

RESEARCH INITIATIVE

Treatment Action!

HIV prevention with positives:

Bad marks for provider-based prevention and (simple, brief, cheap) ways to improve them

by **Mark Mascolini**

INTERVIEWS WITH:

UCSF's **Stephen F. Morin, PhD**

Providers hold key in prevention with positives

CDC's **Kathleen Irwin, MD, MPH**, and
Nicole Crepaz, PhD

New CDC guidelines and data on positive prevention

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Dear reader,

You might assume that HIV-treating clinicians – doctors, mid-level providers, and nurses, among others – make prevention of HIV transmission a priority in daily practice. If so, your assumption is understandable. It's also wrong. According to editor Mark Mascolini, “[E]ven while a raft” of research shows that “simple, regular counseling by HIV providers defuses risky behavior,” between a third and three fourths of HIV providers don’t offer it. In this issue of *RITA!*, Mascolini explores the reasons why.

Still, even while counseling for behavior change is essential, it’s probably not the most important weapon in the clinician’s arsenal. “If every HIV-positive person had an undetectable viral load,” says Joel Gallant of Johns Hopkins University, “the epidemic would be over.” Treating HIV-positive patients with antiretroviral therapy is, he says, the “single most important thing” providers can do to stymie the transmission of HIV. The data support his claims. In a study of nearly 1800 serodiscordant couples, treating the infected partner with antivirals reduced the risk of HIV transmission to the uninfected partner by an astonishing 96%.

“Positive prevention” – helping HIV-positive individuals to stop transmitting the virus – is the focus of this issue of *RITA!*. As Mascolini notes, “Everyone who gets HIV gets it from someone else.” In the United States, where men who have sex with men remain the group most vulnerable to infection, the lifetime risk for viral acquisition is shocking: For white males, it’s 1 in 104; for Hispanic males, 1 in 35; and for black males, 1 in 16. “If you told people they had a 1 in 16 to 104 lifetime chance of dying in a plane crash,” Mascolini asks, “how many people would fly?”

Though some of the numbers are startling, others are heartening. For example, from 1984 to 2006, HIV transmission in the US declined by 90%; it’s declined by more than 33% since 1997. Here, we review the ways – many of them simple, quick and readily available – to help reduce the numbers still further. So if you’re looking not just for a description of the problem, but also for solutions, turn the page.

Until there’s a cure,

A handwritten signature in red ink that reads "Paul".

Paul Simmons, BSN, RN, ACRN
Executive Director

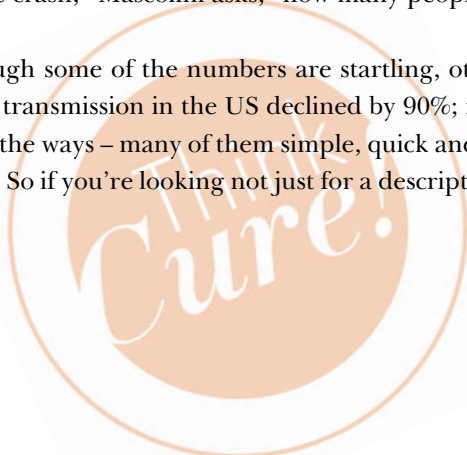


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HIV prevention with positives: Often ignored, yet often effective

By Mark Mascolini

Abstract: Helping HIV-positive people avoid passing their virus to partners—called positive prevention—could dramatically curtail the HIV epidemic if pursued aggressively. Yet, despite ample research showing that clinic-based positive prevention works, providers often neglect this aspect of HIV care. Research suggests many reasons why clinicians avoid talking to positive patients about prevention, from a simple lack of time, to discomfort in discussing intimate (often gay) sex, to the belief that counseling won't change a patient's behavior. Although chances of picking up HIV during condom-free sex may be 1 in 200 or more, those odds look bad when one considers the number of lifetime sex partners some people report. CDC data show that US HIV transmission rates began falling early in the epidemic and kept falling through 2006. Transmission rates probably continued to dwindle after that, but largely because antiretroviral therapy made viral loads undetectable in so many people. Primary high-risk transmission groups include people with high viral loads, sexually active gay and bisexual men, injection and noninjection drug users, and people with mental health problems. But research has also disclosed some unsuspected risk factors, like hunger.

Everyone who gets HIV gets it from someone else. In the United States HIV usually jumps from one person to another during sex, and less often with needle sharing. Antiretrovirals for pregnant

women and blood screening stoutly block the virus from infecting newborns and transfusion recipients. Even in countries with limited perinatal antiretroviral programs, sexual HIV transmission accounts for the bulk of new infections.

So if everyone with HIV stopped having unsafe sex and sharing tainted needles, the epidemic would end.

Yes, pregnant women with undiagnosed HIV or living in places without ready antiretroviral prophylaxis would pass HIV to offspring. But there would be fewer and fewer HIV-burdened pregnant women if HIV-positive men and drug-injecting partners stopped infecting them. So if sexual and drug-sharing transmission can be curbed, HIV infection would not be epidemic. Of course helping HIV-positive people in care stop transmitting their virus would do nothing to stymie transmission from people who don't know they're infected. But it would make a big dent in HIV incidence, and a bigger dent if wider HIV testing succeeds.

You might think, then, that HIV clinicians—a group probably more attuned than any other to the public health consequences of the disease they treat—would make preventing HIV transmission a top priority of day-to-day care. But study after study shows many don't—even while a raft of other research proves that simple, regular coun-

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selling by HIV providers defuses risky behavior. And innovative risk-reduction and screening tools patients can self-administer promise to save clinician time without costing a bundle.

“Positive prevention”—helping HIV-positive people avoid passing their virus to sex mates and injecting allies—clambered several rungs up the US public health ladder in 2003 when the CDC promulgated its guidelines on *Incorporating HIV Prevention Into the Medical Care of Persons Living With HIV*.¹ Until then, CDC experts noted, “HIV prevention in this country . . . largely focused on persons who are not HIV infected, to help them avoid becoming infected.”¹ But to many that oak-to-acorn inversion has the logic of counseling potential car-crash victims to watch for reckless drivers rather than getting reckless drivers to slow down and stay in lane. And focusing on people without HIV had done nothing to stunt HIV incidence—the new infection rate—in the United States. (The CDC will update its positive-prevention guidelines in 2012. See the interview with Kathleen Irwin in this issue of *RITA!*)

If positive prevention languished as a clinical priority for nearly a decade after the CDC unveiled its guidance,¹ results of the randomized HPTN 052 trial pushed this epidemic-arresting strategy to a prime spot in the frontal lobes of HIV clinicians and everyone else who thinks about how the virus spreads.² Although this watershed study involved HIV-discordant couples, almost all of them heterosexual, few doubt that the foremost finding applies to anyone with HIV and that person’s sex mates.

Randomizing HIV-positive partners in 1763 discordant couples to start combination antiret-

roviral therapy (cART) at a CD4 count between 350 and 550 cells/mm³ or to wait for AIDS or a count of 250 cells/mm³, HPTN investigators determined that early treatment cleaved the risk of HIV transmission to the negative partner by a whopping 96% (hazard ratio [HR] 0.04, 95% confidence interval [CI] 0.01 to 0.27, $P < 0.001$).²

Here, dramatically, was proof that keeping viral loads in check with standard cART virtually voided chances of sexual HIV transmission.² The solitary person in the early-treatment group who transmitted HIV to his partner had just begun treatment. When *RITA!* asked top HIV clinician/researchers to name the one or two steps they recommend to keep HIV-positive people from sharing their virus, 16 of 18 said treat them with antiretrovirals, and 7 of those 16 specifically cited HPTN 052.

But “treatment as prevention” will not transform the transmission landscape overnight, even in countries with ready access to antiretrovirals. To blunt HIV incidence in a big way, providers will have to give positive prevention a top-drawer spot in their treatment plans, even if time is short and reimbursement beggarly. This issue of *RITA!* aims to help clinicians focus more sharply on positive prevention and to see what research says on which strategies work best. Although most of the research and guidelines reviewed involve HIV in the United States and countries with a similar epidemic, the major points largely apply to HIV clinics across the world. Interviews with two CDC officials and with Stephen Morin, a top positive-prevention investigator, analyze some of the most telling data. Quick summaries for clinicians appear through this issue, and patient handouts appear in and after the second review article.

Prevention counseling takes back seat in many HIV clinics

Studies that reckon how many HIV providers counsel positive patients on HIV prevention almost all report dreary results. The US Health Resources and Services Administration (HRSA) 2011 *Guide for HIV/AIDS Clinical Care* reports that “one third to three fourths of HIV medical providers do not ask their patients about sexual behavior or drug use.”³

In 1998 and 1999 a CDC team asked 839 Californians with HIV (607 gay/bisexual men, 127 heterosexual men, and 105 women) in six public HIV clinics if a health worker ever talked to them about safer sex or HIV disclosure to partners.⁴ Almost one third (29%) claimed no physician, physician assistant, nurse practitioner, nurse, social worker, health educator, psychologist, or psy-

chiatrist ever discussed safer sex, and 33% could not remember a physician ever mentioning safer sex (**Figure 1**). Only half of the study group said a health worker ever discussed HIV disclosure with them. About 45% of these people had visited their clinic more than 20 times.

Although the US HIV epidemic was dominated by homosexual transmission then and remains so today, multivariate analysis determined that gay/bisexual men were half as likely as heterosexual men to be counseled about safer sex (odds ratio [OR] 0.48, 95% CI 0.28 to 0.81).⁴ The CDC investigators suggested this finding “may indicate that some providers feel uncomfortable talking about homosexual behavior or that they may (mistakenly) assume that MSM [men who have sex with men] already know about the importance of prevention and thus do not need additional information.”

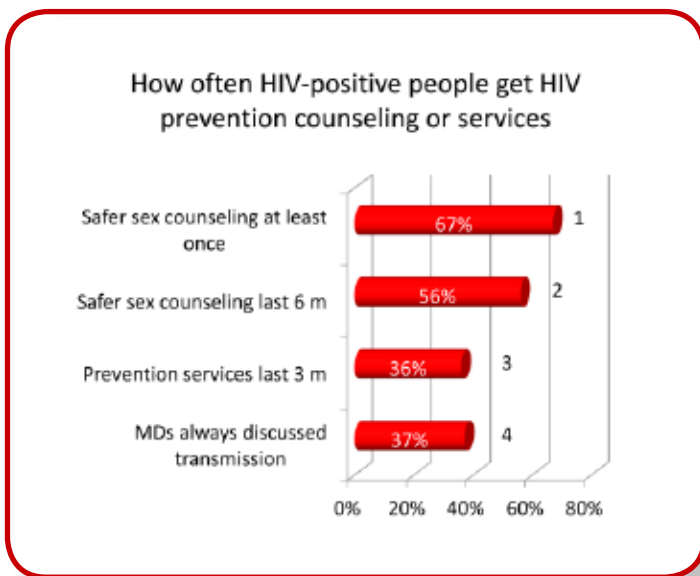


Figure 1. Four studies in the past decade document low to moderate rates of HIV transmission counseling and services offered to HIV-positive people in US clinics. The numbers to the right of each bar indicate the studies described here and in the text. (1) 839 HIV-positive people in six public HIV clinics in California, reported in 2002;⁴ 67% received safer sex counseling by a physician at least once. (2) 413 sexually active HIV-positive people in 16 Ryan White-funded clinics in

9 states, reported in 2004;⁸ 56% discussed safer sex and transmission prevention with a provider in the last 6 months. (3) 3787 HIV-positive people in New York City, San Francisco, Los Angeles, and Milwaukee, reported in 2008;⁵ 36% received HIV prevention services in past 3 months. (4) 317 physicians surveyed in Atlanta, Baltimore, Los Angeles, and Miami, reported in 2008;⁷ 37% of physicians always discussed HIV transmission risk with patients.

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This seeming squeamishness about discussing sex with gays also surfaced in a 2008 study of 3787 HIV-positive people in New York City, San Francisco, Los Angeles, and Milwaukee.⁵ Almost three quarters of this Healthy Living Project group (73%) were men, 50% were MSM, 49% were African American, 26% white, and 19% Hispanic. Median age stood at 41 years.

Only 1356 study participants—a little over one third (36%)—said they received HIV prevention services in the 3 months before their first Healthy Living Project interview.⁵ Compared with other study participants, MSM were twice as likely to report HIV transmission risk behavior (OR 2.04, 95% CI 1.46 to 2.85), but they were 31% less likely to receive HIV transmission risk services (OR 0.69, 95% CI 0.58 to 0.82). Compared with whites, blacks were almost twice as likely (OR 1.93, 95% CI 1.38 to 2.68) and Hispanics 50% more likely (OR 1.52, 95% CI 1.16 to 1.98) to receive such services. People currently taking antiretrovirals were 20% less likely to receive transmission services (OR 0.81, 95% CI 0.74 to 0.89).

Earlier research by this group involving 618 HIV-positive people in 16 publicly funded US clinics found that providers were less likely to counsel people about HIV prevention in the previous 6 months in clinics primarily serving MSM.⁶ This study also traced a correlation between provider belief that behavior change is unlikely in HIV-positive people and chances of HIV prevention counseling. The researchers call this pessimism “provider fatalism,” though it will more likely prove fatal to HIV-positive people or their partners.

A CDC team assessed prevention counseling of positive people in a survey of 317 HIV physicians in Atlanta, Baltimore, Miami, and Los Angeles, 208 of them men and 109 women.⁷ Only 37% of these physicians reported always discussing HIV transmission risk with patients, though 84% always talked about antiretroviral adherence and 65% always discussed prophylaxis for opportunistic infections. Two thirds of these physicians (65%) strongly or somewhat agreed that they had enough time to provide the care and information their patients needed, but only 41% of that group always discussed HIV transmission risk.

Multivariate analysis determined that Hispanic physicians and Asian/Pacific islander physicians were more likely to discuss HIV transmission than other racial/ethnic groups ($P = 0.03$ and $P = 0.0001$), as were physicians who said they had enough time to care for patients ($P = 0.003$) and physicians who cared for fewer patients ($P = 0.05$). The study identified a trend toward more frequent HIV transmission counseling by female physicians (43.5% versus 34.1% of male physicians).

