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The Past, Present, and Future of HIV Prevention: Integrating Behavioral, Biomedical, and Structural Intervention Strategies for the Next Generation of HIV Prevention

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Abstract

In the past 25 years, the field of HIV prevention research has been transformed repeatedly. Today, effective HIV prevention requires a combination of behavioral, biomedical, and structural intervention strategies. Risk of transmitting or acquiring HIV is reduced by consistent male and female-condom use, reductions in concurrent and/or sequential sexual and needle-sharing partners, male circumcision, and treatment with antiretroviral medications. At least 144 behavioral prevention programs have been found effective in reducing HIV transmission acts; however, scale up of these programs has not occurred outside of the United States. A series of recent failures of HIV-prevention efficacy trials for biomedical innovations such as HIV vaccines, treating herpes simplex 2 and other sexually transmitted infections, and diaphragm and microbicide barriers highlights the need for behavioral strategies to accompany biomedical strategies. This challenges prevention researchers to reconceptualize how cost-effective, useful, realistic, and sustainable prevention programs will be designed, delivered, tested, and diffused. The next generation of HIV prevention science must draw from the successes of existing evidence-based interventions and the expertise of the market sector to integrate preventive innovations and behaviors into everyday routines.

Keywords

AIDS; evidence-based interventions; dissemination; review; chronic disease

INTRODUCTION

Human immunodeficiency virus (HIV) is currently impacting 37 million families, with 2.7 million new infections during 2007 (UNAIDS 2008). HIV has been found in every country on every continent and has moved from persons engaging in risk behaviors to general populations. The highest risk behavior for contracting HIV in many communities with generalized HIV epidemics (i.e., not concentrated in high risk groups) is being a married woman in a monogamous relationship, as geography is destiny in HIV (Potts et al. 2008). The global community has rallied to provide the financial, policy, therapeutic, and prevention resources

DISCLOSURE STATEMENT

The authors are not aware of any biases that might be perceived as affecting the objectivity of this review.

needed to stop HIV (Chan 2007). Prevention scientists have designed at least 144 evidence-based interventions (EBIs) to reduce transmission acts (Crepaz et al. 2007), yet these programs have not been broadly diffused (Dworkin et al. 2008). Cross-disciplinary competition over a mythical “magic bullet” for HIV prevention has subsided to support the combination of biomedical, behavioral, and structural (i.e., policy and environmental) strategies integrated in multilevel programs to impact communities (Merson et al. 2008). These approaches may require dramatically different research norms and designs (Chan 2007), moving from randomized controlled trials (RCTs) to fractionalized factorial designs (Nair et al. 2008), randomized encouragement designs, and interrupted time-series designs (West et al. 2008). Concurrently, the need for rapid scale-up to stop HIV also challenges existing scientific norms regarding replication of manualized behavioral EBI with fidelity. This review examines these challenges and summarizes the areas in which prevention science is likely to evolve.

EVIDENCE-BASED INTERVENTIONS TO CHANGE HIV RISK BEHAVIORS

Successes of Evidence-Based Interventions for HIV Prevention

Over the past 25 years, HIV prevention researchers have identified dozens of EBIs that reduce risky acts in RCTs. Meta-analyses that synthesize results from multiple studies confirm that risk reduction in response to EBI ranges between 25% and 50%. For example, EBIs with people living with HIV (PLH) reduce unprotected sex [odds ratio (OR), 0.57], reduce sexually transmitted infections (STIs) (OR, 0.20) (Crepaz et al. 2006), and increase condom use [mean effect size (MES) = 0.16] (Johnson et al. 2006). Interventions for men who have sex with men (MSM) reduce unprotected anal sex (OR, 0.77), reduce numbers of partners (OR, 0.85), and increase condom use during anal sex (OR, 1.61) (Herbst et al. 2005). Among injection drug users (IDUs) and other high-risk drug users, EBIs reduce overall sexual risk (OR, 0.86) (Semaan et al. 2002), reduce frequency of injection (MES = 0.08), reduce other drug use (MES = 0.18), reduce trading sex (MES = 0.33), increase condom use (MES = 0.19), and increase entering drug treatment (MES = 0.11) (Copenhaver et al. 2006). Interventions targeting high-risk heterosexuals find similar effect sizes for sexual risk reduction (OR, 0.81), condom use (OR, 0.69), and reducing STIs (OR, 0.74) (Neumann et al. 2002).

Factors supporting efficacy—Meta-analyses have also identified factors and components that support EBI efficacy. For example, the most efficacious EBIs engage participants with highly interactive activities such as one-on-one, small group, and community-level skill building and dialog (Albarracín et al. 2005). The least efficacious programs use passive, didactic strategies and promote fear-inducing messages that aim to elevate perceived threat of HIV (Albarracín et al. 2005). Almost all EBIs are based in social learning theory or related models of behavior change (Herbst et al. 2005, Smoak et al. 2006). Notably, the theory-based strategies supporting the efficacy of EBI are remarkably common across theories and include provision of information; shaping of attitudes, norms, self-efficacy, and motivation; and building behavioral skills (Albarracín et al. 2005).

Intervention facilitator characteristics—Effective intervention facilitators demonstrate expertise in skills and knowledge as well as empathy with clients. For example, EBIs delivered by trained expert facilitators are more efficacious than are those delivered by clinicians (Crepaz et al. 2006) or lay peers (Durantini et al. 2006). However, health providers and clinicians are effective in EBI designed for people living with HIV (Crepaz et al. 2006) and populations with low power and/or high needs for concrete instrumental help (Durantini et al. 2006). In general, EBIs are more efficacious when interventionists are similar to clients in terms of ethnic, gender, age, behavioral, and background characteristics (Crepaz et al. 2006). Two facilitators are better than one for delivering small group programs (Copenhaver et al. 2006), perhaps by providing

more opportunities to build supportive social networks or meet clients' preferences for credible and empathetic facilitators.

Cost effectiveness—Behavioral interventions are also cost effective (Pinkerton et al. 2001), as are HIV testing and partner notification (Varghese et al. 1999), injection equipment exchange (Holtgrave et al. 1998), and combining behavioral intervention with antiretroviral therapy (Pinkerton & Holtgrave 2000). However, studies of cost effectiveness and cost savings are highly sensitive to contextual variations in local epidemics (Harling et al. 2005), which highlights the importance of tailoring behavioral, biomedical, and structural intervention “mixes” to local priorities (Cohen et al. 2004).

