Published in final edited form as:

Arch Sex Behav. 2015 October ; 44(7): 1833–1841. doi:10.1007/s10508-014-0455-3.

The cost and intensity of behavioral interventions to promote HIV treatment for prevention among HIV-positive MSM

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Abstract

Recently, behavioral prevention interventions for HIV have been criticized as being ineffective, costly, or inefficient. In this commentary, using HIV-positive men who have sex with men (MSM) as an illustrative high-risk population, we argue that the opposite is true – that behavioral interventions for HIV prevention, if implemented with the populations who need them, are affordable and critical for future prevention efforts. We base this argument on recent evidence showing that 1) adherence to antiretroviral treatment (ART) for prevention purposes is necessary to suppress HIV replication and reduce transmissibility, 2) individuals living with HIV have multiple psychosocial concerns that impact self-care and moderate the potential effectiveness of health behavior interventions, and 3) intensive interventions targeting both concerns together (psychosocial and HIV care) can show clinically significant improvement. We follow by comparing the cost of these types of interventions to the cost of standard clinical treatment for HIV with ART, and demonstrate a cost-savings of potential intensive behavioral interventions for, in this case, HIV-positive MSM who have uncontrolled virus. Keeping this evidence in mind, we conclude that individual intervention must remain a mainstay of HIV prevention for certain critical populations.

Keywords

HIV; intervention; prevention; cost; syndemic

With the continuing and steady increase in the number of people living with HIV in the U.S., due to advances in treatment, and the growing number of prevalent cases among men who have sex with men (MSM; Centers for Disease Control and Prevention, 2012a, 2013a), current prevention efforts for this population could certainly be improved. Before the advent of antiretroviral treatment (ART) as prevention, the only known way to prevent the sexual

transmission of HIV was a different bio-behavioral intervention: consistent condom use when having vaginal or anal sex. As an example high-risk population, meta-analytic data from studies conducted during this pre-ART *for prevention* time period suggested that individually-based behavioral interventions to increase consistent condom use among MSM were modestly behaviorally effective, with a 27% reduction in self-reported sexual risk, and were cost-effective (Herbst et al., 2005, 2007).

However, there has been a backlash against individually based interventions for HIV prevention, which seems to have been fueled by the failure of Project EXPLORE (Koblin, 2004). EXPLORE was a large scale behavioral intervention trial among MSM in the U.S. that failed to show a decrease in HIV incidence over time, using the standard of a 35% reduction that had been implemented in vaccine trials (see Kalichman, Zohren, & Eaton, 2014). While the recent, growing emphasis on combination approaches to prevent HIV is critical to making a difference in national incidence rates (e.g., Coates, Richter, & Caceres, 2008; Safren, Reisner, Herrick, Mimiaga, & Stall, 2010), there is still a need for improving individually-based behavioral interventions, and, as we argue here, a role for individual interventions designed for high-risk populations in order to successfully curb the HIV epidemic. Just as the field of general medicine does not conclude, after a failed trial of a specific medication for a particular disease, that no medication will work for that disease, in the case of a failed behavioral intervention trial, we should not conclude that behavioral interventions cannot reduce HIV incidence. This commentary makes this point by focusing on interventions for high risk HIV-positive MSM within the U.S. as an example. Specifically, this commentary argues that individually based behavioral interventions for high-risk HIV-positive MSM need to continue to be considered key components of HIV prevention efforts.

To make this point, we present the following evidence: 1) recent data has shown that individuals with medically-suppressed HIV (i.e., undetectable HIV viral load) are not likely to transmit HIV to their sexual partners, therefore optimizing adherence to ART is a necessary component of secondary prevention, 2) many of the HIV-positive MSM at highest risk for sexual transmission have co-occurring psychosocial concerns or *syndemics* that co-vary with the challenges of maintaining HIV-related self-care (i.e., optimal adherence; using condoms for sex), 3) these co-occurring syndemics likely interfere with the maintenance of long-term behavioral change and consequent risk reduction, 4) interventions that do not directly address these syndemics have shown modest effects on HIV adherence, 5) intensive interventions to promote adherence to ART in the context of addressing syndemic conditions can show at least short-term success, and 6) we estimate that the cost of even the most expensive behavioral interventions that address comorbid syndemics and HIV adherence are less than estimated costs of treating HIV in those who would have acquired the virus without intervention.