Dismal HIV prevention counseling rates also emerged from surveys of 618 HIV-positive people in Ryan White-funded clinics plus in-depth interviews with 16 clinic administrators, 32 primary care providers, 32 support service providers, and 64 patients.⁸ Half of the HIV group was black, one quarter white, and 19% Hispanic. Three quarters were men, 49% heterosexual, and 45% gay or lesbian. The largest proportion of HIV-positive people (48%) was between 35 and 44, while 30% were 45 or older.

Only 27% of 413 patients who had sex in the past 6 months reported having a general discussion about “safer sex and ways to prevent transmission to others” in that day’s primary care visit,

and only 56% did in the last 6 months.⁸ Only 7% reported discussing specific sexual activities that day, and only 27% did in the past 6 months. These people said their clinicians talked about HIV transmission significantly less than adherence to antiretrovirals (41.5%), emotional issues (34%), or diet and nutrition (33%). People attending clinics with set procedures for HIV prevention counseling were twice as likely to report such counseling (OR 2.17, 95% CI 1.41 to 3.32, $P < 0.001$).

Brief provider prevention prompting has big impact

This bad to middling record of provider prevention prompting is particularly vexing because other research offers ample evidence that HIV-positive people curb risky behavior when providers talk to them about it, even briefly. University of Southern California researchers tested the value of “brief safer-sex counseling” by providers at six California HIV clinics.⁹ In this study of 585 sexually active HIV-positive adults, two clinics stressed the positive consequences of safer sex, two stressed the negative consequences of unsafe sex, and two control clinics stressed antiretroviral adherence. About 85% of study participants were men, about 75% were MSM, about 40% white, and about 35% Hispanic.

Stressing the negative worked best in people with two or more sex partners or with casual partners when the study began, cutting chances of self-reported unprotected anal or vaginal intercourse almost 60% (OR 0.42, 95% CI 0.19 to 0.91, $P = 0.03$) when compared with the control group.⁹ This result was similar when the researchers considered only MSM. The negative approach had no measurable impact on risky sex among people with only one partner (who

had low prestudy rates of unsheathed sex) or only a main partner. And stressing the benefits of safer sex did not trim chances of unprotected intercourse compared with the control arm. These researchers concluded that “brief provider-delivered safer-sex interventions are both feasible and effective at HIV clinics that serve a large number of patients.”

HRSA sponsored a 5-year program to see whether HIV prevention strategies in 13 clinics cut transmission risk in positive people.¹⁰ Of the 3556 study participants, 70% were men, 64% were older than 40, 45% were heterosexual, 44% gay, 8% bisexual, 48% African American, 37% white, and 11% Hispanic. Three quarters of these people had at least one sex partner in the past 6 months, and they averaged 5 partners. One fifth of the study group (21%) reported unprotected anal or vaginal sex with an HIV-negative or HIV status-unknown partner in the last 6 months.

Researchers randomized these people to receive prevention counseling by medical providers and/or “prevention specialists” (a social worker or peer educator) or the standard of care.¹⁰ Compared with the standard-of-care group, people who received provider-delivered prevention interventions had a 45% lower sexual transmission risk rate after 12 months (OR 0.55, 95% CI 0.32 to 0.94, $P < 0.03$). People randomized to counseling by a prevention specialist had a 42% lower sexual transmission risk rate at 6 months (OR 0.58, 95% CI 0.35 to 0.96, $P < 0.04$), but that benefit lost statistical significance at 12 months (OR 0.67, 95% CI 0.39 to 1.14, $P < 0.14$). People counseled on prevention by providers *and* prevention specialists did not have a significantly lower sexual transmission risk at 6 or 12 months than the control group.

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The 12-month difference in transmission risk between provider groups and transmission-specialist groups probably reflects the ongoing transmission counseling offered by providers versus specialist counseling delivered only in the days or weeks after initial patient interviews. These researchers concluded that “behavioral interventions are most effective if they are delivered in ‘doses’—such as at routine medical care visits—over time.”¹⁰

There’s another advantage to the provider-only approach: It’s the cheapest way to go.¹¹ After 3 years of the HIV prevention demonstration project just described,¹⁰ the investigators figured costs and cost-effectiveness for the three approaches used: clinical provider alone, prevention specialist (social worker or peer) alone, and provider-plus-prevention specialist. Cost per patient for 3 years averaged \$1004 when only the clinical provider worked with the patient on prevention, \$3173 when only the prevention specialist worked with the patient, and \$3430 when both the clinical provider and the specialist got involved.¹¹ Compared with the lifetime cost of HIV/AIDS care and with other effective HIV prevention interventions, the clinical provider-led interventions proved cost-effective, but specialist-led interventions and provider/specialist-led interventions did not.

A 2001-2002 survey of 614 HIV-positive people interviewed immediately after an HIV clinic visit at one of 16 Ryan White-funded clinics in 9 states divided clinics into those with written HIV prevention procedures, those where providers offered prevention counseling on their own initiative, and those with no prevention procedures.¹² Half of the study group (51%) was black, 25%

were white, and 19% were Latino. Almost three quarters of patients (73%) were men, 48% were heterosexual, and 46% were gay or bisexual. Three quarters (77.5%) were older than 35, three quarters (76.4%) were taking antiretrovirals, and two thirds (66.9%) had sex in the last 6 months.

How often these people got counseled about HIV transmission depended on their clinic’s prevention policy: In clinics with written procedures, 69% said their provider talked to them about HIV transmission in the past 6 months, compared with 56% in clinics where individual providers had to take the initiative, and 45% in clinics with no HIV prevention protocol.¹² Compared with patients whose clinics had no prevention policy, those in clinics with spelled-out procedures had a tripled chance of getting prevention counseling (OR 3.17, 95% CI 1.24 to 8.06, $P < 0.02$). Notably, though, even in clinics with written guidance, almost one third of patients said their provider did not talk about prevention, and overall 43% said they had not discussed safer sex with their provider.

As in two studies reviewed above,^{4,5} heterosexuals in this study were more likely to get prevention counseling in the past 6 months than gays and bisexuals (OR 1.47 in bivariate analysis, 95% CI 1.01 to 2.12, $P = 0.042$).¹² Blacks got counseled more than nonblacks (OR 1.64, 95% CI 1.09 to 2.46, $P = 0.018$), women more than men (OR 1.59, 95% CI 1.09 to 2.32, $P = 0.016$), and sexually active people more than those not active (OR 1.70, 95% CI 1.26 to 2.31, $P = 0.001$). People older than 35 proved less likely to hear their provider talk about prevention than younger people (OR 0.57, 95% CI 0.39 to 0.85, $P = 0.005$), as were people currently taking antiretrovirals (OR 0.57, 95% CI 0.38 to 0.86, $P = 0.007$). The only one of these factors that independently predicted prevention prompting in multivariate analysis in

clinics with written prevention procedures was current antiretroviral therapy, which lowered chances of counseling more than 60% (OR 0.38, 95% CI 0.33 to 0.43, $P = 0.001$).

A faster, simpler approach to prevention with positives

Despite the several just-reviewed studies showing the value of clinician-provided prevention counseling, at least one study identified a counselor who did better than clinicians in getting HIV-positive people to cut back on risky sex: a computer.¹³ This trial randomized 566 HIV-positive people in six Los Angeles clinics to (1) a 10-minute interactive computer program (two clinics), (2) a provider-delivered prevention interaction (two clinics), or (3) standard care (two clinics). Compared with people randomized to provider delivery or standard care, those who pointed and clicked their way through a prevention program reported a significant drop in number of HIV-negative or HIV status-unknown partners. And compared with the standard-care group, computer users claimed a significant drop in vaginal or anal sex without condoms.

Another interactive laptop prevention program, the Positive Steps “Video Doctor,” yielded significant declines in illicit drug use, average days of ongoing drug use, unprotected sex, and number of casual sex partners compared with standard care.¹⁴ This randomized trial focused on 476 HIV-positive people who reported substance use or sexual risk when attending five HIV outpatient clinics in San Francisco. Results for the first two outcomes were statistically significant both 30 and 60 days after the intervention.

An advantage of both of these digital strategies is that they require 0 up-front provider time.^{13,14}

The Video Doctor gives the flesh-and-blood doctor a “cuing sheet” on risks reported by each patient so the provider can follow-up with appropriate questions and, if necessary, referral.

All three positive-prevention experts interviewed in this issue of *RITA!* stress the value of these time-saving approaches for busy HIV practices. And, no doubt, when it comes to intimate questions about sex and drugs, many people with HIV would rather respond to a computer than to a clinician. The table between the two interviews in this issue outlines these and other patient-administered prevention strategies and provides links for more information.

Why providers skip HIV prevention counseling so often

If people with HIV respond to simple HIV prevention counseling from providers—and waiting room laptops—as part of their regular check-up, why do physicians and other practitioners skip this facet of HIV care so often?³⁻⁸ One HIV clinician/researcher told *RITA!* he could think of four reasons: “Time. Time. Time. Time.” Another four reasons are money, money, money, and money. As the CDC delicately notes in its positive prevention guidelines, “Some clinicians have expressed concern that reimbursement is often not provided for prevention services and note that improving reimbursement for such services might enhance the adoption and implementation of these guidelines.”¹

The survey of 317 HIV physicians in Atlanta, Baltimore, Miami, and Los Angeles underlined the importance of time in determining whether clinicians paused to stress positive prevention.⁷ Physicians who strongly agreed they had enough

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time “to provide care and information to patients” were over 3 times more likely to discuss prevention than physicians who said they didn’t have enough time (OR 3.4, 95% CI 1.9 to 6.1, $P < 0.001$). Every additional 20 patients seen monthly lowered chances of always discussing transmission almost 10% (OR 0.92, 95% CI 0.84 to 0.99, $P = 0.05$).

Three studies reviewed above suggest another important reason—provider discomfort in discussing sex with gay or bisexual men,^{4,5,12} though research reviewed below indicates these men pose the biggest transmission risk among HIV-positive people in the United States.

Another already-mentioned study uncovered a nearly nihilistic reason why providers don’t talk to HIV-positive people about prevention—the belief that people with HIV won’t change their behavior.⁶ Besides surveying 618 HIV-positive people about prevention counseling, these researchers conducted 144 interviews with providers, administrators, and patients in 16 publicly funded US clinics. Then they summed pessimistic comments (described as “provider fatalism”) and assigned each clinic a “fatalism score.”

People in high-fatalism clinics proved less likely to report prevention counseling than those in low-fatalism clinics, even after statistical adjustment for clinic characteristics, patients’ sexual risk, and patients’ health status. People in high-fatalism clinics were more likely to be white, gay, educated, and older—a finding that also suggests providers in these clinics assume their patients are sophisticated or disciplined enough to avoid transmission risk on their own.⁶

A separate analysis of these patients found that people in their first year of care were twice as likely to hear from their provider about safer sex and transmission as people in care for more than 1 year (OR 2.35, 95% CI 1.60 to 3.44, $P < 0.001$).⁸ Interviews with these providers confirmed an array of familiar reasons for shunning prevention reminders: lack of time, specialized training, and dedicated funding for staffing. Interviews with some providers evinced a “conflict over their role and responsibility” when they described themselves “as advocates for their patients’ health, rather than as guardians of the public health.” Providers who agreed that HIV clinics should talk to patients about positive prevention did not agree on exactly who should do the talking.

Because research on this question is lean, RITA! asked an impromptu panel of clinician/researchers to offer their insights on why providers don’t spend more time stressing positive prevention (see box). Almost all 18 ticked off the same reasons disclosed in studies outlined above—the (flattering but perhaps unfounded) assumption that patients are avoiding risk without coaching, the belief that primary care doesn’t carry a public health mandate, and too little time:

“My patients often come with lists of issues to deal with and we attend to those first, often leaving little time for issues that would be on my list,” explained Ann Collier. “Other issues of care often seem more important, more pressing, or more rewarding,” David Margolis noted, acknowledging that “this is a problem.” Indeed, too little time may soon become a time-worn excuse for shunning prevention counseling. The forthcoming CDC update on prevention with positives will stress interventions that require little or no clinician time, as discussed in the two interviews in this issue, in the table between those interviews, and in the second review article.

HIV clinician/researchers who offered RITA! opinions on primary prevention

John A. Bartlett, MD
 Duke University Medical Center
 Durham, North Carolina

Cal Cohen, MD
 Community Research Initiative
 Boston, Massachusetts

Ann C. Collier, MD
 University of Washington
 Seattle, Washington

Eric S. Daar, MD
 David Geffen School of Medicine at UCLA
 Los Angeles, California

Steven G. Deeks, MD
 University of California
 San Francisco, California

Carl J. Fichtenbaum, MD
 University of Cincinnati College of Medicine
 Cincinnati, Ohio

Ian Frank, MD
 University of Pennsylvania
 Philadelphia, Pennsylvania

Joel Gallant, MD, MPH
 Johns Hopkins University
 Baltimore, Maryland

Marshall J. Glesby, MD, PhD
 Weill Cornell Medical College
 New York, New York

Richard H. Haubrich, MD
 University of California
 San Diego, California

Charles B. Hicks, MD
 Duke School of Medicine
 Durham, North Carolina

David A. Katzenstein, MD
 Stanford School of Medicine
 Stanford, California

David M. Margolis, MD
 University of North Carolina
 Chapel Hill, North Carolina

Paul E. Sax, MD
 Harvard Medical School
 Boston, Massachusetts

Jonathan Schapiro, MD
 Sheba Medical Center
 Tel Hashomer
 Ramat Gan, Israel

Susan Swindells, MBBS
 University of Nebraska
 Medical Center
 Omaha, Nebraska

Babafemi Taiwo, MBBS
 Northwestern University
 Feinberg School of Medicine
 Chicago, Illinois

David A. Wohl, MD
 University of North Carolina
 Chapel Hill, North Carolina

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Providers probably also look beyond the time taken for prevention counseling itself to what might follow: If a tricky concern does arise during counseling, clinicians may fear they will have little time to deal with it meaningfully. Along the same lines, John A. Bartlett suggested that hearing patients say they haven't backed away from risky sex creates a "burden" for the provider, "and we might wish that we didn't have this information." But that fear, he stressed, does not excuse clinicians from talking about risky sex.

Carl Fichtenbaum underlined the futility some clinician feel in getting patients to avoid transmission-risk behaviors, the "provider fatalism" seen in the 16-center study discussed above.⁶

David Wohl emphasized provider discomfort in talking explicitly about sex. "Even HIV providers used to doing anal paps and hearing about sex toys and meth-fueled nights on the town can get shy when it comes to talking dirty," he offered. "We are also busy and sex talk takes time."

