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Secondary Prevention of HIV Infection: The Current State of Prevention for Positives

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Secondary prevention of HIV infection: the current state of prevention for positives

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Purpose of review

To provide a state-of-the-science review of the literature on secondary prevention of HIV infection or 'prevention for positives' (PfP) interventions.

Recent findings

Early work on PfP focused on understanding the dynamics of risky behavior among People Living with HIV/AIDS (PLWH) and on designing, implementing, and evaluating a limited number of interventions to promote safer sexual and drug use behavior in this population (i.e., PfP interventions). Previous meta-analyses demonstrated that PfP interventions can effectively promote safer behavior. However, the understanding of risk dynamics among PLWH and the extant number and breadth of effective PfP interventions were scant. Recent work has addressed some of these problems, yielding greater understanding of risk dynamics and providing additional, effective interventions. Still, only a modest number of recent, rigorously evaluated, effective interventions have been identified. New ideas for creating stronger, more integrated, and effective PfP interventions have emerged that will guide future intervention research and practice.

Summary

There remains much to be done to understand why, when, and under what conditions PLWH practice risk. Substantial work also needs to be performed to design, implement, rigorously evaluate, and when effective, to disseminate widely, additional, evidence-based PfP interventions targeting diverse populations. Directing such interventions to populations of PLWH at greatest risk for transmission of HIV has the potential to yield significant impact on the pandemic.

Keywords

HIV prevention, People Living with HIV, prevention for positives interventions, secondary prevention of HIV

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Introduction

Approaches to HIV prevention have typically focused on individuals who are HIV seronegative or whose serostatus is unknown [1]. Nevertheless, all HIV infections originate with a seropositive individual, and about one-third of seropositives who know their status continue to practice risky sexual or drug use behavior [2–6]. Moreover, since the advent of antiretrovirals (ARVs), seropositives are thankfully living longer, healthier lives. Yet, if they practice risky behavior, they have the potential to contract other pathogens and to infect others with HIV, even resistant strains of the virus, over extended periods. In the past 10 years, the United States Centers for Disease Control and Prevention (CDC) and international organizations [(e.g., The United Nations Joint Programme on HIV/AIDS (UNAIDS)] have stated that a complete approach to HIV prevention must focus on both seronegatives and seropositives [7–9]. We review recent research on the dynamics of HIV risk behavior among

People Living with HIV/AIDS (PLWH) and on interventions that have been specifically designed to lower levels of risk among PLWH.

Overview

At present, there are about 33.2 million PLWH worldwide [8]. Sub-Saharan Africa has been disproportionately impacted by HIV. There, HIV is primarily transmitted through unprotected heterosexual sex in the general population and accounts for 22.5 million of all PLWH worldwide and 1.7 of the 2.5 million new infections in 2007. The epidemic in the rest of the world is concentrated among men who have sex with men (MSM), intravenous drug users (IDU), sex workers, and their partners [8].

Given the large number of PLWH worldwide, prevention for positives (PfP), which can target diverse preventive behaviors (e.g., safer sexual behaviors and safer needle drug use behaviors), has great potential to impact

the epidemic by leading to behavior change among PLWH who know their serostatus. The percentage of PLWH who know their antibody status varies worldwide and is greater in developed than undeveloped nations [10,11]. Many PLWH respond to the knowledge that they are seropositive, gained from HIV testing, by practicing safer behavior. In a meta-analysis, it was concluded that for PLWH who know their serostatus, rates of unprotected sex with partners of negative or unknown status are reduced by 68% [12]. However, periods during which PLWH abstain from or engage in risk fluctuate over time [13–15]. For those who engage in risky behavior, secondary prevention interventions often encourage more traditional prevention strategies (e.g., consistent condom use, reducing partners, abstinence, serostatus disclosure, and clean injection equipment) to reduce transmission. Harm reduction strategies such as negotiating condom use with specific types of partners (e.g., anonymous partners) [16], sexual positioning to reduce the time and area of mucosal membranes exposed to infection (e.g., a male seropositive partner assuming the receptive role in anal intercourse) [17], and serosorting (e.g., limiting sexual intercourse to persons of similar perceived status) [17] are less effective in reducing risk. However, when offered as part of a combination of strategies (e.g., with consistent condom use outside of the primary relationship), they may help PLWH achieve risk reduction when more traditional strategies fail. To be effective, prevention strategies must be targeted toward contexts in which PLWH are less likely to initiate or maintain safer behavior, acknowledging that risk dynamics vary among subpopulations of PLWH (e.g., women, MSM, and IDU). Recently, biomedical risk