Individuals with controlled virus are not likely to transmit HIV to their sexual partners; therefore optimizing adherence to ART is a necessary component of secondary prevention

In a large, multinational randomized trial (HPTN052), early ART initiation with high levels of medication adherence was demonstrated to significantly reduce sexual transmission risk of HIV between primarily heterosexual, serodiscordant couples (Cohen et al., 2011). Recently, this finding that viral suppression reduced transmission risk was extended to men who have sex with men in an international observational study (Rodger et al., 2014). Although research on treatment as prevention for MSM is only now emerging and questions remain to be answered (Muessig et al., 2012; Rodger et al., 2014), these studies clearly suggest that ART adherence will invariably play a prominent role in preventing the spread of HIV as new prevention efforts rollout.

MSM with HIV who are at highest risk of transmission likely have comorbid syndemics

Researchers have found that multiple psychosocial health concerns can co-occur and interact to create syndemics that synergistically negatively impair health and health behaviors. Stall and colleagues (2003) were the first to document among MSM that psychosocial problems were highly prevalent, that these problems tended to co-vary with each other, and that, generally, the greater number of problems, the greater likelihood of reporting condomless sex and being HIV-positive. Bing and colleagues (2001) used the HIV Costs and Services Utilization Study (HCSUS) cohort to examine the prevalence of psychiatric disorders among a diverse sample of individuals in care living with HIV (N=2,864), of which over 50% reported same-sex sexual partners. They found that almost half (47.9%) met criteria for any psychiatric disorder, and 50% reported any illicit drug use. Thirty-six percent of the sample met criteria specifically for major depression (compared to 7.6% in the NHSDA comparison group). Data from a sample of HIV-positive MSM in care at Fenway Health also found high rates of syndemic conditions. Fifty-three percent of the sample screened in on any mood or anxiety disorder (O'Cleirigh, Magidson, Skeer, Mayer, & Safren, in press) while 39% reported any illicit drug use, and 20% reported binge drinking (defined as having five drinks in one sitting at least once a week; Skeer et al., 2012).

Other studies have documented exceptionally high prevalence rates for other syndemic conditions among HIV-positive MSM. For example, in a probability sample of MSM, Greenwood and colleagues found that 43% reported a history of intimate partner violence in the past five years (Greenwood et al., 2002). A history of sexual abuse has also been shown to be highly prevalent in HIV-positive individuals. In a survey of HIV-positive MSM in six major US cities, childhood sexual abuse was reported by 47% of the sample (Welles et al., 2009). In a community survey of MSM in New York, 44% reported one syndemic problem (including substance use, depression, intimate partner violence, and childhood sexual abuse) and 39% reported two or more syndemic problems. Among the 36% of the HIV-positive MSM in this sample who reported condomless sex, 54% reported two or more syndemic problems (Parsons, Grov, & Golub, 2012). Taken together, the existing evidence suggests

that the mental health burden among HIV-positive MSM is high and complex, developing as multiple syndemic conditions.

Syndemics likely interfere with sexual risk reduction

The types of syndemic problems described above can explain some of the modest results seen in individually based behavioral interventions for MSM. Within the rest of our commentary, we address syndemics in the context of multiple HIV health behaviors, namely ART adherence and condom use. We focus the majority of our paper on the use of promoting ART adherence for HIV prevention as a novel and potentially effective means of reducing transmission risk. However, for the purposes of discussing implications for intervention, we also draw from literature on condomless sex and syndemics, given that empirical evidence for the impact of syndemics on adherence to HIV care is only now emerging (Blashill et al., 2014; Mizuno et al., 2014).

As we noted previously, one of the most intensive behavioral interventions for HIV-negative MSM, Project EXPLORE (Koblin, 2004) failed to show a long term effect on HIV incidence, when contrasting it with twice yearly HIV counseling and testing. Although there was a statistically significant change in self-reported condomless sex in the intervention arm compared to the control group, it was relatively low (14.8% for serodiscordant condomless sex). Within EXPLORE, there may have been study-specific effects that compromised these comparisons, such as the increased amount of time and attention given to study participants in the control arm. Alternatively, the intervention's capacity to make long-term sustained behavioral change may have been moderated by factors interfering with such changes, as shown by the high prevalence of childhood sexual abuse (Mimiaga et al., 2009) and other syndemics in the cohort (Mimiaga, et al., this issue), which contribute to HIV risk.