Some providers, Ian Frank suggested, fear that hammering on consistent condom use may send a pejorative message to the patient, as if the clinician is saying, "You are doing something you know you shouldn't be doing!" He sees value in "getting beyond the condom conversation, which is important, but not the only way to counsel patients about transmission risk."

Paul Sax also stressed that providers must not seem judgmental: "For newly diagnosed patients, or patients seeing you for the first time, it's critically important not to imply blame for the patient being HIV positive," he explained. "Consciously or subconsciously, we may feel that

discussing prevention sends that message—that if only you had followed this prevention advice, you wouldn't be infected."

How often does HIV get transmitted?

TB may jump from one person to the next more readily than HIV makes that leap, but odds of bloodborne or sexual transmission of HIV are not long when one considers (1) the consequences and (2) how often people embrace the risk in a lifetime. Getting transfused with HIV-tainted blood—though rare today—almost always results in HIV infection, with chances estimated at 95-in-100.³ Children born to HIV-positive mothers without antiretroviral prophylaxis stand a 1-in-4 chance of HIV infection. From there, odds drop in people sharing drug-injecting equipment or having condom-free sex (**Figure 2**).

But compared with other risks, sexual HIV transmission chances should inspire caution—if not awe—in people who let HIV near a nick, sore, or porous mucosal wall. For example, the 1-in-150 chance of picking up HIV while sharing injecting equipment exceeds the 1 in 167 risk of dying from heart disease or from an accident in the next 10 years among 45-year-old US men who never smoked¹⁵ and far exceeds the 1-in-1000 risk of dying from pneumonia in the next 10 years among 45-year-old US men who *do* smoke.¹⁵ The high estimate for acquiring HIV during rubber-free male-to-male anal intercourse, 1-in-10, is about the same as the 1-in-10 to 1-in-25 chance of miscarriage in the United States¹⁶ and far exceeds the 1-in-36 chance of rolling snake eyes (one and one) in craps.

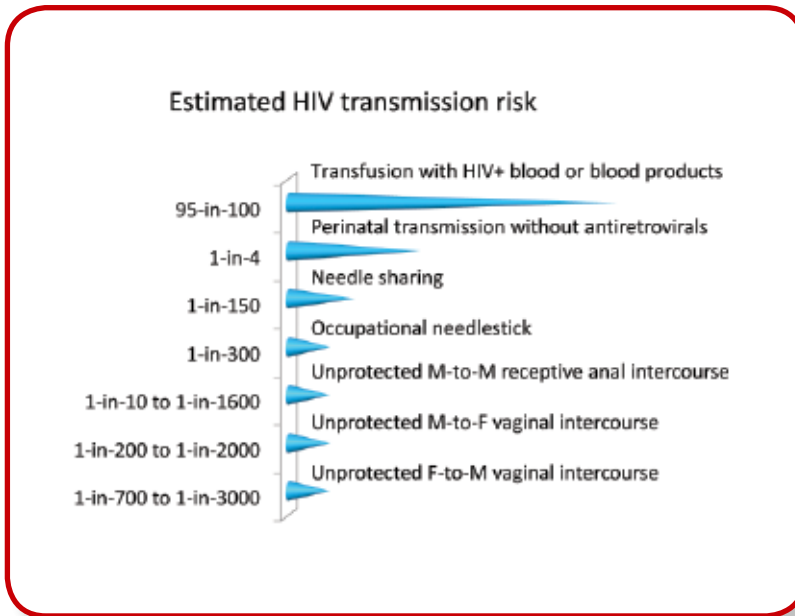


Figure 2. Risk of HIV transmission is generally higher with needle sharing or needlestick injuries than with condom-shirking male-to-male anal intercourse or heterosexual coitus.³ But some research suggests that unprotected receptive anal sex may be riskier than needle sharing or needlestick and that for women unprotected vaginal sex may be as risky as needle sharing or needlestick.

Lifetime chances of HIV infection in the US are downright awful. For the years 2004-2005, CDC researchers estimated that white men in 33 of the United States ran a 1 in 104 chance of getting infected, Hispanic men a 1 in 35 chance, and black men a 1 in 16 chance.¹⁷ Estimated lifetime infection rates for US women were 1 in 588 for whites, 1 in 114 for Hispanics, and 1 in 30 for blacks. If you told people they had a 1 in 16 to 1 in 104 lifetime chance of dying in a plane crash, how many people would fly?

CDC number jugglers offer another way to weigh the risk of getting HIV from a sex partner (**Figure 3**).¹ Starting with the premise that insertive penile-oral sex is the least likely way to pick up the retrovirus, the CDC team uses study data to estimate the relative risk of receptive penile-oral sex (twice as likely), insertive vaginal sex (10 times more likely), receptive vaginal sex (20 times more likely), insertive anal sex (13 times more likely), and receptive anal sex (100 times more likely). Compared with using a condom, the CDC figures, shunning condoms hikes the risk of HIV acquisition 20 times.

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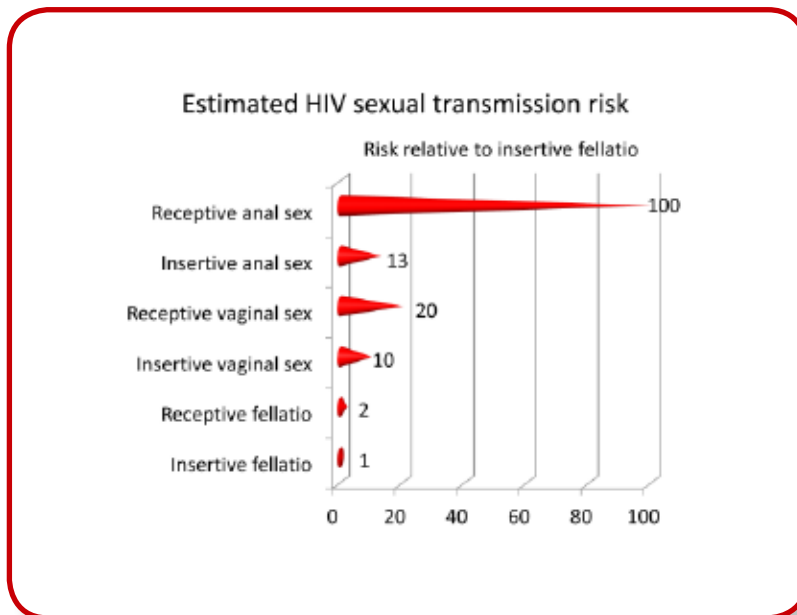


Figure 3. Using data from published studies (and a “best-guess estimate”), the CDC figured the likelihood of getting HIV during sex compared with insertive fellatio as the reference. (Source: CDC. Incorporating HIV prevention into the medical care of persons living with HIV: recommendations of CDC, the Health Resources and Services Administration, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. *MMWR*. 2003;52(No. RR-12).)

Needle sharing and needlestick HIV transmission risk varies according to how much blood gets under the stuck person’s skin. And anal or vaginal transmission risk depends on viral load in the already-infected person and sexually transmitted diseases or open wounds in either partner. A landmark study of 415 HIV-discordant Ugandan couples—one partner positive, one negative—established the tight link between HIV load in plasma and transmission risk in this antiretroviral-naïve group.¹⁸ Viral load averaged 90,254 copies/mL in people whose partner got infected with HIV versus 38,029 copies/mL in

those whose partners stayed HIV-free ($P = 0.01$). Multivariate analysis accounting for other transmission risk factors determined that every 10-fold higher viral load more than doubled transmission risk (OR 2.45, 95% CI 1.85 to 3.26).

A more recent analysis of 235 monogamous Ugandan couples in this same population confirmed the intimate link between transmission risk and viral load (as well as genitourinary disease) in the positive partner.¹⁹ These researchers examined the impact of disease stage, viral load, and other factors on transmission risk in the years

before any of these people took antiretrovirals. They established HIV transmission by HIV sequence analysis.

The HIV transmission rate was about 8 per 1000 coital acts in the first 5 months of HIV infection, when viral load is highest (median 30,000 copies/mL in this cohort).¹⁹ Six to 35 months after infection, the rate fell to about 1.5 per 1000 coital acts as the viral load waned (median 2600 copies/mL 15 months after infection). During chronic HIV infection, transmission rates varied from about 0.5 to 1.0 per 1000 coital acts (median viral load 10,300 copies/mL at study entry and 15,000 copies/mL after 30 months of follow-up). In late-stage infection (median viral load 112,600 copies/mL), transmission rates climbed back above 1 per 1000 coital acts, reaching about 3.5 per 1000 in the 6 to 25 months before death.

Multivariate analysis determined that, compared with a viral load in the lowest quartile, a load in the next-higher quartile tripled the risk of HIV transmission per coital act (rate ratio [RR] 3.31, 95% CI 1.01 to 10.80), a load in the next-higher quartile upped the risk more than 6 times (RR 6.39, 95% CI 2.10 to 19.42), and a load in the highest quartile inflated odds 7 times (RR 7.06, 95% CI 2.29 to 21.81). In a model that also included viral load, genitourinary disease in the initially infected partner doubled the risk of transmission (RR 2.05, 95% CI 1.02 to 4.14).

A recent longitudinal study of 1381 initially HIV-negative gay men in Sydney, Australia figured a per-sex-act HIV risk of 14.3-in-1000 for men who practiced unprotected receptive anal intercourse with ejaculation in the rectum versus 6.5-in-1000 for unprotected receptive anal intercourse with withdrawal before ejaculation.²⁰ The latter rate came close to the 6.2-in-1000 for uncircumcised

men who practiced unprotected insertive anal intercourse, much higher than the 1-in-1000 rate for circumcised men taking the insertive role. The 1.43-in-100 infection rate for receptive partners whose mates ejaculated in their rectum looks big when one considers that the 663 men who took that role reported 56,514 such encounters in 6 years of total follow-up, or 85 per man. Also, these findings underline the iffy protective value of withdrawal during anal sex.

Are US HIV transmission rates changing?

Thanks to busy CDC number summers, the United States has well-estimated and routinely updated counts of HIV prevalence, incidence, and (less often) transmission. But discerning precisely what these tallies say about positive prevention takes an extra army of experts.

In 2008 the CDC heralded a 1977-2006 estimate of HIV transmission with the headline “Dramatic Declines [in HIV transmission] Indicate Success in U.S. HIV Prevention.”²¹ The CDC summary explained work by Johns Hopkins researchers who used CDC data to reckon HIV infections transmitted per 100 HIV-positive people by dividing HIV incidence (the number of new infections) for a given year by HIV prevalence (the overall number of people with HIV) for the same year.²²

Three years after clinicians identified AIDS, in 1984, the Hopkins team figured a transmission rate of 44.4%, meaning 44 out of every 100 HIV-positive people passed the virus to someone else.²² That rate plunged to 11.7% in 1990, to

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7.5% in 1997 (a year or 2 after triple therapy arrived), and to 5.0% in 2006, the final year of the analysis (**Figure 4**). The nosedive from 44 to 5

transmissions per 100 positive people represents an 89% decline. So something—probably many things—were going right.

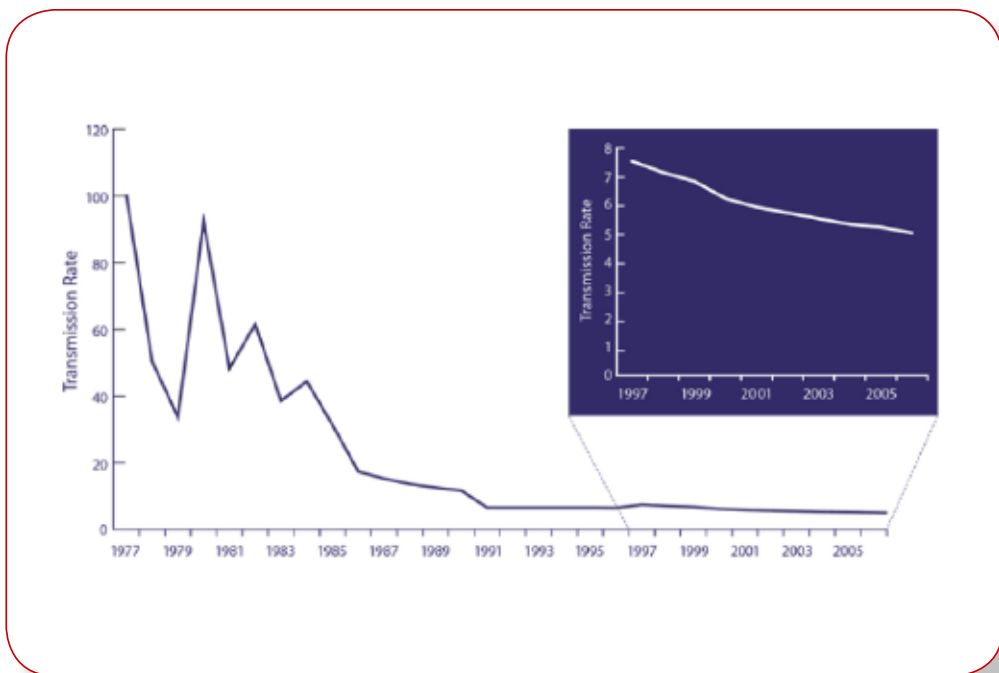


Figure 4. Using CDC data, independent researchers calculated that the US HIV transmission rate swooned from 44 per 100 HIV-positive people in 1984 to 5 per 100 in 2006.^{21,22} But HIV incidence, the numerator in the transmission rate equation (incidence/prevalence), did not keep dwindling after 2006. (Reproduced from CDC HIV/AIDS Facts. HIV transmission rates in the United States. December 2008.²¹)

The Hopkins formula for calculating transmission rate (incidence/prevalence in a given year²²) means transmission would drop if incidence fell and/or if prevalence rose. Indeed, US HIV incidence did tumble from its estimated peak of 130,400 new infections in 1984 and 1985 to about 84,000 from 1986 to 1990, then to about 48,000 in 1991 to 1996.²² From 1997 through 2006, the last year of this analysis, HIV incidence fell no farther.

Over the same years, HIV prevalence climbed steadfastly from about 400,000 cases in 1985, to about 800,000 in 1998, and up to 1.2 million in 2008, the last year for which the CDC made an estimate.²³ These estimates include people with undiagnosed HIV. US HIV prevalence rose so doggedly after combination therapy arrived not because lots more people were getting infected (incidence was flat), but because already infected people were living longer. Much longer. Together, falling (or flat) incidence plus rising prevalence would make the transmission rate (incidence/prevalence) sink.