Limitations of Evidence-Based Interventions and Current Modes of Diffusion

EBIs are not designed for providers or consumers, limiting adoption and diffusion—The successes of EBIs in reducing HIV risk in RCTs demonstrate efficacy in controlled settings with high-quality infrastructure, but EBIs are not necessarily effective when implemented in real-world settings (Green & Glasgow 2006). Several challenges limit the broader impacts of EBIs. EBIs are not designed for providers or consumers. EBIs must be available to providers in user-friendly delivery formats, and providers must have capacity to implement them (Eke et al. 2006a), but there is often a mismatch between what scientists design and what providers have the capacity to implement (Miller & Shinn 2005). For example, when an organization adopts an EBI, staff providers frequently struggle with understanding which activities can be adapted to their perceptions of clients' preferences, how to adapt without undermining program effectiveness, and building the skills and capacities to deliver specific activities (Dworkin et al. 2008). Yet, prevention scientists are clear about the general strategies needed for successful EBI adoption and dissemination. Interdisciplinary design teams with clear roles for clients and providers are essential for developing effective and sustainable EBIs (Fisher et al. 2006). Disseminating EBIs requires training practitioners to understand the intervention's theory, rationale, and nonadaptable “core elements” and to provide guidance on how to modify adaptable key characteristics and activities (Galbraith et al. 2008). Yet, there is very little evidence on how to successfully adopt an EBI or on how to best help providers of HIV prevention services adapt and implement EBIs with fidelity (Dworkin et al. 2008).

Development and dissemination of EBIs is a resource-intensive process that has not progressed as quickly as has our understanding of the epidemiology of HIV (McKleroy et al. 2006). The need to provide health services to 37 million persons infected with HIV leads to implementation of interventions prior to having evidence of effectiveness (Hallett et al. 2007). Direct service providers (e.g., health-care, community-based, and nongovernment organizations and their staff) often develop and implement their own intuitively based interventions focused on the provision of information or on creating intense feelings rather than well-validated EBIs (Fisher et al. 2006). Even when EBIs are administratively mandated or funded (e.g., in the United States), community-based organizations and health providers often face multiple challenges in implementing and adapting EBI with fidelity (Collins et al. 2006a, Dworkin et al. 2008, Rotheram-Borus et al. 2004a). Few EBIs have been consistently implemented in applied settings (Glasgow et al. 2003) resulting in low penetration rates; even the most successful EBIs in the United States rarely penetrate 1% of their target populations (Jensen 2003).

EBIs typically target only one outcome—Typically, EBIs target only one outcome (e.g., HIV transmission) and report on a narrow range of primary risk behaviors (e.g., number of sex partners, unprotected sex). Yet, drug use, physical and daily survival needs, mental health, and social supports may also drive HIV risks or reinforce safe behaviors (Chandra et al. 2005, Collins et al. 2006b). Consumers, providers, and communities might have other priorities that limit engagement in HIV prevention programs and adoption of preventive practices.

Ultimately, EBIs must address environmental barriers to implementing new practices, and EBIs do this much more consistently than is often recognized or reported (Rotheram-Borus et al. 2008). Part of the problem is a reporting bias rooted in funders' priorities, but there were also disappointing results from early prevention research suggesting that multiple-outcome targeted interventions are not effective, being too diffuse in their foci (Goldstein et al. 2004). In the case of HIV prevention, it is clear that multiple outcomes (i.e., medication adherence and sexual risk reductions) are highly correlated, warranting multiple-target interventions (Kalichman 2008). In fact, many successful EBIs do target multiple outcomes proximally related to HIV prevention (e.g., drug use, sex risks, adherence, and quality of life; Rotheram-Borus et al. 2001). Only a few programs have examined long-term outcomes. When examined, the effects of prevention programs are broad and extend beyond the anticipated impact. For example, a family-based program for adolescents whose parents are living with HIV has benefits not only in reducing risk for HIV, depression, and drug use of parents and teens, but teenage pregnancy is reduced and the grandchildren also benefit (Rotheram-Borus et al. 2001, 2004b, 2006a)

Adherence and maintenance are necessary outcomes for all behavior change programs—Behavior changes slowly over time with practice, starting with small steps that accumulate to make large differences. Furthermore, change can only be sustained if incorporated into individuals' daily lives and social relationships that support the new routines. Processes and mechanisms for initially changing a behavior may differ from those that maintain it (Marlatt & George 1998, NIMH Intervention Workgroup 2001). Yet, there is only limited evidence that HIV-related EBIs sustain health behavior changes because most prevention trials have followed participants for one or two years (Sikkema et al. 2005). Most biomedical prevention and treatment programs require adherence to ensure effectiveness (Weiss et al. 2008b) and to prevent negative and unintended consequences such as treatment resistance (Munro et al. 2007). Inconsistent adherence to HIV treatment and preventive behaviors co-occur and have common correlates, and effective interventions should target adherence to multiple outcomes (Kalichman 2008).

Overemphasis of prevention for individuals and couples, not families and communities—Most EBIs are delivered to individuals in one-on-one counseling or small groups (Kelly 1999). Risk behaviors are enacted in routines or practices that are embedded in broader social structures such as marriage, concurrent partnerships, and other partnering norms and opportunities (Kippax 2008). Thus, sustained change requires shifting community and peer norms, modeling influences, reinforcements and cues for behaviors (Curtis et al. 2007, Sikkema et al. 2005), and the broader social structures that shape risk (Kippax 2008, Sumartojo et al. 2000). Families and communities set values and model behaviors from early in life, but few EBIs target families and communities (Rotheram-Borus et al. 2004b). Although the few existing community-level EBIs intervene on a larger scale and in a potentially more cost-effective manner than do intensive individual-focused EBIs (Sikkema et al. 2000), the behavioral targets still have a relatively narrow focus (e.g., condom use).

BIOMEDICAL INNOVATIONS ARE THE WAVE OF THE FUTURE, BUT THE BEHAVIORAL AGENDA IS UNDERDEVELOPED FOR EACH INNOVATION

Biomedical innovations are identified as the wave of the future, but evidence for effectiveness is weak, and the behavioral agendas required for each innovation are underdeveloped and underemphasized. Biomedical interventions, such as HIV vaccines, male circumcision (MC), barrier methods (condoms, diaphragm), antimicrobial products, STI treatment, and antiretroviral medication for treatment and pre- and postexposure prophylaxis have all shown the potential for efficacy in reducing transmission risk but are still in trial phases. Of 31 completed RCTs of these methods, only four to date have shown statistically significant

reductions in HIV incidence (i.e., three on MC and one on comprehensive STI treatment); adherence routines are required to ensure efficacy for all biomedical innovations (Weiss et al. 2008b). In addition, none is likely to be 100% effective in preventing HIV, and all have the potential for behavioral disinhibition. Thus, like other long-standing biomedical cornerstones for HIV prevention (i.e., male condoms and HIV tests), all biomedical innovations will require a behavioral component to support uptake, proper utilization, adherence, and maintenance of safe behaviors by shifting daily routines and norms of populations, a challenging goal.