Looking at secondary HIV prevention studies specifically for HIV-positive MSM, some trials that involved regular assessments of risk behavior have also failed to find differences in consistent condom use between intervention and control conditions, across both individually delivered (Rosser et al., 2010; Safren, O'Cleirigh, Skeer, Elsesser, & Mayer, 2013) and group (Wolitski, Gómez, Parsons, & SUMIT Study Group, 2005) interventions. One such study, Project Enhance (Safren, et al., 2013), specifically recruited high-risk HIV-positive MSM, and purposely sought to address co-occurring psychosocial problems via active prevention case management. In that study, the authors found a moderating effect of one syndemic variable, depression, such that participants who exceeded a clinical cutoff on the depression screening measure in the control and intervention arms did not change their behavior risk behavior substantially. In contrast, among participants who were not clinically depressed, those in the intervention arm demonstrated greater behavior change than those in the control group. Hence, in these two instances, EXPLORE and Enhance, psychosocial moderating variables may be related to the lack of differences between intervention and control conditions. We suggest that the absence of differences in HIV incidence in EXPLORE over time, as well as the lack of significant intervention effects in some secondary prevention trials for MSM, may have contributed to a negative view of individually-based behavioral interventions for MSM.

Syndemics interfere with medication adherence

With recent findings demonstrating that ART adherence markedly reduces transmission risk for HIV-negative partners (Cohen et al., 2011; Rodger et al., 2014), adherence to ART initiated while HIV-infected patients are asymptomatic becomes a critical component of prevention. Syndemic conditions, such as poor mental health and substance use, have also been associated with suboptimal adherence to ART (Blashill, Perry, & Safren, 2011; A. Gonzalez, Barinas, & O'Cleirigh, 2012; Pence et al., 2012; Wagner et al., 2011). For example, a recent meta-analysis (Gonzalez, Batchelder, Psaros, & Safren, 2011) found depression to significantly impact medication adherence in MSM and other key populations. Similarly, a recent systematic review (Binford, Kahana, & Altice, 2012) found that few interventions for HIV-positive persons who use drugs sustained improvements in adherence over time.

In a secondary analysis (Safren et al., under review) of the adherence data from the HPTN 052 trial, lower mental health quality of life was the only variable to predict worse adherence over time in asymptomatic patients initiating ART for the purpose of preventing transmission to their HIV-negative partner. Another recent study (Blashill et al., 2014;) demonstrated that multiple syndemic conditions additively reduced ART adherence, such that greater numbers of syndemic conditions were associated with worse ART adherence. This converges with recent work among persons who use drugs demonstrating that high syndemic burden was related to poorer adherence and lower likelihood of being virologically suppressed (Mizuno et al., 2014).

Together, this evidence demonstrates that the mental health burden among HIV-positive individuals is high and directly interferes with efforts to improve ART adherence and reduce sexual risk. This suggests, in turn, that these syndemic conditions contribute to the most infectious MSM (i.e., those who are not adherent to ART and, thus, likely have transmissible viral load) engaging in, potentially, higher rates of condomless sex. In support of this argument, Mayer and colleagues (Mayer, Skeer, O'Cleirigh, Goshe, & Safren, 2014) found evidence to support this link among one syndemic indicator (substance use), having a detectable viral load (i.e., infectiousness), and condomless sex within a sample of HIV-positive MSM in Boston.

Interventions that do not directly address these syndemics have shown only modest effects on HIV self-care behaviors

Specific to adherence interventions, several meta-analyses have concluded that behavioral interventions have generally shown moderate success (Amico, Harman, & Johnson, 2006; Simoni, Pearson, Pantalone, Marks, & Crepaz, 2006). Simoni and colleagues (Simoni, Amico, Pearson, & Malow, 2008) have also provided a comprehensive review of various modalities to promote adherence (e.g., contingency management, social support interventions). However, many of these interventions reviewed either do not explicitly address mental health or actively exclude those with mental health or substance use concerns from their trials.