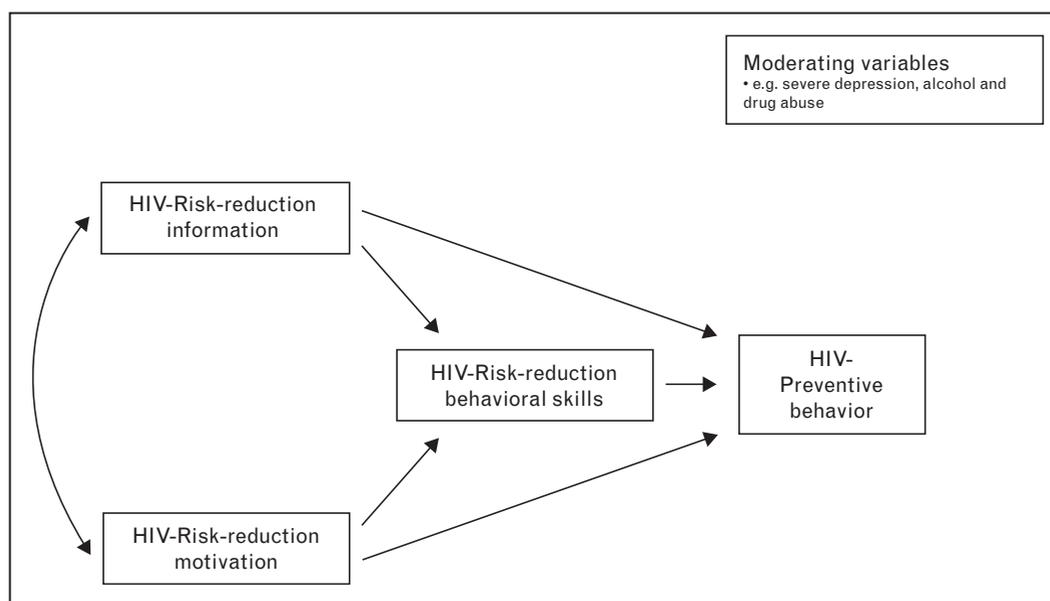
reduction approaches involving adherence to ARVs (to lower viral load) [18,19] have added a promising HIV prevention component.

Risk dynamics

We view the factors that influence risky behavior among PLWH consistent with the well validated Information–Motivation–Behavioral Skills (IMB) model of HIV preventive behavior [20,21]. In terms of the model (see Fig. 1), a PLWH’s level of HIV prevention-relevant information, motivation, and behavioral skills determine his or her level of risky or safer behavior. Specifically, when an individual is informed about HIV transmission and prevention and motivated to practice preventive behavior, they enact critical skilled behaviors, which result in the practice of HIV preventive behavior *per se*. Deficits, or weaknesses, in information, motivation, and/or behavioral skills result in risky behavior. Interventions targeting PLWH that address deficits in IMB model elements will generally increase levels of safer behavior. The efficacy of such interventions may be affected by moderating variables (e.g., severe depression, alcohol, and drug abuse). Although the IMB model and model-based interventions are robust with respect to these variables, at extreme levels, these conditions must be addressed independently (e.g., through separate interventions to eliminate or reduce alcohol or drug consumption) for IMB model-based HIV prevention interventions to be maximally effective.