HIV Vaccines

An HIV vaccine is the ideal hope for a biomedical “magic bullet” to prevent HIV infection. Even if a safe and effective vaccine were developed and disseminated, which is still 5–10 years away (Girard et al. 2006), the primary challenge will be supporting uptake by consumers to reach adequate population coverage (Newman et al. 2004a, 2006; see Jain et al. 2004 for a hepatitis B vaccine example). In addition, it is unlikely that an HIV vaccine will be 100% effective (Girard et al. 2006). Consumer research and epidemiological models suggest that believing that one is protected by a vaccine is likely to increase HIV risk behaviors by 25% to 50% (Crosby & Holtgrave 2006, Newman et al. 2004b). Therefore, although adherence to a series of vaccinations sounds simple, diffusion of vaccines requires reshaping risk perceptions on a population level (Newman et al. 2006).

Despite the strong potential, HIV vaccine research has also had several recent setbacks. In November 2007, the STEP study, a phase II trial of an investigational HIV vaccine by Merck, was cancelled. The unexpected results suggested that not only was the vaccine ineffective in lowering plasma viremia (i.e., HIV virus levels in blood) post infection, which would slow progression to AIDS and potentially reduce infectiousness (a useful secondary benefit if a vaccine does not prevent infection), but the vaccine also may have actually increased the risk of acquiring HIV (Moore et al. 2008). In another more recent setback, the director of the National Institute for Allergy and Infectious Diseases cancelled a planned trial of the National Institute of Health Vaccine Research Center’s HIV vaccine candidate PAVE-100, saying that additional research is needed before the vaccine is ready to be tested in humans (Kaisernet.org 2008).

Male Circumcision

Significant evidence indicates that circumcised men may have a lower risk of HIV infection. Global observational studies typically show that MC provides a two- to eight-fold protection against HIV infection (Morris 2007). Three large RCTs of adult MC conducted in African countries with generalized HIV epidemics showed strong risk reduction, ranging from 48% to 61% (Auvert et al. 2005, Bailey et al. 2007, Gray et al. 2007). Yet, there are mixed data. For example, recent analyses found that STI rates were similar between circumcised and noncircumcised men in New Zealand (Dickson et al. 2008). MC has been dubbed the “surgical vaccine” because it is a one-time procedure, and sexual abstinence is required for only six weeks (Weiss et al. 2008a). However, credible limitations to the MC efficacy trials (e.g., early study termination, short follow-up, low retention rates, and countervailing data) and real-world implementation of MC (e.g., health-care infrastructure capacity, safety, cost-effectiveness, and decreased condom use) suggest that it would be useful to re-examine the recent enthusiasm for immediate and mass scale-up of MC (Green et al. 2008, Weiss et al. 2008a). Like HIV vaccines, MC campaigns will require changes in behaviors at many levels.

Yet, the evidence for the protective effects of MC is strong enough to highlight a disturbing trend of decreasing infant MC rates in the United States, especially among ethnic minority families (Leibowitz et al. 2009). Medicaid does not reimburse costs for MC in 14 states, and MC rates have dropped even more in these states. Latino families in particular do not circumcise

male babies. Health disparities that will become evident 20 years from now are being set in motion with these policies.

Barrier Methods: Male Condoms, Female Condoms, Diaphragms, and Microbicides

Male condoms—The male condom is a long-standing biomedical preventive tool that has been one of the cornerstones of HIV prevention programs since early in the epidemic. Condom use has been found to be highly effective in reducing HIV incidence, as high as 95% when used consistently and correctly (Anderson 2003). However, most persons do not use condoms consistently or correctly, so effectiveness falls to about 70% (Foss et al. 2004). Because consistent condom use has not reached sufficiently high levels in many regions, despite widespread and often aggressive promotion, some suggest that there is a lack of evidence of effectiveness in preventing generalized HIV epidemics (Potts et al. 2008). Yet, condoms clearly cannot be abandoned as a potentially effective strategy. Experience from Uganda with the “ABC” strategy (abstinence, be faithful, use condoms) highlights the importance of strong government commitment and a comprehensive approach to sexual behavior change that incorporates condom use (Kirby 2003, Singh et al. 2003).

The primary challenges to male condom use and the broader ABC strategy are rooted in a lack of attention to gender relations, social inequality, and economic contexts (Dworkin & Ehrhardt 2007). Globally, women account for 60% of HIV infections (Mantell et al. 2006). Young women aged 15–24 are 2.5 times more likely to be infected than are young men, and most infections in women occur within a steady relationship or marriage (UNAIDS 2004). In many situations, women are socially or culturally restricted in their ability to avoid sex or convince partners to engage in condom use or other safer sex practices (Minnis & Padian 2005). Female-controlled preventive methods are needed, particularly products that provide dual protection against pregnancy and sexually transmitted infections.

Female condoms—The female condom has generated evidence to support its efficacy for HIV prevention (Vijayakumar et al. 2006). Although efficacy trials for STI prevention have been conducted for the female condom, no trials have directly examined HIV prevention (Padian et al. 2008). It is a relatively new technology and is challenged by being expensive, unavailable, and unfamiliar (Moore & Rogers 2002). The female condom is also not entirely concealable and so cannot be used consistently without male partners being aware of its use (Mantell et al. 2006).

Diaphragms—Cervical barriers, such as the diaphragm, are established and acceptable contraceptives and recently demonstrated a potential to prevent HIV and STIs (Mantell et al. 2006). However, the only RCT for HIV prevention to date failed to demonstrate efficacy compared to condom use alone, adherence was low, and diaphragm use was associated with decreased condom use (Padian et al. 2007). Yet, there were no differences in infection rates between condom-only users and diaphragm users; thus, it is uncertain whether the diaphragm offers a protective effect for women similar to that of the male condom. Regardless, the diaphragm could be a useful delivery device for microbicides (i.e., antimicrobial agents that kill a microbe on contact) and topical antiretroviral products (Padian et al. 2007).