For interventions focused on reducing sexual risk behavior among HIV-positive individuals, the one meta-analysis (Crepaz et al., 2006) of 12 existing trials found statistically significant effects in reducing condomless sex, and the authors estimated a 43% reduction in prevalence of unprotected sex (with a comparison estimate of 30% prevalence of condomless sex in the general population). Although this would be considered effective, and the authors concluded it was cost-effective for the time, only 5 of the 12 individual studies were significant. The authors noted several defining characteristics of those five studies, one of which was delivering the intervention in an intensive manner, and another being studies that addressed contextual variables, such as mental health. One intervention, published since the Crepaz meta-analysis (2006), that was effective in reducing condomless sex among HIV-positive individuals was the Healthy Living Project (Healthy Living Project Team, 2007), which enrolled participants across all HIV risk groups, including MSM. In this trial, the intervention was intensive and included fifteen 90-minute individual counseling sessions, which addressed multiple quality-of-life and self-care concerns. Accordingly, it could be argued that the Healthy Living Project did, in fact, address co-occurring syndemics in some manner, and, though intensive, was effective at reducing behavioral risk. In short, although modestly effective and successful, behavioral trials for HIV treatment and prevention today have largely not directly addressed mental health, and those that have seem to have shown better success.

Intensive interventions to promote adherence to ART in the context of addressing syndemic conditions can show at least short-term success

Two existing intervention models have explored simultaneously reducing a syndemic variable while also improving adherence. One body of research has focused on integrating the treatment of depression with adherence counseling. In the first study using a cross-over design, the authors found that the intervention successfully improved acute adherence outcomes and reduced depression, with large effect sizes for both outcomes (Safren et al., 2009). In the second study, which recruited a sample of HIV-positive individuals with injection drug use histories, Safren and colleagues found that the intervention improved both adherence and depression, though these effects were not sustained in the long term for adherence (2012).

Separately, Parsons and colleagues have integrated motivational enhancement therapy for problematic alcohol use with adherence counseling (Parsons, Golub, Rosof, & Holder, 2007). Their group found that this intervention improved adherence, as well as biological HIV outcomes (i.e., CD4, viral load) in the short-term. However, similar to the study from Safren and colleagues, gains in adherence were not sustained over time, and their biological endpoint of HIV viral load were not maintained at the 6-month assessment. These intervention models, which each directly address one syndemic condition and ART adherence, have shown strong effects. However, both interventions are notable in that they were not able to maintain adherence gains in the long term, after the intervention was discontinued.

One plausible reason for this finding, given the research we have reviewed on high mental health comorbidity in HIV, is that even these multiple-session interventions may be limited

in their ability to affect lasting gains when they only target one syndemic condition (e.g., depression, alcohol use). Other syndemics that are not directly treated by these approaches may persist in negatively affecting HIV outcomes, such as adherence and, subsequently, viral load. Additionally, similar to medications, it is possible that once gains are made, there is a need for maintenance or booster sessions. Although it seems to be a reasonable conclusion that increased intensity would be beneficial in treating complex mental health problems, to our knowledge, the relationship between increased intervention intensity and stronger intervention effects has not been examined in interventions for ART adherence. We suggest that this hypothesis would be valuable to test in an intervention trial.

The cost of even the most expensive behavioral interventions that address syndemic conditions and HIV-self care are estimated to be less than the cost of treating HIV in those who would have acquired the virus without intervention

We employ the following logical steps to compare the cost of a syndemics-based intensive individual intervention to the cost of treating HIV in the number of potential infections that would occur without such an intervention. We estimate costs using sexually active HIV-positive MSM with biological transmissibility (detectable viral load), as an example at-risk population. 1) First, we estimate the number of transmission behavior acts (i.e., condomless sex) among MSM with uncontrolled virus by using baseline data (pre-study involvement) for the subset of participants who had detectable viral loads and were enrolled in a secondary prevention trial at a community health center (Safren, et al., 2011, 2013). 2) We then use estimates of transmissibility of HIV per act for condomless anal sex among MSM from published studies. 3) Next, we estimate the reduction of transmissibility risk provided by an intensive behavioral intervention that either optimizes adherence to ART, and therefore eliminates HIV sexual transmission risk, or reduces condomless sex. 3) Lastly, we then compare this intervention cost to an estimation of the cost of standard care and treatment for HIV. To do so, we extrapolate rates and costs for every 100 people in our estimates below.