Despite the dwindling estimated transmission rate through 2006, HIV incidence among people 13 and older bottomed out that same year at around 48,000 new infections per year, according to a 2011 CDC study.²⁴ From 2006 through 2009, incidence stayed stuck at that level—48,600 new infections in 2006, 56,000 in 2007, 47,800 in 2008, and 48,100 in 2009. But because HIV prevalence continued to climb, at least through 2008,²³ the CDC's Kathleen Irwin believes transmission rates were falling in those years (see the interview in this issue): If there are more and more people with HIV from one year to the next but incidence (new infections) stays flat, the transmission rate must be dropping.

What these numbers don't explain is why HIV transmission rates appeared to keep dipping in the 15 years since triple therapy arrived. Almost certainly, pushing viral loads to uncountable levels in more and more people stanching transmission considerably.²⁵⁻²⁷ Whether prevention counseling or risk reduction has much to do with waning transmission seems dubious, since these studies also found rising rates of sans-condom receptive anal intercourse,²⁵ vaulting prevalence of infectious syphilis, genital gonorrhea, and genital chlamydia,²⁶ and climbing rates of rectal gonorrhea.²⁷

The CDC incidence study had no trouble pinpointing groups whose new HIV infection rate marooned incidence on a high plateau.²⁴ "The only population with a change in HIV incidence over the entire four-year [2006-2009] period was 13-29 year olds, and within that age group, the only risk group experiencing increases was MSM," the CDC reported. "Among young MSM the estimated number of new infections increased significantly from 2006 to 2009; the increase in incidence in this group was largely driven by a statistically significant increase in new HIV infections of 48% (12.2% annually) in young, black/African American MSM."²⁴

HIV transmitter candidates not hard to find

HIV-positive people unaware of their viral stowaways constitute a deep and covert pool of potential transmitters. In 2006 the CDC figured that HIV-positive but undiagnosed people have a 3.5 times higher risk of passing HIV to a sex partner than people who know they carry the virus.²⁸ Wider HIV screening and earlier diagnosis can

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curtail HIV transmission, and clinicians can promote HIV testing through their positive patients and in their community—topics examined in the preceding issue of *RITA!*.²⁹ But this review focuses on how providers can limit transmission from people who know they have HIV.

The list of likely transmitters is no secret to HIV providers:

- People with a high viral load
- Sexually active gay and bisexual men (MSM)
- Heavy injection and noninjection drug users
- People with mental health problems

But some studies identify transmission-risk groups one might not readily suspect.

→ **High viral load and recent HIV infection.** Ugandan studies of heterosexual couples (discussed above under “How often does HIV get transmitted?”) framed a tight link between viral load and sexual transmission risk.^{18,19} Almost a decade earlier, US researchers found sky-high levels of infectious virus (up to 1000 tissue culture-infective doses per milliliter of plasma) 6 to 15 days after the onset of primary infection symptoms.³⁰ Those loads “fell precipitously” by day 27.

Modeling blood and semen HIV loads in 30 men with known dates of infection or onset of acute HIV symptoms, another US team estimated that—depending on how often they have sex—men with average seminal loads during primary infection would infect 7% to 24% of female sex

partners during the first 2 months of infection.³¹ If either partner has a sexually transmitted disease, those proportions would grow. In Quebec phylogenetic analysis of HIV from 591 people with primary infection and 795 with chronic infection yielded numbers suggesting that early HIV infection accounted for half of HIV transmissions in the whole group.³²

HIV providers understand the higher transmission risk conferred by lofty viral loads, but many people with early infection don’t. In-depth interviews with 34 newly infected people in 6 US cities showed that “most participants knew little about the meaning and/or consequences of acute HIV infection, particularly that it is a period of elevated infectiousness.”³³ Health workers who see acutely or recently infected adults should make sure they understand the link between high viral load and HIV transmission.

→ **Gay and bisexual men.** The CDC’s latest HIV incidence study left no doubt that MSM still comprise the premier risk group in the United States.²⁴ HIV incidence among all people 13 and older remained flat at 48,000 new infections yearly from 2006 through 2009, but the new case rate did grow in one group: boys and men between 13 and 29 years old. Among young blacks, HIV incidence rose 12% annually over those 4 years (**Figure 5**). MSM accounted for 61% of new HIV infections in 2009, and MSM who injected drugs made up another 3%. A versatile few of these newly infected gays and bisexuals may be picking up HIV from women, but most are netting the retrovirus from other MSM.

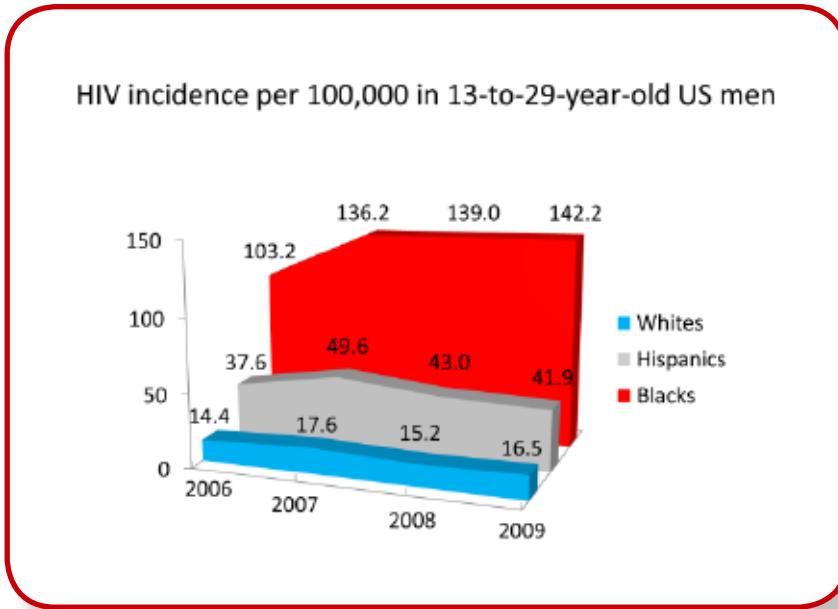


Figure 5. From 2006 through 2009, HIV incidence per 100,000 population rose steadily among black boys and men between 13 to 29, while remaining essentially flat among Hispanic and white boys and men that age.²⁴ HIV incidence in blacks this age was about 3 times higher than in Hispanics and more than 7 times higher in whites.

Studies of HIV-positive people in primary care bear out this torqued-up transmission risk in MSM. In a 15-city US study, 2109 HIV-positive MSM, 1104 women, and 803 men who have sex with women (MSW) completed a computer-assisted survey asking how often they had unprotected anal or vaginal sex with an HIV-negative partner or a partner with an unknown HIV status.³⁴ Compared with MSW, MSM had more than a doubled risk of condom-free sex (OR 2.35, 95% CI 1.84 to 3.00, $P < 0.001$).

In a result that may surprise some, women in this study reported more than a 50% higher rate of risky sex than MSW (OR 1.56, 95% CI 1.19 to 2.05, $P < 0.001$).³⁴ An earlier study of 3723 HIV-positive people in Los Angeles, Milwaukee, New York City, and San Francisco found

that 19% of women, 15.6% of MSM, and 13.1% of MSW had unprotected vaginal or anal intercourse with HIV-negative or status-unknown partners.³⁵ But this study of 1918 MSM, 978 women, and 827 MSW found that fewer than one quarter of women and MSW had 2 or more sex partners, compared with 59% of MSM. Researchers estimated that 30 sex partners of these HIV-positive people would get infected during the 3-month study, and 24 of them (80%) would pick up HIV from MSM.

Modeling HIV transmission data on the basis of partner information provided by 3652 MSM in five US cities, Emory University researchers figured that two thirds of transmissions in these

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men (68%) involve their main sex partner, not casual partners.³⁶ Sensitivity analyses plugging in different variables indicated that transmission from main sex partners may account for 52% to 74% of new HIV infections. Modeling also calculated that 69% of HIV infections resulted from receptive anal intercourse, 28% from insertive anal intercourse, and 2% from oral sex. Model-based estimated HIV incidence in this population was 2.2% per year.

The high transmission rate from main partners reflected more frequent sex with main partners, more frequent receptive anal intercourse with main partners, and lower condom use during anal sex with main partners.³⁶ These findings led the investigators to propose that “couples-based HIV prevention interventions for MSM should be given high priority in the US HIV prevention research portfolio.” Not to mention the HIV clinical care portfolio.

Nearly everyone who follows the US HIV epidemic understands the high and abiding risk of viral transmission from gay and bisexual men. But as noted earlier in this article (see “Prevention counseling takes back seat”), that understanding has not spurred many HIV providers to talk to MSM frankly and frequently about protecting their partners from HIV.

→ **Heavy drug use.** Several studies confirm that using stimulants like crystal meth heightens the risk of HIV transmission. The already-discussed 15-city study of 4016 HIV-positive people in primary care found that stimulant use swelled transmission risk in gay men, straight men, and women ($P < 0.05$).³⁴

A four-city study of 1910 HIV-positive MSM (36% African American) who completed computer-assisted interviews about their 5 most recent partners traced significant links between three types of drug use and unprotected sex partners:³⁷ Stimulant use doubled the risk of unprotected sex with steady partners (adjusted OR 2.10, reference 1.00 to 4.39, $P = 0.050$), and both crystal meth (adjusted OR 1.76, reference 1.16 to 2.68, $P = 0.009$) and other drugs (adjusted OR 1.82, reference 1.16 to 2.86, $P = 0.009$) almost doubled the risk with casual partners. Neither education level nor race/ethnicity affected unprotected sex risk in these analyses. Men who did not disclose their HIV status to partners—including steady partners—had risky sex more often than serostatus disclosers.

A study of 90 HIV-positive MSM found that binge meth users reported more risky sexual behaviors—as well as more social difficulties and physical and mental health problems—than MSM who used meth but did not binge.³⁸ Forty-one of these 90 men (46%) said they binged for periods ranging from 2 to 33 days. Bingers were significantly more likely to be ethnic minorities and to have less education than nonbingers.

A study of 303 HIV-positive male and female African-American crack cocaine users defined bingeing as using as much crack cocaine as you can, until you run out of crack or can't use any more, in the last 30 days.³⁹ Half of these people (51%) reported bingeing for an average 3.7 days, during which they smoked 40 rocks of crack. Almost three quarters of bingers (72%) had sex during their last binge with an average of 3.1 partners. Recent male bingers were more likely than non-

bingers to report lifetime and recent exchange of money for sex and drugs for sex. Recent female bingers were more likely to report lifetime trading of sex for drugs. Multivariate analysis determined that recent bingers were more likely than nonbingers to have high transmission risk scores, to have more sex partners in the last 1 month or 6 months, and never to use a condom during sex in the last 30 days.

Of course injection drug use poses a prodigious risk of HIV transmission, not only because HIV passes from person to person more readily through needle sharing than during sex (**Figure 2**), but also because of the social and psychological factors that boost HIV transmission risk among IDUs. And sharing injection works is not the only way IDUs transmit HIV, as indicated by a case-control comparison of 58 San Francisco IDUs who picked up HIV during follow-up and 1134 controls (matched for gender and date) who did not.⁴⁰ Compared with controls, the IDUs who became infected were almost 9 times more likely to be MSM (OR 8.8, 95% CI 3.7 to 20.5) and 5 times more likely to have traded sex for money in the past year (OR 5.1, 95% CI 1.9 to 13.7). Women with a steady sex partner who injected drugs were almost 70% less likely to become infected (OR 0.32, 95% CI 0.11 to 0.92).

The CDC figures that drug injectors accounted for 36% of AIDS cases since the US epidemic began through 2000.⁴¹ The 2006-2009 CDC study of HIV incidence found that IDUs made up about 10% of new HIV cases in each of those years.²⁴

→ **Mental health and other factors.** Changing mental health in HIV-positive people has complex interactions with HIV transmission risk, as illustrated in a 936-person longitudinal study of positive people enrolled in a transmission-

prevention trial.⁴² This four-city study recruited HIV-positive people from community agencies, AIDS service organizations, and medical clinics for a trial of an individually administered cognitive-behavioral intervention; 851 people had at least one follow-up visit. All study participants had signs of severe neuropsychological impairment or psychosis and reported unprotected vaginal or anal intercourse in the past 3 months with a sex partner whose HIV serostatus was negative or unknown. Participants were randomized to start the Healthy Living Program cognitive-behavioral intervention immediately or after 25 months of follow-up.

Ages ranged from 19 to 66. Most participants (79%) were men, 46% were black, 32% white, and 14% Hispanic.⁴² Almost three quarters of these people (72%) reported having sex with other men, and 43% had less than a high school education. When the study began, 40% of participants had clinically significant depression, 36% had clinically significant anxiety, and 25% had both.

Upon study entry, lower levels of depressive symptoms in the entire study group and higher scores in the Positive States of Mind (PSOM) scale were associated with having *more* HIV-negative partners in bivariate analysis.⁴² In the intervention group, worse anxiety symptoms were related to lower numbers of HIV-negative partners at baseline, and lower PSOM scores were related to *increasing* numbers of HIV-negative partners over time. In the delayed-intervention group, increasing depressive symptoms were related to decreasing numbers of HIV-negative partners over time. For the entire study group, lower PSOM scores from assessment to assessment were “modestly” associated with more risky sex acts, and more anxiety symptoms were associated with more HIV-negative partners. Stephen Morin (Univer-

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sity of California, San Francisco), one of the investigators, discusses this study in an interview in this issue of *RITA!*

A Women's Interagency HIV Study (WIHS) analysis found evidence that poor antiretroviral adherence ups the risk of low condom use in women with HIV.⁴³ This study involved 766 antiretroviral-treated women, 66% of whom reported at least 95% adherence. Among sexually active women, less than 95% adherence doubled the risk of inconsistent condom use (OR 2.17). In the entire study group, poor adherence independently doubled chances of active drug use (OR 2.27, 95% CI 1.39 to 3.33). The WIHS team believes their results "highlight the importance of discussing [sexual behavior and adherence] in relation to one another, particularly with regard to patients experiencing virologic failure."