Microbicides—Antimicrobial agents that can be used discretely, either intravaginally or intrarectally, are under development, but none have proven safe and effective (Hillier et al. 2005, Moore & Rogers 2002). For example, one notable early attempt to use Nonoxonyl-9 (which kills HIV in the laboratory) as a vaginal microbicide actually increased risk for HIV infection among female sex workers by damaging the mucosal barrier that forms part of the body’s natural immune defense against HIV (Hillier et al. 2005). Antiretroviral-based vaginal microbicides are in trials but are also likely to be challenged by adherence requirements, drug

resistance, and less than 100% efficacy (Wilson et al. 2008). Thus, behavioral interventions will be required to integrate consistent use of barrier methods into routine sexual practices to ensure effectiveness (Wilson et al. 2008)

Antiretroviral Therapy as Prevention

Treatment with antiretroviral therapy (ART) for HIV infection has played an important role in the epidemic and has revolutionized how AIDS and HIV disease are treated and prevented. Availability of ART in the early 1990s increased acceptability of HIV testing. Clinical trials demonstrate reductions in morbidity and mortality in patients with HIV who receive a combination of ART drugs (Murphy et al. 2001). Progression from HIV infection to AIDS and mortality without ART typically takes about 10 years; with ART, life expectancy extends an additional 13 years on average (Hogg et al. 2008). ART works by suppressing viral replication and lowering viral loads in blood, the genitals, and other tissues. Thus, treatment with ART holds the potential to lower risk of transmitting the virus by reducing infectiousness. Comparisons of serodiscordant couples (i.e., where only one partner is infected) support the preventive effects of ART on HIV transmission, particularly for people progressing toward AIDS when viral loads soar as HIV overwhelms the body's immune system and infectiousness increases (Quinn et al. 2000). Thus, ART is an effective component of a multilevel prevention effort.

Adherence behaviors for ART are critical for effective viral suppression and to limit emergence of drug-resistant strains of HIV (Wise & Operario 2008). Early therapies had complex dosing regimens, high costs, adverse side effects, and long-term toxicities. The new generations of ART regimens are more effective, better tolerated, and have simplified dosing regimens (Montaner et al. 2006). Nevertheless, adherence remains a critical priority for effective ART, and behavioral and electronic reminder device strategies can be effective in improving adherence (Wise & Operario 2008). In addition, there are concerns and some evidence to suggest that enhanced access to effective treatment may lower vigilance for protective behaviors (Montaner et al. 2006), and low adherence and risk behaviors are highly correlated (Kalichman 2008). Thus, promoting behavioral risk-reduction interventions along with ART access and adherence support must remain a high priority for HIV prevention.

Prevention of mother-to-child transmission—Another success of ART has been in preventing mother-to-child transmission of HIV. In the United States and Europe, an HIV infected pregnant woman who receives ART and has an undetectable viral load has only about a 1% to 2% chance of transmitting HIV to her infant (Fowler et al. 2007). Many industrialized countries have all but eliminated pediatric HIV cases by providing ART during pregnancy and ending with the termination of breast feeding. In the developing world, with no ART intervention nearly 40% of infants will acquire the virus during pregnancy, delivery, or breast feeding (Luo et al. 2007). The use of ART for prevention of mother-to-child transmission in the developing world is both feasible and cost-effective (Chigwedere et al. 2008). Like ART in general, scale-up of this proven preventive strategy is a major challenge.

Pre- and postexposure prophylaxis—The success of ART to reduce HIV viral loads by suppressing viral replication suggests that ART can be used as a chemoprophylaxis method prior to or after exposure to HIV. Use of ART after occupational exposure (i.e., needle sticks in health-care settings) is now routine in the developed world (Pozniak 2004). There is evidence that postexposure prophylaxis (PEP) can reduce the risk of HIV transmission (Mackie & Coker 2000). Advocates have been calling for PEP availability following nonoccupational sexual or injection drug equipment exposures (Martin et al. 2004). Research is also examining pre-exposure prophylaxis (PREP), which involves taking ART for a period prior to anticipated or

possible HIV exposure, particularly for those who may be less empowered to insist on condom use (Youle & Wainberg 2003).

Until the approval of the antiretroviral drug Tenofovir in 2001, it was thought that PREP and regular use of PEP would not be feasible due to the safety concerns of long-term ART use. Tenofovir (and the combination of Tenofovir and Emtricitabine), however, has a good safety profile and infrequent side effects (Paxton et al. 2007). The use of PREP and routine nonoccupational PEP remains controversial due to the potential to increase high-risk sexual behavior. However, several studies demonstrate that PEP does not necessarily lead to an increase in high-risk behavior (Martin et al. 2004, Schechter et al. 2004). In the United States, PEP and PREP have been largely confined to studies of white, middle-class MSM who may be less inclined to decrease protective behaviors given availability of this experimental biomedical innovation (Shoptaw et al. 2008). If current studies of PREP prove that the drug regime is safe and effective, several issues will need to be resolved, including who will receive the drug and how it will be administered (Coates & Szekeres 2004). Behavioral interventions will be required to accompany any PREP and routine PEP interventions to support dissemination, proper utilization, adherence, and maintenance of preventive behaviors.

Treatment of Sexually Transmitted Infections as HIV Prevention

Evidence suggests that STIs, particularly those that cause genital lesions, increase the risk of HIV infection. For example, a meta-analysis of 19 longitudinal studies found that relative risks or the risk ratio (RR; a ratio of the probability of an event occurring in an exposed group versus a nonexposed group) for acquiring HIV was significantly higher for people with herpes simplex virus 2 (HSV-2) among heterosexual men (RR = 2.7), women (RR = 3.1), and MSM (RR = 1.7) (Freeman et al. 2006). HSV-2 is the cause of 80% all genital ulcerations, and 40% of sexually active adults are HSV-2 antibody positive (Corey et al. 2004). Population-attributable risk percentages for HIV infection with HSV-2 infection range from 19% to 47%, with the latter estimate reflecting areas with the highest HSV-2 prevalence such as sub-Saharan Africa (Corey et al. 2004).

Therefore, STI diagnosis and treatment have the potential to be key HIV prevention strategies by preventing biologically synergistic infections and as sentinel events for HIV surveillance (Aral & Peterman 2002, Detels 2001). Although one RCT of broad-scale syndromic treatment of STIs found a 40% reduction in HIV (Grosskurth et al. 1995), five other trials found no effect (Gray & Wawer 2007). Disappointing results have also come from two recent RCTs of HSV-2 suppressive therapy on HIV acquisition (Celum et al. 2008, Watson-Jones et al. 2008). Despite biological evidence for STI treatment as a potentially efficacious HIV prevention method, efficacy trials are challenged by limitations in study design, treatment coverage and adherence, and acceptability (Kaldor et al. 2008, Lagakos & Gable 2008, Weiss et al. 2008b).

Rapid Routine HIV Testing

HIV testing and counseling are also long-standing cornerstones in HIV prevention by enabling treatment and risk reduction for PLH. There is substantial evidence that testing HIV sero-positive results in significant reductions in transmission acts among PLH but not among those testing sero-negative for HIV (Holtgrave & McGuire 2007). Meta-analyses find that PLH aware of their sero status are at least half as likely to engage in sexual risk behaviors compared to unaware PLH (Marks et al. 2005), and modeling suggests that unaware PLH in the United States are at least 3.5 times more likely to transmit HIV (Marks et al. 2006).