In the sample of HIV-positive MSM in care (Safren, et al., 2011, 2013), there were 71 sexually active men with a detectable viral load who reported any condomless sex with unknown or HIV-negative status partners. On average, these men engaged in 13 condomless sex acts with HIV-negative or unknown status partners in the three months prior to study enrollment. Using this average, this translates into 52 acts per year. For every 100 people, this translates to a potential 5,200 transmission acts.

In one recent meta-analysis, Baggaley (2010) estimated 1.4% transmissibility per act of unprotected receptive anal intercourse with an HIV-positive partner. Jin and colleagues (2010) estimated a 1.43% transmissibility rate for unprotected receptive anal intercourse, .62% for insertive anal intercourse when uncircumcised, and .11% for insertive intercourse when circumcised. For ease of calculation, we use 1% as a rough estimate of transmissibility across these findings and sexual position, however, see Table 1 for number of new infections per year at different levels of transmissibility. Note that neither estimate (Baggaley nor Jin) accounted for viral load (i.e., viral control) in their estimation. Hence,

this estimate of 1% overall is conservative, since the samples in the meta-analyses likely included some MSM who had suppressed viral load and some that had uncontrolled virus.

In our number of transmission acts above, partners were of unknown or negative status. Because transmissibility also depends on the HIV-status of the sexual partners of HIV-positive MSM, a conservative estimate is that only $\frac{1}{4}$ of partners are HIV-negative (see Table 1 for number of infections per year at different proportions of HIV-negative partners). Accordingly, of the 5,200 acts per year per among 100 HIV-positive MSM with a detectable viral load, this scenario would estimate that approximately 1,300 acts are with HIV-negative partners. At 1% transmissibility, this yields 13 new HIV transmissions per year (see Table 1).

One recent meta-analysis of behavioral interventions for HIV prevention among HIV-negative MSM (Herbst et al., 2007) found decreases in any condomless anal intercourse ranged from 27–43%. The Healthy Living Project (2007), which we previously described as one of the few effective prevention interventions for HIV-positive individuals, found reductions in transmission risk acts of 22% (at 10 months), 23% (at 15 months), and 36% (at 20 months) when compared to the control condition. Thus, we estimate a 25% reduction as a conservative, lower bound estimate of reductions in transmission risk behavior following a behavioral intervention. We should point out that although our focus is on the potential secondary prevention benefit of increasing adherence to ART among HIV-positive MSM, the advent of adherence for prevention is new enough that estimates of reductions in transmissibility as a direct result of increased adherence are unavailable. Hence, we use estimates from sexual risk reduction interventions, as they are similar health behavior interventions conducted with similar populations (MSM).

With 13 transmissions per year, a 25% reduction in transmission risk amounts to 3.25 infections averted per year (see Table 2 for infections averted at different assumptions of intervention effectiveness and across proportions of HIV-negative partners). Again, this assumes a 1% transmissibility estimate per act, with 5,200 condomless sex acts with unknown or negative partners, assuming only one-quarter of these are actually negative (i.e., some of the unknown partners will be positive). In Table 3, we estimate infections averted at different levels of intervention effectiveness at 5% transmissibility per act, to present an alternate scenario at a higher transmission rate.

The CDC estimates costs for treating a single case of HIV is \$379,668 (in 2010 dollars) over a lifetime (Schackman et al., 2006). This estimate includes costs of inpatient and outpatient care utilization, costs of ART regimens and standard regimens for opportunistic infections, as well as standard laboratory tests (e.g., t-cell count, viral load assays). The cost of 20 sessions of psychotherapy with the highest trained potential interventionists, doctoral-level clinical psychologists, is approximately \$100 per session when covered by high-end commercial insurance, and this was also the case in 2010. For 20 sessions, this is \$2,000 for a course of treatment. For every 100 people who might receive this treatment in the course of a year, this cost would be \$200,000. This estimate also assumes more sessions than most intensive behavioral interventions are designed for and with a provider with the highest level of training. If treating HIV over a lifetime costs \$379,668, this then results in a lifetime cost-

savings of \$179,668 for every one infection averted. Assuming a syndemics-based behavioral intervention, per the above calculations, results in only 3.25 infections averted, the total cost-savings would be \$283,921 for every 100 HIV-positive persons with detectable virus who receive the intervention.