Even being hungry may boost the risk of unsafe sex, at least among IDUs taking antiretrovirals. Researchers in British Columbia reached that conclusion in a longitudinal study of 420 IDUs

enrolled in the AIDS Care Cohort to Evaluate Exposure to Survival Services from 2005 through 2009.⁴⁴ Almost three quarters of this group (71%) suffered from food insecurity, marked by hunger due to lack of access or means to acquire food. People with food insecurity were marginally less likely to have an undetectable viral load (31% versus 39%, $P = 0.099$). Multivariate analysis that controlled for age, gender, marriage or cohabitation, binge drug use, homelessness, and antiretroviral use determined that food insecurity almost tripled the risk of unprotected sex (adjusted OR 2.68, 95% CI 1.49 to 4.82).

The second review article in this issue of *RITA!* scrutinizes diverse strategies for helping HIV-positive people avoid transmitting their virus. One of the clinician/researchers we polled for their opinions on this question, Babafemi Taiwo (Northwestern University, Chicago), offered this admirably succinct advice: "1. Test as many people as possible. 2. Treat as many infected patients as possible." But the next article will ask readers to endure considerably more detail.

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Providers hold key in prevention with positives

An interview with **Stephen F. Morin, PhD**

*Professor of Medicine
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Department of Medicine
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Dr. Morin was among the first scientists to undertake behavioral research on HIV prevention. Besides his ongoing investigation of HIV prevention—much of which focuses on prevention in positives—he has helped recommend structural changes in the AIDS Drug Assistance Program and has studied racial and ethnic disparities in access to HIV medication. From 1987 through 1997, Dr. Morin worked as principal legislative assistant to Representative Nancy Pelosi, then on the Labor-HHS-Education Appropriations Subcommittee, which funds most of the federal response to AIDS.

Provider-patient prevention exchange can take only 90 seconds

Mascolini: What does your research and others' tell us about which HIV-positive people in the United States have the highest risk of transmitting their virus sexually or by needle sharing?

Morin: The greatest transmission risk continues to be sexual transmission, even among injectors. In the United States, being a man who has sex with men (MSM) is the greatest predictor of HIV transmission risk. Most sexual transmissions occur among MSM, and MSM have the highest probability of transmission.

Much of my research has looked at how clinical settings can be used to reach men who have sex with men and other HIV-positive people who may be at risk of transmitting to others. We've been looking at everything from very simple com-

munications from providers to very complicated multisession interventions delivered by prevention specialists. (See "What are effective HIV prevention models for use in health care settings?")

Mascolini: Your work shows that prevention interventions delivered in clinical care settings can be effective in reducing HIV transmission risk.¹⁻³ But clinicians say they don't have enough time or they're uncomfortable talking about sex or they don't think they can change patient behavior. How can clinicians get beyond these negative perceptions?

Morin: We started examining this issue by looking at the opportunity for prevention in clinical settings.^{4,5} Those early studies found that prevention interventions in clinical settings were unusual, and we found that there was considerable difference of opinion among providers about their

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What are effective HIV prevention models for use in health care settings?

Excerpted from: How can HIV prevention be integrated into health care settings? Center for AIDS Prevention (CAPS) Fact Sheet 68. July 2010. Prepared by Carol Dawson-Rose, Janet Myers, and Karen McCready. <http://caps.ucsf.edu/factsheets/prevention-in-health-care-settings/>.

Positive STEPs is a training intervention to help HIV care providers deliver prevention counseling to their patients. The model was effective in improving provider attitudes, comfort, self-efficacy and frequency of delivering prevention counseling.¹

Partnership for Health is an EBI (CDC's Effective Behavioral Intervention) for providers in HIV clinics. Medical providers are trained to deliver brief risk-reduction counseling to their patients. All clinic staff are trained to integrate prevention messages into the clinic setting, and counseling is supplemented with written information for all patients. The intervention was effective in reducing unprotected intercourse by 38% among patients who had two or more sex partners.²

Positive Choice is an interactive "Video Doctor." Patients at HIV clinics complete an in-depth computerized risk assessment and receive tailored risk-reduction counseling from a "Video Doctor" via laptop computer and a printed educational worksheet. Providers receive a Cueing Sheet on reported risks for discussion during the clinical encounter.³

Provider-Delivered Counseling. In a large federal demonstration project, brief counseling messages delivered by primary care providers in clinic settings were most effective in reducing risk among HIV-infected patients, although there were also benefits in programs delivered by prevention specialists and HIV-infected peers.⁴

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role in prevention.⁴ Some providers argued that they were advocates for their patients, that their primary responsibility was improving health outcomes, and that they did not play a significant role in public health, which was other peoples' responsibility. Other providers argued that of course sexual health was part of taking care of any patient and that frank discussions about sexual risk and transmission were part of their responsibility in improving health outcomes. You had a range of provider attitudes on this issue.

We found that in order to get providers more involved, one has to start by working to minimize the burden on providers and to simplify the process of conducting the risk assessment. The most useful and efficient provider-based interventions last about a minute and a half. You have to structure the situation so the provider is comfortable and has some guidance about how to deliver a prevention message in a very brief amount of time.

Mascolini: And do your findings show that such brief interventions can be effective?

Morin: Yes, we actually found it to be the most effective and most cost-effective of various interventions that we looked at.²

Looking for chances to address acute HIV infection

Mascolini: Your work indicates that people with acute HIV infection don't understand the high transmission risk associated with their new infection.⁶ You also found that newly infected MSM cut back on sex and risky sex in particular.⁷ Do HIV clinicians see acutely infected people often enough to have an impact on prevention at this critical juncture?

Morin: Yes, providers see acutely infected patients often enough to have an impact. Among all their patients, the proportion of people with acute infection is very low. Even in those low numbers, however, they can still have an impact because diagnosing acute infection—when the viral load is so high—can have such a big impact on transmission outcomes.

We find that many providers do not have sufficient information about sexual history or risk in their HIV-negative patients. If they did, they would probably do more screening for acute infection. One of the interventions we've recommended is a provider awareness campaign that encourages providers to screen for HIV and STIs [sexually transmitted infections] in clinical settings when people present with certain symptoms.

Mascolini: Who would mount such campaigns?

Morin: It could be done through specialty organizations, though any of the professional groups, or through networks at the local level. Most of these campaigns have been done in discrete jurisdictions, like New York City.

Screening for mental health and substance abuse in the waiting room

Mascolini: A study you coauthored found complex and evolving interactions between mental health and HIV transmission risk.⁸ Can you summarize the clinically relevant take-home findings?

Morin: The important takeaway messages from that study are that there is a high prevalence of mental disorders in the population of people

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with HIV, and if clinicians treat depression and other mental health issues they can improve antiretroviral adherence and improve clinical outcomes. The relation between the mental health issues and substance abuse issues is very significant as well.

In terms of prevention in positives, these findings point to a need to screen for both mental health and substance abuse in the course of treating people with HIV. These kinds of brief screenings can be done in waiting rooms, the same way you can screen for transmission risk on handheld devices in waiting rooms. If you make it efficient and don't put the burden on the provider, you greatly increase the likelihood that it will get done as part of routine clinical business. [See the table following this interview for a summary of four patient self-administered interventions.]

Depending on patient responses on the handheld device, the provider can be alerted to the need for intervention. If there's no problem, the provider is not cued. If there is a problem, there's a prompt in the electronic medical records to raise the issue. That may mean directly intervening with a message or it may mean referral for specialty care.

Mascolini: Are clinical practices adopting this approach?

Morin: It depends on how technology-savvy the practice is. Practices that have electronic medical record prompts tend also to be more flexible in terms of screening procedures that cue providers when to intervene and when not to.

Serosorting, written procedures, and HPTN 052

Mascolini: Your research shows that MSM adopt serosorting if they learn they're positive⁷ and that behavioral intervention can cut HIV transmission from positive people by promoting serosorting in MSM.⁹ But other work shows that serosorting has a modest protective effect when compared with condom use.¹⁰ Do you think clinicians should encourage serosorting in HIV-positive MSM?

Morin: You have to look at the relative contribution of serosorting. It's not your first-line strategy for prevention. But among people who are unlikely to use condoms, serosorting can be better than nothing. The primary risk in serosorting is among negative men as opposed to positive men. In fact, many MSM who start serosorting with positive partners after seroconverting were serosorting with negative partners and ended up getting infected.

If you're talking about clinicians working with positive patients and trying to reduce the risk of onward transmission to new partners, discussing serosorting is one task. And if positive MSM are serosorting for positive partners, there are other risks that need to be discussed, including STIs and the challenge to the immune system posed by additional infections.

Mascolini: You've found that clinics with written procedures on positive prevention do a better job delivering positive prevention counseling.³ What other practical steps can medical

practices and providers take to promote better prevention services?

Morin: How do clinics get to the point of having written procedures? It usually takes some kind of leadership at a practice level to adopt written procedures as an important thing to do. And that leadership ultimately results in training and procedures, which then get implemented in a clinical setting. If you have that leadership, if you have those written procedures, then prevention interventions are likely to occur. If you don't have the leadership and don't have the written procedures, it's far less likely to occur. The AIDS Education and Training Centers can be a good resource for providers interested in this issue [<http://www.aids-ed.org/>. Go to "Topic Index" at the bottom of the home page, then click on "Prevention with Positives."]

Mascolini: Will results of HPTN 052¹¹ change the way US HIV physicians and patients think about antiretroviral therapy?

Morin: They should. We've not studied whether it's led to a change in practice. However, you would expect that it would at a minimum start a conversation for clinicians working with serodiscordant couples, because treating the infected partner early can clearly have a beneficial effect in not infecting that negative partner. And I think that message is out there in the clinical community.

HPTN 052 showed that earlier antiretroviral treatment and viral suppression not only prevent onward transmission, but also promote better health outcomes in the infected individual.¹² For

discordant couples, suppressive antiretroviral therapy taken by the infected partner has a benefit for both partners.

Is positive-prevention research making a difference?

Mascolini: HIV incidence remains flat in the US,¹³ suggesting that HIV-positive people continue to transmit their virus at about the same rate. After all the time and effort you've spent studying positive prevention, do you see any signs that providers or patients are doing better in cutting HIV transmission risk?

Morin: It's hard to say. Let me put it this way: The last 2 years have seen a significant shift in the CDC's approach to HIV prevention—and the approach in the United States—with a clear focus on prevention through the National HIV/AIDS Strategy.¹⁴ The new strategy also emphasizes treatment outcomes and reducing disparities between different populations. All of that, along with coordination efforts, have put a greater emphasis on the importance of viral suppression as a clinical outcome.

That is being communicated in clinical practices and will increase, one, the frequency of testing among those at risk and, two, the proportion of that population with HIV that is virally suppressed. And as you increase that proportion, or lower community viral load, you should see a decrease in the number of new infections.^{15,16} This approach is a different way of thinking for this country—a shift from exclusive condom promotion.

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We have yet to see what the impact will be on the CDC projections of new infections. It will take a while for this new approach to take hold and have a significant impact on transmission rates.

Mascolini: What other findings from your work or other work on positive prevention would you like to stress for clinicians caring for HIV-positive patients?

Morin: It's been clear for a long time that, in terms of cost-effectiveness, the more you intervene with HIV-positive people and give them a significant role in HIV prevention leadership, the better off you're going to be. Just focusing on at-risk HIV negatives is not as cost-effective as working with people who are aware of their infection and who are willing to partner with the provider in trying to prevent onward transmission.

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Patient Self-Administered Risk-Reduction and Screening Programs

Intervention	Aim	Tools	Brief description
Positive Choice Video Doctor ¹	Eliminate or reduce sex risk behaviors or illicit drug use in HIV-positive people	Laptop, printed educational worksheet, cuing sheet for providers	Patients in HIV clinics complete in-depth computerized risk assessment and receive tailored risk-reduction counseling from a "Video Doctor" via laptop and printed educational worksheet; providers receive cuing sheet on reported risks for discussion during patient visit.
Motivational interviewing ²	Enhance motivation of HIV-positive people to reduce number of HIV-negative and status-unknown sex partners	Waiting room computer	Ten-minute self-administered interactive program that (1) assesses personal values, (2) encourages personal responsibility and responsibility toward others, (3) provides feedback on congruence between personal values and behavior, (4) encourages self-efficacy to implement new actions.
Safe in the City ³	Lower incidence of HIV and other STIs	Waiting room posters directing attention to a personally viewed video	Twenty-three-minute video viewed in STI clinics depicts couples overcoming barriers to safer sexual behaviors; animated segments show correct condom use.
STI self-screen ⁴	Detect asymptomatic gonorrhea and chlamydia in HIV clinic patients	Multiple self-swabs to detect rectal, urethral, and pharyngeal pathogens, followed NAAT	During routine blood-test visit, nurse-led screening relying on self-swabbing by patients with no STI symptoms, followed by staff-conducted NAAT for <i>Neisseria gonorrhoeae</i> and <i>Chlamydia trachomatis</i> .

NAAT, nucleic acid amplification test; STI, sexually transmitted infection.

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Sorting out CDC data and guidelines on preventing HIV transmission from positives

An interview with
Kathleen Irwin, MD, MPH, FIDSA

(Fellow of the Infectious Diseases Society of America)

and

Nicole Crepaz, PhD

Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention

Dr. Irwin leads the guidelines development team for the Division of HIV/AIDS Prevention. In collaboration with HIV experts at CDC, the Health Resources and Services Administration (HRSA), and several national HIV organizations, including organizations that represent people living with HIV (PLWH), she is updating guidelines for prevention of HIV transmission from PLWH.



Kathleen Irwin, MD, MPH



Nicole Crepaz, PhD

Dr. Crepaz is a Project Officer for the HIV/AIDS Research Synthesis Project (PRS), which conducts systematic reviews and meta-analyses to evaluate behavioral interventions for risk reduction and for linkage to care, retention in care, and medication adherence among HIV-positive people. The PRS group produces a compendium of evidence-based behavioral interventions (EBIs) (<http://www.cdc.gov/hiv/topics/research/prs/index.htm>), which are recommended to the Replicating Effective Programs (REP, http://www.cdc.gov/hiv/topics/prev_prog/rep/index.htm) for developing user-friendly packages of materials. The completed intervention packages are passed on to the DEBI (Diffusion of Effective Behavioral Interventions) project for dissemination to providers (<http://www.effectiveinterventions.org/en/home.aspx>).

Statements are those of the interviewees and do not necessarily represent the official position of the US Centers for Disease Control and Prevention.

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What's new in updated CDC guidelines for prevention in positives?

Mascolini: Why did the CDC first issue guidelines on incorporating HIV prevention into medical practice and why is an update necessary?