Yet, an estimated 25% of PLH in the United States are unaware of their sero status (Glynn & Rhodes 2005). High stigma is a major barrier to testing and receiving results (Chesney & Smith 1999). Risk screening and targeted testing are unreliable (Klein et al. 2003). Requirements for

pre- and posttest counseling for all HIV testers burdens health-care providers, but there is little evidence that counseling changes behaviors (Holtgrave & McGuire 2007). Therefore, the Centers for Disease Control (Branson et al. 2006) and others (Rotheram-Borus et al. 2006b) have recommended universal, opt-out routine HIV testing in general health-care settings, with posttest counseling provided only to HIV positives. Routine testing can result in three-to four-fold increases in HIV testing compared to standard physician referral (Greenwald et al. 2006a) and identification of at least half of the positive cases that would have otherwise been missed (Greenwald et al. 2006b).

Rapid testing technologies have emerged that are easy for providers to administer, have low patient burden (i.e., a finger prick) and have no laboratory needs, making test results available within 20 minutes (Janossy & Shapiro 2008). Ultimately, scale-up costs and infrastructure, and low consumer demand due to potential for HIV-related stigma, are the largest barriers to expanded HIV testing (De Cock et al. 2006). We anticipate that repeat rapid consumer-controlled HIV tests, similar to pregnancy tests, will soon become the norm.

STRUCTURAL FACTORS AND STRUCTURAL INTERVENTIONS

Most preventive interventions focus on the proximal causes of HIV infection (i.e., sexual behavior). However, distal or “structural” factors also drive HIV transmission, most broadly through marginalization of at-risk populations that limits access to treatment and prevention resources, and also by shaping the general socio-environmental context in which HIV risk and preventive practices are produced (Parker et al. 2000, Rhodes et al. 2005, Sumartojo 2000). For example, economic instability and societal transitions may increase sexual mixing via survival sex work, migration, and greater population density (Van Donk 2006). Structural, epidemiological, biological, and behavioral risks of HIV infection share significant overlaps in the web of causation with other infections (i.e., hepatitis B and C, STIs, tuberculosis, and malaria), diseases (i.e., mental illness and addiction), and social problems (i.e., homicide, violence, and crime) (Poundstone et al. 2004). These constellations of risks and disease have an observable synergy with HIV (Freudenberg et al. 2006, Singer et al. 2006). Thus, “structural interventions” have been highlighted for their potential to address distal drivers of HIV epidemics and intersecting health and social problems.

Structural interventions that work by altering the context in which health is produced and reproduced have a long history in public health and typically involve regulatory, funding, and other policy-style mechanisms to enhance the availability, acceptability, and accessibility of preventive services or behaviors (Blankenship et al. 2006). Early and important structural interventions for HIV include universal precautions for a safe blood supply; funding support for HIV testing, prevention, and treatment; clean syringe availability for IDUs; and 100% condom-use policies in sex-work establishments in Thailand and Asia (Rojanapithayakorn 2006). Four important types of structural interventions have been recommended for future HIV prevention efforts (Blankenship et al. 2006): (a) community mobilization, (b) service integration, (c) economic interventions such as microfinance, and (d) contingent funding reform to remove gag rules that prevent organizations from supporting effective prevention strategies in local contexts (i.e., syringe exchange, drug-substitution treatment, and harm reduction for sex workers) in order to receive funding. Notably, structural interventions are not advocated as replacements for behavioral and biomedical interventions but rather should be incorporated into comprehensive, multilevel, and multisectoral responses (Sumartojo et al. 2000).

THE NEXT GENERATION OF HIV PREVENTION

Behavioral, biomedical, and structural interventions are needed to prevent HIV. Behavioral interventions have been successful but suffer from low uptake, and few have been designed to

accompany the biomedical innovations on the horizon. Biomedical advances hold promise, but most are years away from dissemination, not likely to be 100% effective, and require broad uptake and adherence. The impact of structural interventions is difficult to assess using scientific standards of evidence, but structural interventions are innately tied to behavioral and biomedical preventive efforts via funding and policy decisions (Padian et al. 2008). Prevention researchers, donor agencies, and policy makers must reframe their norms on design, delivery, and diffusion of EBIs and biomedical preventive technologies. Some sources of innovation for the next generation of HIV prevention may include (a) basing EBI development and adaptation on common factors underlying the efficacy of all EBIs; (b) creating a science of design and dissemination of EBIs using a continuous quality improvement (CQI) paradigm rather than a model of replication with fidelity; (c) utilizing business principles from marketers and entrepreneurs to facilitate design, diffusion, and utilization; (d) reframing prevention from a disease-management framework into a wellness perspective that reinforces HIV as a chronic disease; and (e) moving prevention from health-care settings and personnel to community sites and leaders.

Common Factors to Support Dissemination and Adaptation of Evidence-Based Interventions

The current mode of disseminating EBIs uses a technology-transfer framework, with emphasis on fidelity to specific core elements in each EBI (Eke et al. 2006b). This approach has limited evidence for success due to a lack of integrated dissemination research and because local adaptation was not considered in designing the dissemination initiative spearheaded by the Centers for Disease Control and Prevention (Dworkin et al. 2008). In contexts where EBI dissemination infrastructure is not available (e.g., in developing countries or organizations that do not receive EBI dissemination funding), the urgency of the HIV epidemic has required implementation of interventions to run ahead of evidence for effectiveness (Hallett et al. 2007). Adopting and implementing an EBI is a resource-intensive process (McKleroy et al. 2006). Staff persons in agencies who wish to implement EBIs often do not have the skills or capacities to pull a manualized EBI off the shelf and implement it effectively (Dworkin et al. 2008).

EBIs are currently disseminated with a goal to maintain fidelity to core elements (i.e., the factors believed to be responsible for an EBI's efficacy), which vary dramatically in scope and specificity across EBIs (Rotheram-Borus et al. 2008). There is no consensus on the level at which to define core elements and the causal mechanisms implied. There are not typically data on the EBI to identify that specified core elements are indeed the causal mechanisms necessary for behavior change or for program success. Core elements are typically defined by the EBI researcher-developers and may (or may not) incorporate key skills, specific activities, target population characteristics, and/or recruitment and outreach strategies, or intermediate outcomes that intervention participants should achieve to support behavior change. All EBIs also include core elements that suggest the importance of building skills and social support, yet the specificity and explicitness of these factors are quite variable across EBIs (Rotheram-Borus et al. 2008).