Information necessary for PLWH to practice prevention involves knowledge about HIV transmission and

Figure 1 Three fundamental determinants of HIV risk and preventive behavior among seropositives



Adapted from [20].

prevention (e.g., knowing that condoms and abstinence prevent HIV transmission) [22], knowledge of contraception and safe reproductive planning [23,24], and not possessing incorrect information (e.g., myths that being on ARVs invariably prevents transmission, believing that how a partner 'looks' indicates their serostatus [25], or that risky behavior with other PLWH is 'safe') [26].

Motivation to practice prevention involves having favorable attitudes toward practicing specific Pfp behaviors (e.g., condom use, disclosing one's serostatus, adhering to ARVs, and so on) and perceiving social normative support from important others, such as one's sexual partners or family, for these actions. Behavioral skills for prevention involve the ability to keep condoms on hand and to use them even in the face of countervailing elements (e.g., partners who do not want to use condoms, being under the influence of drugs or alcohol, and so on). Critical behavioral skills also involve the ability to negotiate safer sex, to leave unsafe situations, to substitute safer for risky behavior, to disclose one's status, and to adhere to ARVs, among others.

Consistent with the IMB model, past work on risk dynamics among PLWH has indeed found that individuals' levels of HIV prevention information, motivation, and behavioral skills are associated with levels of risky and preventive behavior [4,27,28]. For information, recent studies [23,24,26,29–32] have further demonstrated the importance that knowledge of HIV transmission risk plays in lowering risk-taking behavior across diverse samples of PLWH.

With respect to motivation, past studies [4,27,33] have shown that pro-prevention attitudes and social norms among PLWH are associated with preventive behavior. In more recent work, perceived responsibility and motivation to protect one's self and one's partners predict increased safer behavior among PLWH [32,34–36]. Further, supportive peer norms facilitate safer injection behaviors among seropositive IDUs [37,38]. Fertility desires [23,31,39,40], cultural taboos [30,41], and stigma [29,42,43] surrounding sexual activity and same-sex behaviors [44,45] decrease risk reduction motivation.

With respect to behavioral skills, skills for consistent condom use, safer sex negotiation, and disclosure help PLWH to reduce risk [4,27,46–48]. In our own work with PLWH, we consistently find, across studies, a relationship between self-reports of risk reduction behavioral skills and practicing lower levels of risky behavior (Amico KR, personal communication). Recent work demonstrates that skills for not sharing injection drug paraphernalia lower risk behavior in PLWH who are IDUs [37]. Sexual risk reduction among PLWH may also be achieved by increasing skills to reduce alcohol consumed prior to intercourse

[49] and enhancing skills that facilitate safer sex discourse and disclosure of antibody status [22,49].

Concerning moderators, or factors that will affect the relationship of PLWH's levels of information, motivation, and behavioral skills, with their levels of safer or risky behavior, research continues to identify factors such as extreme poverty [50], housing instability [13,51], intimate partner violence [52], mental health concerns [37,38,42,53,54], and substance use [49,55,56] that may need to be targeted prior to, or concurrent with, addressing risk reduction behavior change in behavioral interventions. By addressing relevant moderating factors, barriers to behavior change can be reduced. Treatment of severe addiction and mental illness may also improve one's capacity to attend to behavioral interventions.

Early prevention for positives interventions

For many years, the focus of HIV prevention interventions was those presumed to be seronegative. Beginning with the second decade of the epidemic, this focus was urgently expanded to PLWH [57]. The overall goals of Pfp interventions are to prevent HIV transmission to others and to ensure optimal health in PLWH [7]. Many Pfp interventions focus on safer behavior, which prevents HIV transmission to others and keeps PLWH from acquiring additional pathogens. To date, relatively few Pfp interventions have had a joint focus on preventing risk and enhancing ARV adherence. This can affect both infectivity and transmission of resistant HIV strains and also safeguard health of PLWH. Thus far, very few Pfp interventions have focused broadly on improving seropositives' health.