To suggest the possible magnitude of cost-savings, we further extrapolate savings based on the total HIV burden among MSM within the United States. The CDC estimated that, as of 2010, there are 596,600 MSM living with HIV in the US (Centers for Disease Control and Prevention, 2013b). Of those men, 79% (or 471,314) are diagnosed, or aware of their infection, and of those diagnosed, 310,232 are not virally suppressed (Centers for Disease Control and Prevention, 2012b). Meta-analytic (Crepaz et al., 2009) work has estimated that 13% of HIV-positive MSM engage in condomless anal sex with partners who are HIV-negative. A recent CDC study of HIV-positive adults in medical care found that 6% of MSM engaged in condomless anal sex while virally unsuppressed with HIV-negative or unknown partners (Mattson et al., 2014). To give weight to the meta-analytic data, but acknowledge the limitation of not knowing viral suppression at the time of sex, we would use the estimate that approximately 10% of HIV-positive MSM are aware of their HIV serostatus and engage in condomless sex with HIV-negative partners, but are not virally suppressed. We base our calculations off of these 31,023 men, assuming they are the ones who are accessible for clinic-based behavioral intervention.

Retaining our estimate of 52 transmission acts per year per person, with 310,232 HIV-positive MSM that are not virally suppressed, this yields approximately 1,613,206 (1.6 million) acts per year in this group. With 1% transmissibility per act, this yields approximately 16,132 new infections per year. If behavioral intervention reduces sexual risk by 25%, intervention then would result in 4,033 infections averted per year. Keeping costs of intervention at \$2,000 per person, the total cost of behavioral intervention for 310,232 individuals would be approximately \$62 million. With a lifetime cost of treating HIV at \$179,668 for every new infection and, in turn, approximately \$5.6 billion costs in care for those 16,132 new infections in a single year, behavioral intervention results in a cost-savings of \$5.5 billion by averting 4,033 infections.

We acknowledge that it is unlikely that behavioral intervention will be able to easily or rapidly reach HIV-positive MSM who are unaware of their HIV diagnosis. Additionally, we do not estimate costs of other types of interventions for mental health concerns in HIV (e.g., psychopharmacological), although these modalities could also be worth comparing to the costs of standard treatment if they were shown to independently improve adherence. Intervention effects may also decline or dissipate with time and so the potential sustained cost-savings of intervention are unclear. Lastly, our estimate of the costs of HIV treatment over a lifetime is based on the most recent published data, although this is several years old (2010). These costs do not include complementary treatments (e.g., psychopharmacology) and are not adjusted for changing costs of HIV treatment either due to scientific advances or new healthcare legislation. That said, psychotherapy reimbursement rates from insurance companies has been stagnant for approximately the past decade, and hence those costs are not changed.

However, we also suggest that not all HIV-positive MSM will need as intensive a behavioral intervention (i.e., 20 sessions, here). Further, as the Affordable Care Act extends the reach of mental health parity, public and private payers should increasingly cover evidence-based interventions for syndemic conditions, both of which would reduce the costs of intervention. These limitations notwithstanding, we cautiously suggest a high behavioral and financial impact of intervention at a national level.

Conclusion

In this commentary, we have focused on the critical role that complex mental health problems may play in reducing the success of current interventions for ART adherence for HIV prevention. To date, previous interventions both for improving adherence and for reducing transmission risk behavior have shown only modest success. Calls have been made to recognize that co-occurring syndemic conditions likely reduce the efficacy of such interventions (Safren, Blashill, & O’Cleirigh, 2011; Safren et al., 2010). Taken together, this suggests that HIV-positive MSM who are both biologically (i.e., virally uncontrolled) and behaviorally (i.e., engaging in condomless sex) at risk for transmission are also less likely to benefit from brief, scalable public health interventions (e.g., passive “messaging” strategies, brief health behavior change interventions that do not account for syndemic variables). Instead, these MSM may require intensive, individual behavioral interventions that target multiple syndemic conditions in the context of addressing overall HIV self-care. We acknowledge that more holistic interventions that simultaneously address ART adherence and mental health may only be one of several effective options for moving the field of HIV prevention forward. However, in light of the literature we have reviewed, we propose that syndemic-focused interventions are likely a viable and appropriate approach to addressing complex behavior change in certain vulnerable populations (e.g., HIV-positive MSM).