Despite apparent differences among EBIs, the programs share underlying common factors (Rotheram-Borus et al. 2008), principles (M.J. Rotheram-Borus, B.L. Ingram, & D. Flannery, manuscript in revision), processes (Ingram et al. 2008), theory-based strategies (Albarracin et al. 2005), and other practice elements (e.g., Chorpita et al. 2007, Garland et al. 2008, Kaminski et al. 2008) that support EBI efficacy. For example, at the broadest level of abstraction, common factors in EBI (i.e., what all effective programs do or should do) are argued to include: (a) establishing a framework to understand behavior change; (b) conveying issue-specific and population-specific information needed for healthy actions; (c) building cognitive, affective, and behavioral self-management skills; (d) addressing environmental barriers to implementing

new behaviors; and (e) providing tools to develop ongoing social and community support for adherence and maintenance of healthy practices (Rotheram-Borus et al. 2008).

Rather than promote replication with fidelity to specific EBIs and activities reflected in core elements, fidelity to common factors that are consistently implemented in every EBI will focus on effective practices across EBIs (Rotheram-Borus et al. 2008). If prevention modules were built on the common components across the shared evidence base, existing EBIs could be more broadly framed as prototype models including all core elements. Ideally, EBIs then would be more broadly accessible to more communities in less time, more quickly developed to meet the evolving epidemic, and more easily replicated and adapted to local priorities and preferences; in addition, the design cost could be lower (Chorpita et al. 2005). By utilizing common core elements as anchors for EBI fidelity, prevention providers would build capacities each time they implemented and adapted an EBI. These capacities would be more readily generalizable for each new EBI adopted, implemented, and adapted.

Science of Delivery or Implementation

We need and lack a science of delivery and dissemination. The funding and political will are now in place to support global scale-up of HIV prevention, treatment, and care (Chan 2007). However, a paradigm shift is needed to support integration of research into the design and evaluation of programs in conjunction with scale-up (Chan 2007, Cooper et al. 2007, Madon et al. 2007). Currently, we build preventive EBIs in a lockstep manner, from efficacy to effectiveness to dissemination over a 20-year time frame (Flay et al. 2005). A CQI paradigm (Rapkin & Trickett 2005), rather than replication with fidelity to specific EBIs, would ensure faster but effective adaptation and diffusion of preventive interventions (Rotheram-Borus et al. 2004a).

These approaches require reframing norms on application of the gold-standard RCT and adopting dramatically different research designs. Although RCTs are typically used only for early-stage efficacy trials and are not considered viable for larger-scale effectiveness trials, there is precedence for using RCTs in national-level public health programs (Feachem 2004). Fractional factorial designs, which systematically test different combinations of intervention components (adopted from CQI processes in engineering), can identify the independent and synergistic effects of intervention components in multicomponent interventions (Nair et al. 2008). It is typically not feasible to implement RCTs that can accomplish this goal, yet almost all interventions incorporate multiple components (Nair et al. 2008). When RCTs are not feasible to implement at all, alternative designs such as randomized encouragement designs and interrupted time series designs can still provide valid information regarding the causal effects of interventions, often with greater external validity than that of RCTs (West et al. 2008). Biomedical RCTs often fail to demonstrate efficacy because of real-world limitations of non-adherence and lack of statistical power to detect effects in comparison with standard-care controls, often a condom-promotion-only program (Weiss et al. 2008b). Thus, alternative designs show great promise, particularly if used in conjunction with RCTs as part of a larger research program (West et al. 2008).

Ultimately, a programmatic research agenda is needed to identify how to effectively disseminate EBIs identified in efficacy trials. This agenda might include, for example, analyzing existing EBI manuals to identify common factors, gathering data from EBI providers and facilitators regarding real-world implementation, and conducting consumer research among prevention clients or end-users. Utilizing a CQI paradigm for research and evaluation would support alternative standards of evidence (Flay et al. 2005), new research agendas would emerge, and far more attention would be focused on building platforms for global dissemination of EBIs.

Business Principles Leveraged to Scale Evidence-Based Interventions

Private enterprise, not science, knows how to engage consumers to influence their preferences, habits, and loyalty to products and services over time, including health-promoting products (Curtis et al. 2007). Private entrepreneurs replicate and diffuse quality products in hundreds of thousands of sites simultaneously. We advocate employing the product development and marketing expertise of the private enterprise world to increase the uptake, scalability, and sustainability of EBIs (Rotheram-Borus & Duan 2003). Marketing approaches that can specifically support dissemination of EBIs include (a) consumer research, (b) systematic efforts to build sustainable distribution channels, and (c) improved products and service developments or selection (Maibach et al. 2006). Again, prevention researchers, policy makers, and donors need to reframe their norms on how best to engage end-users with highly attractive prevention products and services.

Wellness Perspective and Integration of Prevention for All Local Health Priorities

A paradigm shift is also needed to support integrated prevention, treatment, and care for HIV (Weis et al. 2008). The health-care system has the responsibility for HIV care, yet the system is overwhelmed by HIV: more than one million health-care workers are needed immediately (Shah 2008). Costs to train the needed health-care providers will require billions of dollars of investment. Yet, 65,000 physicians and 75,000 nurses immigrated from developing countries to the United Kingdom during the 1990s (Shah 2008), and the drain continues. In Zimbabwe, 1200 physicians were trained in-country, but only 360 remain (Shah 2008). Health care alone cannot meet the challenge of HIV.

From the consumer's perspective, the health-care provider is not the desirable person responsible for prevention. Historically, and certainly in the context of overwhelming and overlapping HIV and tuberculosis epidemics, systems for delivering health care are not consumer friendly. Clinic waiting lines are long, clinics are difficult to access, and, in many countries, are expensive (World Health Org. 2007). Globally, one billion people do not have access to health care (Shah 2008). Consumers often struggle to know whether a problem is severe enough to require treatment; the responsibility and choice for seeking care is with the consumer. Consumers who decide to seek care often face a complex process that involves getting referrals to the right clinic, dealing with long wait times for appointments, taking time off from work or taking children out of school to accommodate the health-care provider's available appointment times, paying high rates that are frequently not covered by insurance, and wondering how long the appointment will last and whether it will successfully address the problem about which they are concerned. These are difficult challenges to overcome.