Irwin: The guidelines issued in 2003¹ were to encourage HIV care providers to incorporate HIV prevention in their medical practices by addressing three issues known to curb HIV transmission: early, continuous care, sexually transmitted infection (STI) screening and treatment, and partner services.

The update we're working on now is more comprehensive and will include new evidence that has accumulated since 2003. Because of that new evidence, the new guidelines broaden the domains of prevention strategies. The most important difference with the upcoming guidelines is that they focus on actions of clinical *and* nonclinical providers—health departments and community-based organizations.

Mascolini: What new issues will the revised guidelines address?

Irwin: The updated guidelines will present new evidence and/or new recommendations in several domains:

- Special considerations for groups with unique HIV prevention needs
- Linkage to and retention in care
- Risk assessment and risk reduction
- Partner services
- Antiretroviral treatment and its role in prevention

- Medication adherence
- STI services
- Referral to other medical and social services
- Sexual and reproductive health
- Preventing HIV transmission during pregnancy
- Policy, legal, and ethical considerations
- Monitoring and evaluation

I can summarize some of the highlights of these new domains and revisions in domains covered in the 2003 guidelines.

The **special considerations** section addresses issues that may affect minors, adolescents, men who have sex with men (MSM), migrants, immigrants, pregnant women, illicit drug users, sex workers, the homeless, prisoners, persons with mental illness, and other groups that may have unique HIV prevention needs or are medically marginalized. These issues include stigma and legal, financial, language, cultural, and transportation barriers to accessing services or adopting HIV prevention methods.

The section on **risk assessment and risk-reduction** interventions includes new evidence on strategies for risk assessment and reduction, in particular, brief assessments and interventions that can be done in community or clinical settings. Some of the interventions that clinicians may find attractive include those that can be done by patients in the waiting room without taking clinician time, such as self-administered risk assessment and computer or print tools that provide risk reduction messages tailored to their risk. [For examples, see the table preceding this interview.]

A chapter on **antiretroviral treatment and prevention** highlights new evidence from a randomized controlled trial that found that antiretroviral therapy prevented heterosexual transmission in HIV-discordant couples from several countries.² This new section also presents information from other, less rigorously designed studies in heterosexual and MSM couples that indicates that antiretroviral treatment prevents sexual HIV transmission by lowering genital viral load. The new section on medication **adherence** summarizes new information about effective clinic-based and community-based interventions to support long-term antiretroviral adherence.

Another new section describes **referral to other medical and social services**, including mental health, drug rehabilitation, and syringe exchange services, and housing. This section summarizes new evidence that these services are essential to support the health and antiretroviral adherence of HIV-positive individuals as well as to prevent HIV transmission.

A section on **sexual and reproductive health care** for women and men addresses strategies to prevent sexual transmission, including conception methods that reduce risk of sexual and perinatal transmission and the latest evidence on interactions between hormonal contraceptives and some antiretroviral medications. This part of the new guidelines also describes family planning and emergency contraception to prevent unintended pregnancies. Another section assesses preventing **HIV transmission during pregnancy** and refers to the latest guidance on antiretrovirals for pre- and postexposure prophylaxis to prevent perinatal transmission. A new recommendation will discourage prechewing infant food by HIV-positive persons.

A section on **policy, legal, and ethical issues** will provide updated information on policy and legal environments that affect HIV prevention with PLWH, HIV disclosure and the negative consequences of criminalization of PLWH, standards for privacy and confidentiality, disparities in access to prevention services for PLWH, and implications of health reform on providing prevention services to PLWH.

A new section on **monitoring and evaluation** urges both clinical and community organizations to monitor or evaluate their HIV prevention strategies, either through quality-improvement initiatives, which are usually done in clinical settings, or through more classic program evaluation, usually by community-based organizations and health departments.

The revised guidelines update advice on **linkage to and retention** in HIV care because new evidence confirms the importance of early HIV care and staying in care for support of adherence, risk reduction, and behavioral interventions. In addition, the updated section on **partner services** refers to the 2008 CDC guidelines on partner services³ and new CDC guidance on using the Internet to contact partners. The updated partner guidelines stress that clinicians have an important role in helping their index patient—the HIV-infected person who has an HIV or STI diagnosis—think through a plan about how they want to notify their partner, either by themselves, through the health department, or with the clinician's help. The revised section on **STIs** refers to the 2010 CDC STI treatment guidelines,⁴ which lay out recommended STI screening tests and frequency, as well as treatment strategies.

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Mascolini: Will the revised guidelines differ from the 2003 guidelines in other important ways?

Dr. Irwin: The 2003 prevention-with-positives guidelines did not emphasize actions that could be taken by organizations such as health departments and community-based organizations, so many of their HIV prevention efforts continued to focus on reducing risk behaviors among HIV-negative persons. Because CDC and HRSA want to drive down HIV transmission rates even further, the updated guidelines will more fully engage all HIV prevention providers by including recommendations for health departments and community-based organizations that provide testing, linkage to care, antiretroviral adherence support, referral for substance abuse, mental health, or housing, and other services that support prevention in people with HIV. The new CDC funding announcements for health departments and community-based organizations also stress more activities with HIV-positive people to prevent transmission.

CDC's Medical Monitoring Project (<http://www.cdc.gov/hiv/topics/treatment/MMP>) is also tracking delivery of prevention services to people living with HIV in more than 20 areas in the US from 2007 through 2013. It will be able to evaluate implementation of several services that were recommended by the 2003 prevention-with-positives recommendations, the upcoming recommendations, and other CDC and federal agency recommendations that relate to prevention with positives: delays in entry to care, frequency of care visits, factors associated with receipt of treatment, treatment adherence, use of HIV prevention services, and screening tests. Data from the

Medical Monitoring Project are expected to be released periodically over several years, including at least 1 year after the expected 2012 release of the upcoming prevention-with-positives recommendations.

Mascolini: What are the CDC's plans for releasing the updated prevention-with-positives guidelines?

Irwin: We expect to release the revised guidelines sometime in 2012, both online and in the *MMWR*. The Division of HIV/AIDS Prevention is planning several activities to disseminate the guidelines and train providers in their use. We will also distribute implementation materials and tools to help providers in clinical facilities integrate prevention activities into HIV medical care, such as offering prevention counseling in waiting rooms or in other time-efficient ways. We also plan to spread the word about the new guidelines for clinical and nonclinical providers through continuing education and conference presentations.

Did transmission from positives slow after the 2003 CDC guidelines?

Mascolini: After the original positive-prevention recommendations came out in 2003,¹ the CDC reported little change in US HIV incidence from 2006 through 2009.⁵ Given this flat incidence, did the original guidelines do any good?

Irwin: You are correct that HIV incidence has been fairly stable from 2006 to 2009. However, this stable incidence has occurred during a period when the number of people living with HIV in

the US has steadily increased.⁶ The combination of stable incidence and increasing prevalence indicates a declining rate of transmission from people living with HIV.

The HIV transmission rate in the US though 2006 declined consistently by 3% to 4% each year; this represents a nearly 90% reduction since 1984 (early in the epidemic) and a more than 33% reduction since 1997.⁷ The Division of HIV/AIDS has not yet calculated the change in transmission rate from 2003 (when original guidelines were published) to the present, but that can now be done with reasonable precision using recent estimates of new infections through 2010 based on surveillance data published in August 2011.

When interpreting transmission rate changes from 2003 through 2010, it is important to keep in mind that the 2003 guidelines, like all guidelines, take time to be adopted into practice. As an example, a survey of 417 HIV physicians in 4 cities found that they were more likely to counsel patients about prevention if they were familiar with antiretroviral treatment guidelines that encouraged prevention counseling.⁸

Although the Division of HIV/AIDS Prevention did not sponsor a comprehensive evaluation of the uptake of the 2003 guidelines, scientists at CDC and other institutions have evaluated the extent of implementation of several interventions recommended by the 2003 guidelines in focused studies, interventions to increase implementation such as use of STI screening in HIV care clinics,⁹ use of risk-reduction interventions,¹⁰⁻¹³ and interventions to increase medication adherence.^{14,15}

Also, as I mentioned earlier, the combination of stable HIV incidence and increasing HIV prevalence indicates some success in reducing the transmission rate. That may be partially attribut-

ed to HIV prevention approaches highlighted in the 2003 guidelines. Discussions are underway to evaluate awareness and uptake of the upcoming guidelines by clinical and nonclinical providers. The updated prevention-for-positives guidelines will continue to stress prevention counseling at both initial and follow-up visits.

Overcoming provider reluctance to address prevention in positives

Mascolini: US physicians I surveyed listed several reasons why they don't counsel their patients on positive prevention, including lack of time, discomfort in discussing specific sex practices, and the perception that they can't change patient behavior. From your personal point of view as someone who studies these issues, can those obstacles be overcome?

Crepaz: These are all commonly cited barriers to provider-delivered prevention,^{8,16-20} and overcoming these obstacles is critical. Some evidence in the literature shows that HIV medical care providers with training can successfully conduct an HIV prevention intervention with their clinic patients.²¹ Training increases frequency of provider-patient discussions of safer sex and assessment of sexual activity.²⁰⁻²²

Staff training should focus on understanding and utilizing the provider's personal strengths, enhancing communication skills, practicing brief behavioral counseling, giving prevention messages, and providing booster trainings as needed. Clinics with established procedures for HIV prevention counseling are more likely to deliver such services to HIV-diagnosed patients.¹⁶ Some studies in the pipeline are testing computer-based interventions that can be integrated into clinic flow

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with minimal disruption and that supplement prevention efforts of providers—for example, the NIMH/CDC DHAP Epidemiology branch comprehensive prevention for people living with HIV (https://www.fbo.gov/index?s=opportunity&mode=form&id=f218809367e97758d060ea3012cacb26&tab=core&_cview=0).

From my personal point of view, there is no easy fix for these obstacles. However, they can be overcome by offering providers with needed training and prevention tools (such as computer-based interventions), obtaining providers' buy-in, and incorporating their input into the training and improvement plan.

Irwin: Although we recognize that some physicians face the barriers you describe, studies indicate that many physicians routinely provide prevention services to people with HIV. For example, a survey of randomly sampled HIV-positive men and women in six public HIV clinics found that, on average, 71% reported that their provider had talked with them about safer sex at least once, and 50% reported specific discussions about disclosure to partners.²³ A self-administered survey of HIV-infected men in San Francisco and New York City found that about three-quarters had been counseled about safe sex by their provider.²⁴ And a review of medical records of 1334 HIV-infected MSM from eight HIV clinics during 2004-2006 found that more than two-thirds were annually screened for syphilis, a practice recommended by the 2003 guidelines.⁹

Some studies indicate that physicians with extensive experience in HIV care or a large volume of HIV-infected patients may be more likely to establish systems for routine delivery of preven-

tive services than those who see few HIV-infected patients. For example, in a recent study of 165 experienced HIV physicians in the Bronx and Washington, DC, fewer than 10% said they rarely or never spoke with their HIV-positive patients about important issues such as sexual partners, sexual partners' HIV status, use of condoms, and sexual practices.

The CDC's Medical Monitoring Project (<http://www.cdc.gov/hiv/topics/treatment/MMP>) is tracking what proportion of HIV-positive persons in care reported receiving prevention counseling from their healthcare provider in the preceding 12 months. The results of this study are promising but are not yet available for release; we will provide them as soon as they are available.

Also, several interventions have been developed and shown to be effective in encouraging HIV clinical sites to provide prevention services, including those that do not require provider time.^{10-13,25-28} Examples include the "Safe in the City" waiting room video¹¹ and Positive Choice, a computer-based prevention intervention designed for use in the waiting room and outpatient clinics and requiring little or no clinician time.¹³ The 2012 prevention-with-positives guidelines will highlight these interventions for clinical settings as well as non-clinic-based interventions to increase prevention behaviors. The "Ask, Screen, Intervene" training curriculum is an example of another clinician intervention to support prevention with positives in clinical settings (www.cdc.gov/hiv/topics/treatment/pic/ppt/PIC_Workshop.ppt).

Finally, the recent HPTN 052 study found that antiretroviral therapy that suppresses viral load can reduce heterosexual transmission to uninfected partners by more than 95%.² The updated prevention-with-positives guidelines will

stress the role of antiretroviral use to prevent heterosexual transmission. With this information in hand, providers can use routine discussions about antiretroviral therapy and adherence as an entrée to discussing prevention in a context they are comfortable with.

Meta-analyses back value of behavioral intervention for prevention

Mascolini: Dr. Crepaz, can you give an overview of your meta-analysis involving HIV-positive people²⁵ and suggest the key take-home messages for HIV providers in the United States?

Crepaz: The 2006 paper presents findings from a meta-analysis of 12 controlled trials conducted in the US and published between 1988 and 2004.²⁵ We systematically searched the HIV prevention literature to identify interventions that were specifically designed to reduce HIV-related risk behaviors (such as unprotected sex and needle sharing) or biologic outcomes (such as STIs) in HIV-positive people. The meta-analysis technique allows us to quantitatively synthesize the findings across studies, estimate the overall effect size of interventions, and identify factors that are associated with intervention effects. We found interventions significantly reduced unprotected sex and decreased acquisition of STIs. A limited number of studies have evaluated intervention effects on injection drug use behaviors, and the evidence is not conclusive.

Several intervention characteristics were found to be associated with reductions in unprotected sex: interventions guided by behavioral theory; specifically focused on HIV transmission behaviors in more than two thirds of intervention sessions; provided skills building; delivered individually; delivered by healthcare providers

or professional counselors; delivered in settings where people living with HIV receive care or services; and addressed a myriad of issues related to coping with one's serostatus, medication adherence, and HIV risk behaviors. This meta-analysis also indicated that more intensive HIV interventions—that is, those with 10 or more intervention sessions and lasting 20 or more hours or more than 3 months—were more efficacious than briefer interventions.

The meta-analysis findings suggest some take-home messages for HIV providers:

1. HIV providers play an important role in changing patients' behavior.
2. Clinic settings are an ideal place for delivering prevention messages and interventions.
3. There is a need to address a whole range of issues faced by HIV-positive patients—for example, coping with one's serostatus, medication adherence, HIV risk behaviors, mental health, and substance abuse. But to see the effect on reduction in HIV risk behaviors, patients need to receive sufficient "doses" of interventions.

