnerships HIV Incidence 	<ul style="list-style-type: none"> Observational study Population-based open cohort study Unit of analysis: individual Random selection of participants, non-random assignment to HTC 	<ul style="list-style-type: none"> VCT non-acceptors residing in same communities as HTC acceptors 	<ul style="list-style-type: none"> Increased condom use with regular partners among HIV+ women Increased risk-taking among HIV negatives No difference in HIV incidence between testers and non-testers
Corbett <i>et al.</i> (6), 2007	Harare (Zimbabwe)	<ul style="list-style-type: none"> HIV incidence 	<ul style="list-style-type: none"> Cluster-Randomized controlled trial of intensive HTC provision at the workplace Prospective cohort or seronegative employees Unit of analysis: individual and groups of businesses Selection criteria for businesses unknown, 	<ul style="list-style-type: none"> Workers in businesses allocated to standard HTC services by external providers 	<ul style="list-style-type: none"> No difference in HIV incidence between control and intervention groups

Study, Year	Setting	Outcome measures	Study design	Comparison group	Main findings
Cremn <i>et al.</i> (61), 2010	Manicaland (Zimbabwe)	<ul style="list-style-type: none"> New sexual partner <12 months Sex in the last month Multiple concurrent partners Condom use Visits to beer halls 	<ul style="list-style-type: none"> Observational study Population-based open cohort study Unit of analysis: individual Random selection of participants, non-random assignment to HTC 	<ul style="list-style-type: none"> Non testers living in the same area 	<ul style="list-style-type: none"> Reduction in the number of new partners in HIV+ and HIV- women No other behavioral changes recorded
Huchko <i>et al.</i> (62), 2009	Kisumu (Kenya)	<ul style="list-style-type: none"> Composite measure of risk behavior (based on information on sex with non-spouse, unprotected sex with non-spouse, anal sex, transactional sex) 	<ul style="list-style-type: none"> Cross-sectional observational study with self reports of past HTC Unit of analysis: individual Random selection of participants, non-random assignment to HTC 	<ul style="list-style-type: none"> Non testers living in the same area 	<ul style="list-style-type: none"> Women who had HTC in the last 1 to 2 years has reported less risk behavior in the past 12 months Men who had HTC reported more risk behaviors in the past 12 months
Turner <i>et al.</i> (63), 2009	Zimbabwe and Uganda	<ul style="list-style-type: none"> Number and proportion of unprotected sex acts 	<ul style="list-style-type: none"> Observational study Prospective cohort of health facility clients and –Uganda only– members of high risk populations Unit of analysis: individual (women only) Non-random selection of participants, non-random assignment to HTC 	<ul style="list-style-type: none"> Before-after comparison of behaviors of women who received HCT 	<ul style="list-style-type: none"> Reduction in the number (not proportion) of unprotected acts among HIV positives No change among HIV negatives
Kalichman <i>et al.</i> (64), 2010	Cape Town (South Africa)	<ul style="list-style-type: none"> Number of sexual partners Unprotected/protected vaginal and anal intercourse 	<ul style="list-style-type: none"> Observational study Prospective cohort of STI clinic patients Unit of analysis: individual Non-random selection of participants, non-random assignment to HTC 	<ul style="list-style-type: none"> Before-after comparison of risk behaviors at baseline and at 12 months 	<ul style="list-style-type: none"> Reductions in number of sexual partners and unprotected intercourse occurred in both seroconverters and clients who remained negative

Study, Year	Setting	Outcome measures	Study design	Comparison group	Main findings
Kabiru et al (38), 2010	Kisumu (Kenya)	<ul style="list-style-type: none"> Concurrent sexual partnerships Unprotected sex Risky sexual partnerships (casual partner or commercial sex worker) 	<ul style="list-style-type: none"> Observational study Retrospective life history data Unit of analysis: individual Random selection of participants, non-random assignment to HTC 	<ul style="list-style-type: none"> Study participants who did not have HTC 	<ul style="list-style-type: none"> One time HIV-testing has little effect on most measures of safe sexual behavior (may even be associated with concurrency for men) Repeated testing is associated with safer sexual behavior