Initially, two intervention models emerged to reduce HIV transmission by PLWH [47]. One employed the same HIV prevention strategies used with populations at risk for HIV (e.g., HIV testing and counseling). This reduced risk in many PLWH, especially those with serodiscordant partners, but failed to effectively change or maintain safer behavior for others [12,14,27,47]. The limitation of this model was likely that it involved a 'one time' intervention during a period of acute anxiety and also failed to address relevant information, motivation, or behavioral skills factors specifically relevant to reducing risk in the context of living with HIV [4,6,20,21,47]. More recent models for Pfp interventions have stressed understanding and addressing the dynamics of risky behavior for PLWH and integrating HIV prevention with other care and support services [4,12].

Despite the relatively recent emphasis on Pfp [1], prior to 2006, there were several individual-level and group-level Pfp interventions that yielded mixed results [57–65]. This suggested that successful Pfp interventions may

demand information, motivation, and behavioral skills content [48] and other elements (e.g., substance abuse and mental health services) to address complex dynamics of living with HIV that were not incorporated in some early interventions. It also indicated a need to expand traditional prevention messages of ‘consistent condom use with all partners, for all sexual behaviors’ [4,6] and explore additional prevention objectives (e.g., concurrent HIV testing and safer sex with secondary partners) that may prove to be more practical, though less effective, intervention strategies for some PLWH [4].

Two meta-analyses [66,67] have emerged that demonstrate the overall potential for efficacy of PfP interventions, including those reviewed above, when taken as a whole. These meta-analyses also highlight the conditions under which PfP interventions are most likely to be effective. Each reviews interventions published primarily through 2004, and although they are very helpful, given the increasing emphasis on PfP interventions, a newer, updated meta-analysis would be welcome as new studies accumulate.

Crepaz *et al.* [66] reviewed 12 pre-2004 PfP intervention trials meeting stringent criteria, many including information, motivation, and behavioral skills (IMB) intervention components, and reported that this body of research, overall, greatly reduced PLWH’s levels of unsafe sex, decreased sexually transmitted infections (STIs), and would likely be cost-effective in terms of health outcomes [66]. Unfortunately, intervention effects on needle-sharing were non-significant. Over the sample of interventions, those that were most effective had the following characteristics: they used behavioral theory, were targeted to change HIV transmission risk behaviors, were given either by healthcare providers or counselors, were intensive, and were delivered over a period of more than 3 months at the individual level and at sites in which PLWH receive medical care and other services. The most effective interventions also included a skills-building component and addressed one or more issues related to HIV risk behavior, medication adherence, or mental health.

The meta-analysis by Johnson *et al.* [67] revealed similar results. Data from 15 trials meeting stringent criteria were reviewed, and again, PfP interventions reduced risk with respect to unsafe sex compared with control conditions. Interventions did not reduce reported number of sex partners. In this meta-analysis and in that by Crepaz *et al.* [66], the effect sizes for condom use were equal to or stronger than in earlier meta-analyses of HIV prevention interventions for HIV-negative populations. In the meta-analysis by Johnson *et al.* [67], interventions were most successful at improving condom use if the sample included lower numbers of MSM or participants who were younger. Interventions with information,

motivation and behavioral skills components were more effective overall. As none of the interventions included in the meta-analysis targeting seropositive MSM had all the requisite IMB components, future research must ascertain whether such interventions would, as expected [68], be effective.

More recent work on prevention for positives interventions

An extensive literature review of recent Pfp interventions identified a reasonable number of newer studies. Of these, many involved descriptions of interventions that had been designed and implemented but not evaluated for outcomes [69–76]. We also found a number of recent Pfp interventions that involved rigorous intervention outcome studies. Most were interventions to increase safer sexual and drug use behaviors, which also protect PLWH from other pathogens. A number of them involved secondary prevention with respect to other health outcomes (e.g., interventions to favorably impact mental health and immune functioning) relevant to PLWH. We will discuss recent interventions to decrease risky sexual and drug use risk behavior in PLWH below.