Developing countries also cannot broadly mount categorically funded (i.e., disease-specific) programs, such as HIV prevention (Halperin 2008). The health-care budgets are so low as to demand horizontally integrated care, which involves providing care in a single setting for a variety of diseases (Capacity 2008). This is true for all African countries as well as in the developed world. Yet, efficacious HIV prevention programs have been designed for vertically integrated health-care systems only (i.e., HIV prevention, and not prevention for other diseases, is provided and organized at the clinic, hospital, township, provincial, and national levels) (Myer et al. 2007). HIV prevention programs typically address a single outcome (reducing HIV transmission or providing HIV care) and are categorically funded and vertically integrated. The Global Fund, the U.S. President's Emergency Plan for AIDS Relief (a commitment of \$15 billion over five years, from 2003–2008), the World Bank, and private donors (e.g., the Gates Foundation and the Clinton Foundation) typically limit funding to HIV-related care only, although this trend is changing. In 33 of 41 African countries (70%), the total health-care budget is less than \$30 per person, and only two countries spend more than 10% of their annual budgets on health care. In contrast, the United States spends 15.4% of its annual

budget on health care, at \$6096 per person annually (World Health Org. 2007). South Africa spends \$390 per person annually, more than double the annual expenditures of 36 other African countries, reflecting 8.6% of its annual budget.

Because HIV is receiving \$5 billion annually, it has been argued that HIV is draining resources from other life-threatening diseases (Halperin 2008). Approximately 300–500 million cases of malaria could be cured for five years with \$1.5 billion (Sachs 2008). The challenges of tuberculosis, malnutrition, alcohol abuse, and depression cannot be addressed if HIV absorbs the primary prevention and care resources. Promoting healthy relationships and routines from cradle to maturity is one health-protection strategy that reduces the burden on the health-care system, especially for chronic diseases (which HIV has become).

A wellness framework also shifts the existing associations of HIV away from negatively sanctioned sex and drug behaviors. Framing HIV around sex and drug behaviors facilitates and maintains stigma globally (Dorfman et al. 2005, Schneider et al. 2006). Being HIV positive provides evidence that one has engaged in illicit social behaviors (MacPhail et al. 2008): HIV is perceived as just punishment for such violations in China (Li et al. 2007), the United States (Herek et al. 2003), South Africa (Delius & Glaser 2005), and Uganda (Bikaako-Kajura et al. 2006). Many churches are unwilling to deliver HIV prevention programs because sex and drug behaviors must be discussed, which may be misperceived as endorsement of risky acts (Kaisernetwork.org 2005, McKoy & Petersen 2006). HIV-positive adults are often unwilling to get tested for HIV because it would reflect acknowledgment that they have engaged in risk acts (Bell et al. 2007, MacPhail et al. 2008, Obermeyer & Osborn 2007). Even more problematic is that HIV-positive status is often not disclosed because it may be seen as a public acknowledgment of illicit social behavior.

However, increasing evidence demonstrates that unprotected sex and drug use are directly linked to a lack of goals and a sense of meaning to one's life (Patrick et al. 2007). Unprotected sexual acts or needle-sharing behaviors are not discrete actions, but rather are embedded in daily lives that lack a sense of meaning, coherence, and consistency. Across cultures, healthy daily routines are embedded in a family life that has meaningful and supportive interactions, reflective of one's values, and in which family resources are allocated in line with these values (Weisner 2002). With these characteristics, family and members of strong social networks help each other create prosocial roles and identities for themselves and especially for children, who acquire the healthy habits that buffer and sustain an individual through hard times. When encountering risky situations (e.g., offers of drugs or sexual pleasure), the short-term reward of pleasure cannot be overcome unless there is an important long-term reward to sustain motivation in the moment (McClure et al. 2004). Perceptions of a future, pleasurable daily life, and sexual acts that are embedded within a meaningful relationship, provide the motivation to refuse potentially risky sex and drug use. Building family wellness serves as the foundation for combating HIV and simultaneously sidesteps the stigma that is generated with a narrow, targeted focus on sex and drugs. Although sexual relationships and drug use must still be directly addressed in prevention programs, the framework is placed in the meaning of one's life, not in a single type of interaction.

A wellness framework also places HIV risk on a par with risky behaviors associated with other chronic diseases. Five risky behaviors account for more than 50% of all morbidity and mortality globally: what we eat, and how much we eat, exercise, use alcohol, and smoke cigarettes (McGinnis & Foege 1993). Chronic diseases resulting from these five behaviors is predicted to increase by 54% over the next 20 years, further bankrupting the health-care system, especially in the developing world (DeVol & Bedroussian 2007). With the exception of smoking, the patterns of eating, exercising, and drinking, as well as forming meaningful social and sexual partnerships, are behaviors rooted in everyday routines. Small changes in a family's

behaviors reverberate and make huge cumulative differences in the health outcomes of each family member. For example, encouraging family members to have serially monogamous partnerships rather than concurrent sexual partnerships could virtually eliminate HIV in Africa (Epstein 2007). Building healthy daily routines among families in a family wellness framework and setting is an alternative strategy for delivering HIV prevention.

AIDS has been reframed as a chronic illness with the introduction of ART (Beaudin & Chambré 1996). The skills and support required for people living with HIV to manage their health are common across all chronic illnesses (Ingram et al. 2008). The objectives of chronic disease interventions include improving the independence and quality of life of the person (Kennedy et al. 2001, Willison & Andrews 2005). Regardless of the chronic disease, the targets of behavior change are the same, including adoption of a healthy lifestyle (e.g., sufficient sleep, moderation in use of alcohol, good nutrition, weight control, smoking cessation, exercise, and regular health care); adherence to treatment protocols, particularly medication; mental health goals such as stress management and reduction of anger and depression; and communicating effectively with health professionals (Creer et al. 2004). If the chronic disease is contagious, an additional goal is to prevent transmission. Evidence-based self-management interventions for different chronic diseases have demonstrated success in achieving improved health outcomes; the World Health Organization included as a best-practice strategy to improve clinical care and outcomes for chronic conditions: “Educate and support patients to manage their own conditions as much as possible” (Epping-Jordan et al. 2001). This applies to both HIV and other local health priorities envisioned in horizontally integrated disease-prevention and wellness promotion.

Disruptive Innovations

We need a disruptive innovation (Bower & Christensen 1995) in HIV prevention. With disruptive innovations, an existing service or program often “overserves” needs, and a simpler, less-expensive alternative is provided that meets most of the same needs in a manner that is “good enough” for the majority of the consumer market. The new, good-enough service is more accessible, scalable, replicable, and sustainable. Examples of disruptive innovations in health care include “minute clinics” in retail pharmacies that provide treatment by nurse practitioners for the ten most common health problems (Schmit 2006, California Healthcare Foundation 2006); *Doc in a Box* converts shipping containers into health clinics that enable rural farmers to become health providers for common problems in their local community for approximately \$1500 (www.doc-in-a-box.net); and distance learning and similar information technology innovations that enable expert information and consultation support to be provided virtually in remote and resource-limited settings (DelliFraine & Dansky 2008, Sorensen et al. 2008). This model of thinking about innovations has the potential to revolutionize lives in positive ways for HIV prevention and the host of other local health challenges faced by communities globally.