One important thing to point out is that the intensive interventions evaluated in my meta-analysis were conducted in places where HIV-diagnosed persons received care or services (such as medical care sites, methadone maintenance centers, and community agencies) as individuals or in groups. Currently, there is insufficient evidence to support the efficacy of multi-session, intensive, group-level HIV interventions in busy healthcare settings. Multidisciplinary teams and co-location of care and service may be needed to make multi-session interventions more feasible in healthcare settings. This issue certainly warrants further examination.

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Since publication of the meta-analysis, several risk-reduction interventions for HIV-diagnosed persons that have been published. Recently published studies conducted in clinic settings^{13,28,29} have demonstrated the effectiveness of screening HIV-diagnosed patients for HIV/STI risk behaviors during their clinic visits and using results to guide individually tailored brief prevention counseling by care providers. Given that HIV-diagnosed persons differ in their risk and prevention needs at different points in time, risk screening to determine the types of interventions that work best for HIV-diagnosed persons may allow intervention resources to be applied most appropriately. HIV providers may consider incorporating this approach into their clinics.

Mascolini: Did your meta-analyses uncover important differences between risk-reduction interventions that work for HIV-positive people²⁵ versus people at risk for HIV?³⁰⁻³²

Crepaz: There are a few factors that seem to work both for HIV-positive people and for people at risk for HIV when you review all four of these meta-analyses.^{25,30-32} All found that interventions that are theory-based (usually addressing personal knowledge, attitude, motivation to change, and readiness to change) and provide skill training are critical for interventions to work. These are the underlying mechanisms of behavioral change that are applicable to HIV-positive people and also people at risk for HIV.

However, there are certainly differences between risk-reduction interventions that work for HIV-positive people and for people at risk for HIV, although these differences are not explicitly pointed out in these meta-analyses. From my point of view, HIV-positive persons face issues different

from people at risk for HIV—for example, how to disclose HIV-seropositive status to others without being stigmatized, when to start HIV treatment, how to ensure medication adherence and regular clinic visits, whether the cost of treatment will be covered, how to manage HIV symptoms, and treatment side effects. People at risk for HIV face none of these issues. But for HIV-positive persons, these issues may negatively impact their behaviors and thus they need to be addressed with prevention efforts.

Mascolini: All four of your meta-analyses found that multiple or intensive theory-based interventions are among the most effective.^{25,30-32} Does this mean clinicians have to plan multi-session, theory-based, culturally tailored risk-reduction programs and pay someone to conduct them regularly?

Crepaz: All four meta-analysis did point out that interventions based on behavioral change theories work better. The common components of these theories are personal knowledge, attitude, motivation to change, readiness to change, social norms, social support, communication, perceived behavioral control, self-efficacy, and outcome expectations. While all four meta-analyses suggest that more intensive theory-based interventions are efficacious, the feasibility of conducting this type of intervention in busy clinics is still a question.

We also found that conducting formative research to identify the most relevant behavioral determinants that affect participants' behavior is a critical component. This is consistent with the findings from HIV clinic settings where HIV providers first screen HIV-diagnosed patients for HIV/STI risk behaviors and use the information to guide

individual prevention counseling based on motivational interviewing and strength-based principles. As I pointed out in my previous answer, there is increasing evidence suggesting that risk screening and brief, tailored prevention counseling reduce HIV risk behavior among HIV-positive clinic patients. This type of intervention is often brief but routinely offered to patients during their clinic visits.

After reviewing and incorporating the recent literature, we recommend the following screening and prevention strategies in the updated prevention-with-positives guidelines:

- Screen HIV-diagnosed persons for sex or drug use behaviors (including alcohol and injection and noninjection drug use) at the initial visit and subsequent routine visits (at least twice yearly) or periodically, as the provider deems necessary.
- Use risk screening information to guide prevention messages individually tailored to the HIV-diagnosed person's needs and circumstances, with the goal of increasing safer behaviors.
- Become familiar with available resources and make referrals to prevention specialists within or outside the clinic who can offer intensive HIV prevention interventions as needed.

Mascolini: Do your meta-analyses^{25,30-32} suggest differences in effective behavioral interventions for MSM versus black heterosexuals versus Hispanic heterosexuals versus IDUs?

Crepaz: Our meta-analyses point out more common components than differences in effective behavioral interventions for the groups you list. This is not surprising because, as I pointed out earlier, common components address the underlying mechanisms of behavioral change which, in general, apply to various groups.

I would make the same argument as I did in answering your question about whether there are differences in effective behavioral interventions for HIV-positive persons versus people at risk. From my point of view, the prevention needs may be different for MSM, black heterosexuals, Hispanic heterosexuals, and IDUs as each group (and individual) faces different issues or barriers that prevent them from engaging in safer behavior. For behavioral interventions to work well, it is important to engage the individual and community of interest to identify the issues and barriers to behavioral changes. A participatory approach is likely to yield a better outcome.

Mascolini: Overall, what do your meta-analyses^{25,30-32} say about the impact of behavioral interventions delivered by providers versus counselors or peers?

Crepaz: For HIV-positive persons,²⁵ interventions delivered by providers and counselors seem to work better than interventions delivered by peers. This may be confounded by the finding that interventions delivered in settings where HIV-positive persons receive routine services or medical care are more effective. In other words, selection bias may favor interventions with people in routine care because HIV-positive people who seek and sustain care are probably more motivated than HIV-positive people who do not. The other meta-analyses, in which the majority of study participants are at risk for HIV,³⁰⁻³² suggest that providers, counselors, and peers are equally effective in impacting participant's behavior.

Mascolini: Do these studies or other research you know say whether behavioral interventions continue to lower risk behavior after the formal intervention period ends?

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Crepaz: Yes, our meta-analyses evaluated the intervention effects after completion of the formal intervention period.^{25,30-32} The common follow-up assessment is 3 or 6 months after completion of the entire intervention. Few studies conduct a follow-up assessment after more than 12 months.

There is evidence that behavioral interventions work after the interventions end—mostly after 3 or 6 months and sometimes 12 months after completion of intervention. However, we do not know if the interventions still work further out, after 12 months.

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Eight strategies to trim transmission risk in people with HIV

By Mark Mascolini

Abstract: Working with HIV-positive people to tell their sex and drug-injecting partners they have HIV is the first step in prevention with positives. Step 2 is encouraging positive people to consider starting antiretroviral therapy, with an eye toward reaching and maintaining an undetectable viral load. Clinician experience in the United States suggests that results of HPTN 052 have opened another avenue to discussing starting antiretroviral therapy. Because most sexually transmitted infections (STIs) remain asymptomatic, appropriate screening for STIs is essential to limiting HIV transmission risk from positive people. Despite data confirming low HIV transmission risk in people with an undetectable viral load, providers should continue to stress condom use. Circumcision lowers the risk of HIV transmission from positive heterosexual men. But the CDC and other groups urge caution in considering circumcision for gay men because of limited evidence in this population and because the risks of circumcision remain largely unexplored in them. Serosorting limits HIV transmission in gay men who do not use condoms but cannot be recommended as a primary prevention strategy. Clinicians should remember that most HIV transmissions from injection drug users come during sex, not needle sharing. Plentiful evidence shows that behavioral interventions can help HIV-positive people refrain from transmission-risk behavior. Some of these interventions involve little or no provider time and

can be completed by patients using hand-held devices in the waiting room. The CDC plans to stress these time-saving strategies in its 2012 prevention-with-positives guidelines.

Reasons why clinicians fail to engage HIV-positive patients on transmission risk almost outnumber reasons why clinic-based prevention strategies work. The first article in this issue ponders both lists of reasons. This article probes clinic-based strategies for bridling transmission from positives—with a focus on strategies that take little provider time and won't break the clinic budget.

First step in positive prevention: telling partners

Before providers can lift a finger—or prescription pad—to prevent HIV-positive people from transmitting their virus, they've got to know who's positive. That's why the CDC and others are pushing hard to test as many people as possible, regardless of perceived HIV risk. Once a person gets diagnosed and referred to care, the provider must address another urgent priority—making sure the new patient's partners know.

For an array of reasons easy to imagine, people with HIV often avoid telling sex partners they're infected. One study of 675 HIV-positive men who have sex with men (MSM) in six US cities found

that 30% told no sex partners they had HIV in the past 90 days.¹ Another study discussed below recorded a 7% notification rate.²

HIV providers must remember that most states and some local governments have laws regulating HIV disclosure to partners; many states also regulate disclosure by clinicians to third parties at high risk of getting infected by already positive patients.³ Some health departments give HIV-positive people a set time to notify partners. If the partners don't show up for counseling and testing by the end of that "contract period," the health department gives them the news.³

CDC guidelines advise providers to ask all positive people at their first visit whether they've told sex and needle-sharing partners they have HIV.³ And keep asking at follow-up visits, the CDC says, because many patients will have found new partners in the interim. (The CDC is releasing revised and greatly expanded guidance on prevention with positives in 2012. See the interview with the CDC's Kathleen Irwin in this issue.)

A 1992 trial that randomized newly diagnosed people to physician- or self-notification of partners found that physicians successfully notified 78 of 157 sex or needle-sharing partners (50%), while patients themselves notified only 10 of 153 partners (7%).² Among notified partners, 23% had HIV.

Second step to positive prevention: undetectable viral load

Long before HPTN 052 offered sumptuous proof that triple antiretroviral therapy slashes the risk of HIV transmission in HIV-discordant couples, plentiful evidence forged a fast link be-

tween lower viral loads and slimmer chances of transmission. That principle became clear well before the dawn of triple therapy, when US and French investigators found that zidovudine taken by pregnant women and newborns sliced the risk of mother-to-child transmission 67.5% (95% confidence interval [CI] 18.4 to 32.5, $P = 0.00006$).⁴

In ensuing decades, one trial after another showed that one drug is better than none, two are better than one, and three are best in cutting chances of vertical HIV transmission, clearly because each stronger regimen lowers viral load more. Testing three triple regimens in 730 women, the Mma Bana study in Botswana found that more than 90% of women across the three groups had a viral load below 400 copies/mL at delivery and through follow-up.⁵ Six months after delivery, the HIV transmission rate in this breast-feeding population was 1.1%—equivalent to rates in formula-feeding Western populations.

The same principle applies to sexual or parenteral transmission of HIV. In the seminal study of 415 HIV-discordant Ugandan couples before antiretroviral therapy became available, none of 51 people with a viral load below 1500 copies/mL infected their partner.⁶ In a study of 253 antiretroviral-naive HIV-discordant monogamous Ugandan couples, the researchers divided HIV-positive partners into four equal groups reflecting their HIV load: under 3090 copies/mL, 3090 to 14,450 copies/mL, 14,450 to 75,850 copies/mL, and over 75,850 copies/mL.⁷ Compared with people in the lowest viral load quartile, those in the next higher quartile had a 3.31 times higher risk of transmitting HIV, those in the quartile above that had a 6.39 times higher risk, and those in the highest quartile had a 7.06 times higher risk. (**Figure 1**).

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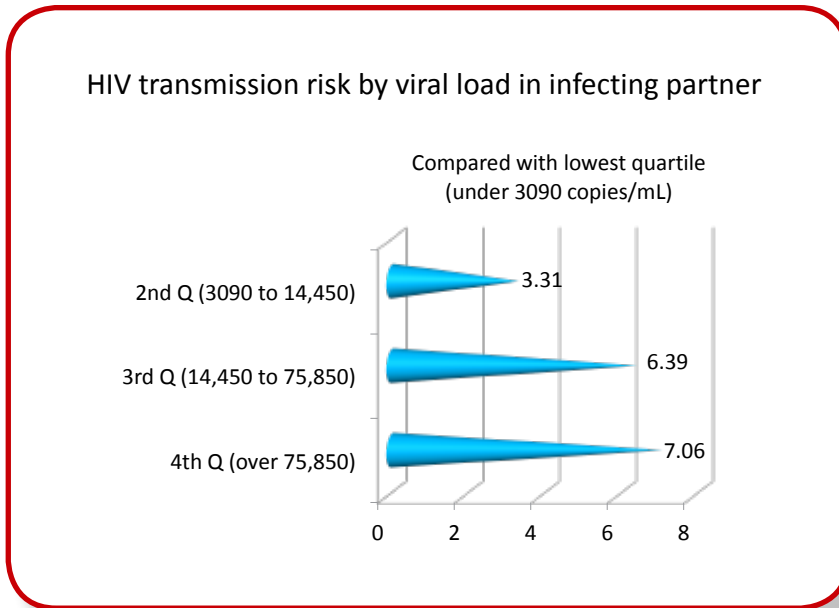


Figure 1. Higher viral load in the HIV-positive partner of HIV-discordant couples independently raised the risk of HIV transmission by the indicated rate ratios. Transmission risk rose with each higher viral load quartile (Q) in this study of 253 antiretroviral-naïve monogamous Ugandan couples.⁷

Though HIV incidence data from HIV-discordant heterosexual African couples may not apply precisely to gay and straight couples in the United States and similar countries, this research certainly offers keen insights into how viral load may affect transmission. A canny modeling study relied on data prospectively collected from 3381 HIV-discordant African couples from 2004 to 2008, including 108 with genetically linked HIV transmissions.⁸ The model predicted that every 0.74 log (about 5.5-fold) lower viral load cut heterosexual transmission risk 50%, regardless of starting viral load in the population and other HIV-related population traits.

Meta-analysis of 11 studies involving 5021 heterosexual couples counted 461 HIV transmissions, only 5 of them from an antiretroviral-treated partner.⁹ No one with a viral load below 400 copies/mL passed HIV to a partner. These couples lived in three African countries, Brazil, India, Spain, Thailand, and the United States.

Population-based modeling studies show that, as communities start using robust antiretroviral combinations, “community viral load” drops, followed by HIV incidence (the new infection rate).¹⁰⁻¹² For example, British Columbia’s centrally controlled antiretroviral program allowed

researchers to figure that individual use of triple therapy soared 547% from 1996 to 2009, reaching only 837 people in 1996 and 5413 in 2009 ($P = 0.002$).¹¹ Over the same period, the number of new HIV diagnoses dwindled 52%, from 702 to 338 per year ($P = 0.001$). On an annual basis, the number of people on combination therapy correlated inversely—and tightly—with the number testing positive (-0.89 , $P < 0.0001$).