Recall that Crepaz *et al.* [66] suggested that Pfp interventions situated in healthcare settings were especially effective. Two studies published recently by J. Fisher *et al.* [15] and Cornman *et al.* [77] focused on linking HIV prevention with clinical care for PLWH. In work performed in the United States [15], researchers taught physicians how to have IMB model-based ‘conversations about prevention’ with seropositive patients using Motivational Interviewing for intervention delivery [78]. Intervention recipients decreased risk behavior over time; those receiving the standard-of-care with respect to prevention actually increased risk, highlighting the cost of doing nothing. Cornman *et al.* [77] then adapted these clinic-based procedures to the healthcare system and the HIV risk dynamics in South Africa, and in an intervention delivered by HIV counselors rather than physicians (due to cost considerations and scarcity of physicians), reported similar outcomes.

Another intervention tested in outpatient clinics [79•] involved ‘positive choice’, an interactive software program designed to perform a risk assessment and provide tailored risk reduction counseling for PLWH based on Motivational Interviewing. It framed behavior change for PLWH more to protect the patient’s own health than to protect others, a strategy suggested in some recent Pfp commentaries [80]. Patients reporting risk behavior were randomly assigned to the intervention, including a ‘video doctor,’ or to a control condition. The former led to less risk behavior involving illicit drugs and less unprotected sex than the control condition.

In Uganda, Bonell *et al.* [81] assessed the secondary prevention effects of ARV initiation coupled with a behavioral intervention involving sexual risk behavior counseling and free condoms. Overall, the intervention reduced sexual risk behavior by 70% over 6 months. Although there was no control condition, these findings suggest the potential of linking prevention with African ARV rollouts. Note that intervention participants appear to have decreased risk behavior even though they indicated increasing sexual desire and having more opportunities to meet new partners after initiating ARVs.

Jones *et al.* [82] randomly assigned seropositive Zambian women attending a hospital clinic to a group-based or individually based intervention; there was no control condition. The group-based condition included three sessions with a focus on group cohesion, skills building and practice, and experimentation and feedback on sexual barrier products. The individual-level intervention offered information in a standard health education format, skills training, and access to videos and written materials. Sexually active individuals used sexual barriers and male condoms more in the group condition than in the individual condition. There were no between-condition differences for use of female condoms, lubricants alone (to counter dry sex), or lubricants with condoms, all of which increased in both conditions.

Several recent PfP interventions have been performed outside of clinical care settings. For example, Lightfoot *et al.* [76] adapted a successful community-based Pfp intervention initially implemented with youth in the United States to Ugandan youth living with HIV. Participants were randomly assigned to an intervention or control condition. Youth in the intervention used condoms and decreased number of sexual partners more than controls. On the basis of studies [28,83,84] that showed that PLWH with childhood sexual abuse engage in more risk behavior, Sikkema *et al.* [84] created a coping-based intervention to lower their risk. It involved 15 sessions, and the control condition was a therapeutic support group. Intervention participants reduced unsafe sex more than controls for up to 12 months.

Recent interventions have attempted to lower risk behavior among drug using PLWH. The Interventions for Seropositive Injectors - Research and Evaluation (INSPIRE) study [85] recruited seropositive IDU in four cities and randomly assigned them to a 10-session intervention involving peer mentoring or to a control condition consisting of a video-based discussion intervention. Both conditions reduced injection risk and sexual risk behavior compared with baseline, but the intervention condition was not differentially effective [85,86]. The EDGE study [87] randomly assigned PLWH with ongoing methamphetamine use to a safer sex interven-

tion or to a time-matched diet and exercise intervention. EDGE participants practiced greater safer behavior at 8-month and 12-month intervals. Margolin *et al.* [88] employed more unorthodox intervention methods to reduce impulsivity in drug using PLWH. Individuals were randomly assigned to a 'spiritual self-schema therapy' intervention (which integrates cognitive and Buddhist psychologies for increasing safer behaviors) or to a standard-of-care control condition. Those in the intervention decreased impulsivity and drug use and exhibited more motivation for abstinence, HIV prevention, and medication adherence.