Lastly, we have chosen to focus on HIV-positive MSM as an example at-risk group, based on the high prevalence of HIV and the complex mental health burden within this population. However, we believe that many of the issues we have outlined above regarding the need for intensive, behavioral interventions for HIV prevention may be usefully applied to other populations. For example, syndemic indicators and their relationships with HIV health have also been described among persons who use drugs (Mizuno, Purcell, Knowlton, Wilkinson, Gourevitch, & Knight, 2014), HIV-positive women (Meyer, Springer, & Altice, 2011), and transgender women (Brennan et al., 2012; Operario & Nemoto, 2010). Thus, approaches similar to those we have described that address multiple, interactive mental health concerns in combination with adherence to ART would appear to be potentially beneficial for these populations. Additionally, a meta-analysis of psychological interventions on the use of medical services found a significant cost offset (20%) for such interventions, particularly those considered behavioral medicine interventions (Chiles, Lambert, & Hatch, 1999). That said, pathways to HIV risk and treatment non-adherence differ across all of these risk groups and this might suggest the need for tailored interventions.

Evidence we have presented on the limitations of current interventions suggests that innovative treatments that target the interactions between mental and behavioral health will be necessary as prevention efforts move forward. For some populations, such as HIV-

positive MSM with uncontrolled virus, these interventions may need to be complex, to affect complex behavior change, and intensive, to maintain effects in a clinically meaningful way. However, we have also argued, by using estimates from the literature, that such interventions for the appropriate at-risk population may not only be cost-effective, but may be potentially cost-saving. We conclude that individual-level behavioral interventions are necessary and affordable for high-risk HIV-positive MSM and must remain incorporated into prevention efforts using appropriately creative and intensive designs.

Acknowledgments

Support for author time on the manuscript came from National Institutes of Health grants K24MH094214 and P30AI060354 awarded to the first author.

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Table 1

Estimation of the number of infections in 100 individuals per year, assuming 5,200 transmission risk behavior (TRB)¹ acts per year

Percent infectiousness per act	Serostatus of Partners			
	If all TRB partners are negative	If 3/4 of TRB partners are negative	If 1/2 of TRB partners are negative	If 1/4 quarter of TRB partners are negative
<i>Number of TRB acts (across)</i>	<i>5,200</i>	<i>3,900</i>	<i>2,600</i>	<i>1,300</i>
0.50%	26	19.5	13	6.5
1%²	52	39	26	13
2%	104	78	52	26
5%	260	195	130	65

¹Transmission risk behavior acts defined as condomless receptive or insertive anal intercourse

²Conservative estimate based on recent meta-analytic and longitudinal studies

Table 2

Number of infections averted by intervention, assuming conservative transmissibility at 1% per act and 5,200 transmission risk behavior (TRB)¹ acts per year for 100 people

Intervention effectiveness	Serostatus of Partners			
	If all TRB partners are negative	If 3/4 of TRB partners are negative	If 1/2 of TRB partners are negative	If 1/4 of TRB partners are negative
<i>Number of new infections</i>	52	39	26	13
Infections averted if intervention reduces risk by 25%	13	9.75	6.5	3.25
Infections averted if intervention reduces risk by 20%	10.4	7.8	5.2	2.6
Infections averted if intervention reduces risk by 10%	5.2	3.9	2.6	1.3

¹ Transmission risk behavior acts defined as condomless receptive or insertive anal intercourse

Table 3

Infections averted by intervention, assuming high transmissibility at 5% per act and 5,200 transmission risk behavior (TRB)¹ acts per year

Intervention effectiveness	Serostatus of Partners			
	If all TRB partners are negative	If 3/4 of TRB partners are negative	If 1/2 of TRB partners are negative	If 1/4 of TRB partners are negative
<i>Number of infections</i>	260	195	130	65
Infections averted if intervention reduces risk by 25%	65	48.75	32.5	16.25
Infections averted if intervention reduces risk by 20%	52	39	26	13
Infections averted if intervention reduces risk by 10%	26	19.5	13	6.5

¹ Transmission risk behavior acts defined as condomless receptive or insertive anal intercourse