HIV testing is an example of an overserved need in HIV prevention. When the HIV test was first developed in 1985, no viable treatments existed, and HIV was a death sentence. MSM and IDU were the two populations linked to HIV; both were stigmatized populations that became further stigmatized because of HIV (Herek et al. 2003). Therefore, the developed world generated norms and procedures that protected the identity of HIV-positive persons by guaranteeing anonymity, providing choices on whether to know one’s status, and providing one hour of pre- and posttest counseling regarding transmission risks. This standard was shipped globally and was required by donor agencies in countries with health-care budgets far lower than \$30 per person at that time. Now, 28 years later, multiple prophylactic treatments exist; HIV testing leads to reductions in transmission acts that benefit society as well as the individual; HIV-positive persons immediately reduce transmission acts upon learning their

sero status; and HIV pre- and posttest counseling does not change risk behaviors among HIV-negative testers. Yet, we know that pre- and posttest counseling are not delivered with any fidelity, and the technology exists for learning one's sero status by using dried blood spot (2.5 ml of blood), with results available in 20 minutes. Now an industry has been generated, an industry that will have economic consequences if this technology is encouraged and allowed to blossom. The needs for HIV testing are overserved by our current practices, especially in the developing world. A disruptive innovation for HIV testing may be to broadly distribute cheap, rapid, consumer-controlled HIV tests in a diverse range of settings, including bodegas, pharmacies, and market stalls, that place the decision with the consumer on when to test and what to do if testing positive. The technology moves from health care to community and from one industry to a broad distribution system.

Other examples exist in the world of HIV. Recently, a Swiss team found that highly individualized ARTs provided in resource-rich settings result in virologic outcomes similar to those of programmatic ARTs delivered in resource-limited settings (Keiser et al. 2008). Thus, programmatic ART with generic drugs that does not require quarterly monitoring of viral load and CD4 (a primary indicator of immune functioning and AIDS progression in HIV-positive patients) may also be a disruptive innovation. Building on these prototypes and the successes of EBIs and biomedical advances, the next generation of HIV prevention can hope to meet its broad goals: universal access to prevention, treatment, and care and elimination of the global HIV pandemic.

SUMMARY

HIV prevention research over the past 20 years has demonstrated both successes and challenges. Neither existing behavioral interventions nor the future wave of biomedical advances is likely to be 100% effective. Ultimately, a combination of behavioral and biomedical interventions, supported by structural interventions, will be needed. Current behavioral interventions that have been shown to be effective in lowering risky acts still suffer from low uptake, and few if any have been designed to accompany the biomedical innovations that are expected in the future. To be effective on a large scale, both behavioral and biomedical prevention research must move beyond the laboratory and into real-world dissemination and scale-up. This next generation of HIV prevention interventions must draw from the successes of existing evidence-based practices from HIV and other chronic diseases in order to improve dissemination and eventual uptake. This process can be facilitated through designing programs based on common factors, creating a science of delivery formats, utilizing business principles, and reframing prevention into a wellness perspective.

A series of meta-analyses among MSM, IDU, and people living with HIV have demonstrated that EBIs can reduce risky acts by 30%. Studies have also demonstrated the cost-effectiveness and cost savings of many HIV related interventions. Although much effort has been devoted to development and evaluation of HIV prevention efforts, there is still relatively little uptake of these programs. When there is EBI implementation, replication with fidelity is also a major challenge, and little attention has been devoted to helping providers and service organizations successfully adopt evidence-based interventions. Each EBI must target the needs of two audiences: (a) the providers who deliver the program and (b) the end users or consumers who may benefit from acquiring the information, skills, or support provided by the program. The needs of each audience must be addressed by each EBI to ensure effective dissemination. The hothouse research environment does not typically evaluate the preferences, capacities, or desires of either audience in designing new programs; however, in order for broad diffusion to occur, the focus in the initial design must be on providers and consumers.

Ultimately, we advocate for a shift in how HIV prevention programs are framed, recognizing the need for a shared set of preventive outcomes; a science of delivery format; an exploration of business principles as aids in design, diffusion, and utilization; and a reframing of prevention into a wellness perspective. Focusing on common factors and recognizing similarities across intervention approaches can assist both researchers and providers who wish to use EBIs. Doing so moves the attention away from particular theoretical models of behavior change toward a focus on effective practices. Furthermore, a spirit of collaboration among intervention researchers will be fostered if they can work to understand what their EBIs share rather than how their models differ. Successfully identifying the common factors that underlie EBIs will make it easier for programs to be adopted by providers and will allow new interventions to be developed faster, improvements that will prove to be very important as the pandemic continues to change and grow. We also need to be able to examine the common and unique factors of EBIs that target the same outcomes and to identify programs that focus on different outcomes but using similar delivery formats. Furthermore, the needs of both providers and end users must be considered in each EBI; in order to take a more market-driven approach, we need to build or purchase the infrastructure for these audiences.

The next generation of HIV health-care providers must integrate local health priorities into their general prevention services if destigmatization and rapid scale-up are to be viable. Movement from health-care settings to community settings will respond to the reality of HIV as a chronic condition. These shifts require a new set of methodologies and strategies that will require all prevention scientists to learn new skills, make new social networks and collaborations, acquire different knowledge bases, and reframe their existing norms. The same common factors that are necessary to achieve successful behavioral change that is sustained over time are needed by scientists to shift our current models and paradigms to defeat HIV. There is a need for structural changes among scientists that parallel the changes by consumers and providers who are battling the HIV epidemic on a daily basis.

Glossary

Evidence-based interventions (EBIs)	interventions that are grounded in consistent scientific evidence through randomized-controlled efficacy trials showing improved outcomes
RCTs	randomized control trials
Scale-up	the process of bringing an evidence-based intervention into a real-world setting
Meta-analyses	combining the results of several research studies to address a set of related research hypotheses
PLH	people living with HIV
Odds ratio	the odds of an event occurring in one group compared to the odds of it occurring in another group
STIs	sexually transmitted infections
MES	mean effect size
MSM	men who have sex with men
IDUs	injection drug users
Cost effectiveness	the ratio of an intervention's cost compared to an alternative in terms of incremental cost and effect

Biomedical innovations	approaches to HIV prevention based on the biological sciences including vaccine, microbicides, male circumcision, and antiretroviral treatments
Microbicides	antimicrobial agents that if applied topically to mucosal surfaces might act as a chemical barrier to prevent sexually transmitted infections
ART	antiretroviral therapies
Postexposure prophylaxis (PEP)	an antiretroviral drug administered immediately after exposure to HIV with the intent of reducing the likelihood of contracting HIV
Pre-exposure prophylaxis (PREP)	an antiretroviral drug administered prior to potential HIV exposure with the intent of reducing the likelihood of contracting HIV

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