Another large trial, the Healthy Living Project [89], involved recruiting risky PLWH from four groups (IDU, MSM, primarily heterosexual men, and women) in four cities. Fifteen Pfp sessions were administered in the intervention group; there was also a wait-list control group. Risky behavior was lowered in the intervention group over intervals from 5 to 20 months, with the largest reduction at 20 months. All of these differences disappeared by the 25-month follow-up, perhaps demonstrating the need for booster sessions.

The future of prevention for positives interventions

Extant Pfp interventions have generally been 'stand alone' projects in which PLWH have been recruited for interventions that focus on reducing risky practices. Future Pfp interventions should be broader in their objectives than a narrow focus on safer behaviors *per se*, broader in the populations targeted, and substantially more integrated into an array of medical, social, psychological, and other services that PLWH may need. In effect, we need to recognize the role of a spectrum of services in facilitating Pfp. Further, we must seriously consider designing and integrating Pfp interventions so that they have the potential to continue, when needed at each medical visit, rather than ending precipitously, as most Pfp interventions do (for exceptions, see [15,77]). When Pfp (and other HIV prevention interventions) end, the effects tend to decay [89], yet Pfp must be a lifetime enterprise. Many elaborations on these themes, which follow below, are discussed in detail in excellent studies by Temoshok and Wald [90], Remien *et al.* [91••], and West *et al.* [92••].

To cast the widest possible net, future Pfp interventions should include early identification of PLWH through broad-based HIV testing initiatives, especially within 'high risk' populations [93]. Outreach could include targeting individuals who practice high-risk behaviors, their social networks, those with diseases with pathways to infection similar to HIV, patients in STI clinics, young women attending antenatal clinics, and others. 'Opt out'

testing could be incorporated in medical facilities offering routine and emergency care [93]. When individuals are tested and have access to treatments earlier, they are prescribed ARVs and have lowered viral loads and decreased infectivity earlier, can be exposed to Pfp interventions earlier, and have opportunities to improve their health and protect others [90,91**]. The act of being identified as HIV infected leads to safer behavior [12], safety that is likely augmented biologically by ARVs. When individuals are not identified early, they may practice risk during periods of high infectivity, and opportunities for promoting their own and others' health are missed (e.g., delivering behavioral and biomedical interventions to reduce horizontal and vertical transmission) [90,91**].

In addition to casting a wider net for targets for intervention, future interventions must address other pressing psychosocial needs of PLWH (e.g., substance use, mental health, and reproductive health needs) more aggressively through referral and vigorous follow-up. For example, Pfp programs must be directly linked with alcohol and drug treatment programs, as alcohol and drug use increase risk behavior among PLWH [56,94,95]. Pregnancy desires of women and their partners, which are also associated with risky sex among PLWH, contribute to both horizontal and vertical HIV transmission [91**] and have not been well addressed in past Pfp interventions or by some reproductive health service providers [96]. Inclusion of relevant content in interventions as well as referrals to reproductive health professionals can result in relatively safer techniques for achieving pregnancies (e.g., only having unprotected sex at times of highest fertility, adhering to ARVs, and cesarean delivery) [96]. For PLWH who do not want to become pregnant, barrier methods can prevent pregnancy and HIV transmission. In addition to linking PLWH with care, next generation Pfp programs must help keep individuals in care, as this enhances general health and Pfp-relevant outcomes [97,98]. Those who remain in care can access Pfp programs, have their ARVs monitored, their adherence enhanced, be checked for viral load and resistance, and be treated for co-morbid conditions.

Pfp programs must also provide effective referrals for homelessness and financial emergencies, for gender and other violence, provide access to clean needles (where possible), to male and female condoms, and to other critical services. For many PLWH, HIV is part of a syndemic (i.e., the interplay of multiple social and health problems that mutually facilitate risk for negative outcomes) [99], which must be addressed using multiple intervention methods. Many of these syndemic conditions (e.g., co-occurring alcohol and drug use, extreme poverty, homelessness, and violence) have been shown, independently, to produce risk behavior. This suggests

that for Pfp to be optimally effective, we must integrate Pfp with care, treatment, and other critical ancillary services in a 'treatment cocktail' and must exploit all potential synergies [90,91**]. This may involve individuals with different specialties working together, referring to each other, or even cross-training and possessing knowledge of each other's specialties.

In this vein, consider a nonadherent patient on ARVs who is practicing risky sexual and IDU behavior. An optimally effective Pfp intervention for this PLWH – or any PLWH – must address any behavioral (e.g., risky sex, drug use, and nonadherence) or biological element (e.g., inadequate ARV regimen and co-morbid conditions), or their interaction, which may affect infectivity to others (e.g., viral load and/or viral resistance). Behavior and biology interface in critical ways. For example, often, risky behavior and nonadherence to ARVs, with its biologic consequences, co-occur. Those likely to have resistant virus may be especially apt to practice risky behavior [91**,100]. Addressing these issues from only a behavioral or biological perspective is insufficient; a synergistic approach with input across specialties is critical. Such integration may be easier when prevention occurs in a clinical setting. Effective Pfp needs to include behavioral approaches to reduce risk, medical approaches to deal with drug resistance and infectivity, and, on occasion, mental health, addiction, and other interventions.

To have the most significant effect on the epidemic, future Pfp programs need to target populations in greatest need. As 70% of new HIV infections occur in sub-Saharan Africa [91**], this region is a critical focus. The ARV rollout there will reduce stigma, increase HIV testing, and bring people into care in which they can be exposed to Pfp interventions [15,101]. As we noted earlier, special attempts should also be made worldwide to target Pfp programs to PLWH with high HIV infectivity [92**]. It may also be critical to target Pfp to those new to ARVs who may become more risky as they feel better. Further, PLWH who are refractory to brief interventions, and who have characteristics that make them especially likely to practice risk behavior, should be triaged to more intensive Pfp. All such interventions should include behavioral and biomedical components.

Finally, few extant Pfp interventions have been widely disseminated, without which it is impossible for them to impact the epidemic [102]. It is unclear whether interventions developed and tested predominantly in resource-rich environments with particular HIV risk dynamics and healthcare systems will work in different contexts [91**]. Note, however, that several Pfp interventions developed in the United States were modified, tested, and found to work in Africa [76,77]. One of these involved using lower cost intervention personnel (e.g.,

HIV counselors rather than physicians [76]), an adaptation needed when disseminating interventions to resource poor settings. Kalichman *et al.* [103] showed that other significant changes may be made in PfP intervention protocols, possibly without affecting outcomes. Note also that widespread dissemination of PfP will necessitate critical organizational level interventions (e.g., to counteract negative attitudes toward PfP interventions or staff feelings of inefficacy to change behavior of PLWH) [104] and will also need to promote integration of PfP across levels of healthcare organizations in order to integrate PfP and medical services [90,91**].

Conclusion

Extant work on PfP has addressed both the dynamics of risk and the reduction of risk-related behaviors among PLWH. In light of this review, future PfP work that aims to integrate both behaviorally and biologically based prevention is likely to yield a more substantial impact on the current pandemic. As life circumstances and subsequent risk dynamics evolve throughout an individual's life span, PfP messages and support must be adapted to meet this variation in context within resource-constrained settings and across different subpopulations of PLWH. Thus, future work on PfP must consider systematically performing positive prevention across a continuum of social and care services in order to improve both the overall health of PLWH and help to address other risk-related factors (e.g., fertility desires, mental illness, and substance use).

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Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 338).

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