With all these findings pointing (insistently) in the same direction, no one could be surprised that antiretroviral therapy stymied sexual HIV transmission in HPTN 052.¹³ But the magnitude of that effect was stunning. The trial enrolled 1763 HIV-discordant couples in nine countries, 97% of them heterosexual and 94% of them married. Everyone had a CD4 count between 350 and 550 cells/mm³, and no one had taken antiretrovirals. The investigators randomized HIV-positive partners in these couples to start antiretroviral therapy immediately or to wait till their CD4 count dropped to 250 cells/mm³ or they had an AIDS disease.

The Data and Safety Monitoring Board pulled the plug on HPTN 052 early when results through February 2011 showed that 28 couples had a genetically confirmed HIV transmission, only 1 of them in the early-antiretroviral group. Starting antiretrovirals immediately chopped the HIV transmission risk by 96%. Because the 1 genetically linked transmission in the early-antiretroviral group probably occurred before treatment made the positive partner's viral load undetectable, HPTN 052 confirmed earlier nonrandomized studies that found no sexual HIV transmissions from people with an undetectable viral load.

“Drinking the Kool-Aid” on treatment as prevention

Long before HPTN 052 confirmed that antiretrovirals taper HIV transmission rates, the CDC cautioned that undetectable virus in plasma does not necessarily mean virus-free semen, rectal secretions, or genital or pharyngeal fluids.^{3,14,15} And an unreadable load in plasma depends on steady adherence and staying free of other sexually transmitted infections. Even certain vaccinations can hike viral load. On top of that, some studies show that doing well on antiretroviral therapy can make people reckless in bed. So even universal treatment of diagnosed people will not tamp down their transmission risk completely.

But it's a big step in that direction. Of the 18 top HIV physicians who responded to RITA's survey on positive prevention (see box on page 13), 16 listed reining in HIV with antiretrovirals as a prime strategy, and 7 of those 16 cited HPTN 052.¹³

“The single most important thing clinicians can do to prevent transmission is to treat their HIV-positive patients with antiretroviral therapy, our most effective form of prevention,” wrote Joel Gallant (Johns Hopkins University). “That doesn't mean that other forms of prevention don't matter anymore,” he added. “It's still important to talk about behavior change and condom use, for example. But if every HIV-positive person had an undetectable viral load, the epidemic would be over.”

David Wohl (University of North Carolina) seconded that opinion, noting that HIV incidence in HPTN 052 “was pretty low in the control

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group not treated with antiretrovirals.” That means the “prevention measures in the control [arm]—pretty standard stuff—seemed to have an effect. That said, I have really drunk the Kool-Aid when it comes to use of antiretrovirals to prevent transmission.”

Others believe HPTN 052 opens an avenue to discussing positive prevention with their patients. “I’ve been pleasantly surprised how the ‘treatment-as-prevention’ message from 052 has facilitated discussion about prevention in clinical practice, and how motivating prevention can be for people considering starting therapy,” said Paul Sax (Harvard Medical School).

Steven Deeks (University of California, San Francisco) agreed, noting that “in my recent experience, this public health aspect of treatment has been a great motivator for some individuals to seek care and begin therapy, so I am optimistic transmission rates will decline.”

Some HIV-positive people who may not want to start treatment for their own health “will opt for treatment to prevent transmission,” Ian Frank (University of Pennsylvania) is finding. As a corollary to this emerging attitude, Frank suggested, treatment as prevention “can be particularly motivational for people in discordant couple relationships” and for another patient subset—HIV-positive people looking for a partner but assuming no HIV-negative person would consider a relationship. Now, Frank noted, a positive person with well-controlled infection can tell a potential partner, “I have a low risk for transmission of my infection because my viral load is undetectable,” and that “can change someone’s outlook” on finding a partner.

Risk screening and STI testing for positive prevention

Besides treating people to make their viral load too low to tote, what else should HIV providers do to help patients avoid dispatching their virus to others? HIV Medicine Association (HIVMA) primary care guidelines prescribe four essentials:¹⁶

1. Screen people for high-risk behavior at each visit.
2. Ask patients about sexually transmitted infection (STI)-related symptoms at each visit.
3. Give a general message about risk reduction at each visit.
4. Tailor messages for patients who report high-risk behavior.

Do providers have to keep hammering on prevention at every visit? The CDC thinks so. “Clinicians should recognize that [HIV transmission] risk is not static,” the 2003 guidelines state.³ “Patients’ lives and circumstances change, and a patient’s risk of transmitting HIV may change from one medical encounter to another.”

The HIVMA guidelines, freely available online,¹⁶ boast an ample section on risk screening in people with HIV, including a list of questions most clinicians should feel comfortable asking (**Table 3 in Reference 16**). HIVMA guidelines also feature pointers on carrying out the four steps listed above.

CDC positive-prevention advice spells out recommendations on screening for transmission risk and STIs (**Table 1**).³ The CDC stresses that

Table 1. CDC advice on screening HIV-positive people for transmission risk and STIs

Screen HIV-positive adults for HIV transmission risk behaviors in a straightforward, nonjudgmental manner. Screening should be done at the initial visit and subsequent routine visits, at least once a year.

Any indication of risky behavior should prompt a more thorough assessment of HIV transmission risks.

Ask HIV-positive adults about STI symptoms at the first and every following routine visit.

Regardless of reported sexual behavior or other epidemiologic risk information, such signs or symptoms should always prompt diagnostic testing and, when appropriate, treatment.

At the first visit screen all HIV-positive adults for laboratory evidence of syphilis and all HIV-positive women for trichomoniasis.

Screen for cervical chlamydial infection at the first visit in all sexually active women under 25 years and other women at increased risk, even if asymptomatic.

At the first visit consider screening all HIV-positive adults for gonorrhea and chlamydial infection.

Because of the cost of screening and the variability of gonorrhea and chlamydia prevalence, decisions about routine screening for these infections should be based on epidemiologic factors. [But see results of the large British self-screening study discussed in the text.¹⁷]

Repeat STI screening at least annually if the patient is sexually active or if earlier screening revealed STIs.

STI screening should be done more frequently (for example, every 3 to 6 months) for asymptomatic people at higher risk.

At the first and each subsequent routine visit, question HIV-positive women of childbearing age to identify possible current pregnancy, interest in future pregnancy, or sexual activity without reliable contraception.

Ask women whether they suspect pregnancy or have missed their menses and, if so, test them for pregnancy.

STI, sexually transmitted infection.

Source: Centers for Disease Control and Prevention. Incorporating HIV prevention into the medical care of persons living with HIV: recommendations of CDC, the Health Resources and Services Administration, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. *MMWR*. 2003;52(No. RR-12).⁵

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most STIs are asymptomatic, so these risky infections remain masked unless lab tests uncover them. CDC and HIVMA guidelines outline asymptomatic STI screening advice by (1) initial versus subsequent patient visit, (2) gender, and (3) risk (**Table 2**).

Patients can even test themselves for gonorrhea and chlamydia in an HIV clinic, according to results of a large London study.¹⁷ In this nurse-led self-screening program, HIV-positive men and women are invited to collect specimens by self-swabbing. Diagrams on rectal, pharyngeal,

and vaginal self-swabbing are posted in clinic rest rooms. Staff screens samples with nucleic acid amplification tests.

The 976 screens completed over 8 months in people without STI symptoms disclosed 143 infections (14.6%), at rates of 17.4% in MSM, 2.1% in heterosexual men, and 1.5% in women.¹⁷ Six people with a self-detected STI had a transient spike in HIV load. Among 78 people taking antiretrovirals at STI diagnosis, 72 had a viral load below 40 copies/mL and 6 had a load between 40 and 70 copies/mL. The researchers recommend

Table 2. CDC and HIVMA guidelines for screening to detect asymptomatic STIs

First visit			
All patients	Women	Patients reporting receptive anal sex	Patients reporting receptive oral sex
<ul style="list-style-type: none"> ■ Serologic test for syphilis (ie, nontreponemal test, such as RPR or VDRL) ■ Consider urine-based (first-void specimen) NAAT for gonorrhea ■ Consider urine-based (first-void specimen) NAAT for <i>Chlamydia</i> species ■ Serologic tests for hepatitis B and C (if hepatitis B negative, vaccinate) 	<ul style="list-style-type: none"> ■ Examination of vaginal secretions for <i>Trichomonas</i> species ■ Cervical specimen for NAAT for <i>Chlamydia</i> species for all sexually active women aged <25 years and other women at increased risk 	<ul style="list-style-type: none"> ■ Culture of rectal sample for <i>Neisseria gonorrhoeae</i> ■ Culture of rectal sample for <i>Chlamydia</i> species 	<ul style="list-style-type: none"> ■ Culture of pharyngeal sample for <i>N gonorrhoeae</i>

Subsequent visits

All sexually active patients

- Screening tests for STIs should be repeated at least annually

Asymptomatic persons at higher risk

- More frequent periodic screening (eg, every 3 to 6 months) if any of the following factors are present:
- Multiple or anonymous sex partners
 - History of any STI
 - Identification of other behaviors associated with transmission of HIV and other STIs
 - Sex or needle-sharing partner(s) with any of the above-mentioned risks
 - Developmental changes in life that may lead to behavioral change with increased risky behavior (eg, end of a relationship)
 - High prevalence of STIs in the area or in the patient population

NAAT, nucleic acid amplification test; RPR, rapid plasma reagin; STI, sexually transmitted infection; VDRL, venereal disease research laboratory test for syphilis.

Sources: Centers for Disease Control and Prevention. Incorporating HIV prevention into the medical care of persons living with HIV: recommendations of CDC, the Health Resources and Services Administration, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. *MMWR*. 2003;52(No. RR-12).³ Aberg JA, Kaplan JE, Libman H, et al. Primary care guidelines for the management of persons infected with human immunodeficiency virus: 2009 update by the HIV Medicine Association of the Infectious Diseases Society of America. *Clin Infect Dis*. 2009;49:651-681.¹⁶

STI screening for MSM every 4 months and annual testing for heterosexuals. They suggest this approach “may address some of the barriers to screening in this population.”

The Health Resources and Services Administration (HRSA) 2011 *Guide for HIV/AIDS Clinical Care* includes a useful table (on pages 134 and 135) suggesting questions to ask and assessments for (1) sexual practices, (2) partner notification, (3) STI screening, and (4) drug and alcohol use.¹⁸

Getting HIV-positive people to don condoms

Condoms are lots easier to make than antiretrovirals, lots cheaper, and lots easier to get to people with HIV. Yet this low-tech latex sheath stops HIV transmission dead if used properly. No one has figured out how much condoms have stunted the epidemic’s growth, but they certainly had a hand in Uganda’s dramatic drop in HIV prevalence from 18% in 1992 to 6% in 2002.¹⁹ And

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a recent study from India suggests that a pilot prevention program stressing condom use and other measures may have averted over 100,000 new HIV cases in 5 years.²⁰

In a systematic review of five studies, WHO researchers figured that consistent condom use by MSM cuts HIV transmission risk 64% and STI acquisition risk 42%.²¹ WHO guidelines for HIV prevention and treatment in MSM strongly recommend condoms for MSM and transgender people, noting that “water- and silicone-based lubricant use is key for the correct functioning of condoms during anal sex.”²¹

The first figure in 2003 CDC prevention guidelines suggest how to tailor messages on condom use for HIV-positive people.³ The opening question might be, “How often do you use condoms when you have sex?” If the person says never or sometimes, the next question could be, “What do you plan to do about using condoms in the future?” And if the person has no plan, an appropriate follow-up may be, “Do you know that you could catch an STI that way, and it could make your HIV infection worse?”

CDC authorities urge physicians to supply condoms to HIV-positive patients,³ and HRSA guidelines say physicians should hand out condoms *and lubricant*.¹⁸ HRSA details condom-use pointers providers can give patients, as well as suggestions for people who complain about lack of sensitivity with condoms (**Table 3**).

Circumcision works . . . for some

Three randomized trials established that medical male circumcision cuts the risk of HIV acquisition in heterosexual African men.²²⁻²⁴ WHO now

endorses circumcision for heterosexual men in countries with high HIV prevalence,²⁵ and some African countries gave circumcision a prominent place in their HIV prevention agenda. But WHO does not recommend circumcision for gay or bisexual men and, in fact, advises against it: “Not offering adult male circumcision to prevent HIV and STI acquisition is suggested over offering it to MSM and transgender people.”²¹ Although WHO aims these guidelines at MSM in low- and middle-income countries, the agency recommends making this document available to men in high-income countries as well.

What makes WHO take this negative stance? WHO cited a Cochrane Database systematic review decocting 20 studies of male circumcision for HIV prevention in MSM.²⁶ Three studies of 1792 men determined that circumcision did not protect MSM who primarily practiced receptive anal intercourse (odds ratio [OR] 1.20, 95% confidence interval [CI] 0.63 to 2.29). Seven studies of 3465 men who mostly practiced insertive anal sex yielded evidence that foreskin removal did lower their HIV acquisition risk almost 75% (OR 0.27, 95% CI 0.17 and 0.44).²⁶

The Cochrane review found no evidence that circumcision protects gays or bisexuals from syphilis, herpes simplex virus 1, or herpes simplex virus 2.²⁶ Cochrane rated overall evidence quality low in these studies and stressed that *no studies* analyzed adverse effects of circumcision.

Surveying all these findings, WHO guideline writers decided “it is not clear if the benefits outweigh the risks [for MSM] at this point in time, as male circumcision, like any other operation, carries some risks.”²¹ On top of that, WHO cautioned, “there are significant concerns regarding its acceptability and implementation among MSM

Table 3. HRSA condom use advice for HIV-positive people**General advice**

- Use a new latex or polyurethane condom with each sex act (oral, anal, or vaginal).
- Make sure that the condom is undamaged and that its expiration date has not passed.
- Carefully handle the condom to avoid damage (for example, from fingernails or teeth).
- Being sure the condom roll faces out, unroll the condom onto the erect penis before any genital contact with a partner.
- Ensure that the tip of the condom is pinched when applying it to the top of the penis to eliminate air in the tip that could cause breakage during ejaculation.
- Use only water-based lubricants with latex condoms. Oil-based lubricants (such as mineral oil, cooking oil, massage oil, body lotion, and petroleum jelly) can weaken latex or cause it to break, although they are fine with polyurethane condoms.
- Adequate lubrication during intercourse helps reduce the risk of condom breakage.

Advice for people who complain about lack of sensitivity with condoms

- Apply a drop of lubricant inside the condom (not more, because it increases the risk that the condom will come off).
- Use polyurethane condoms instead of latex because they conduct heat and may feel more natural.
- Use insertive (female) condoms, which are not as restrictive to the penis.
- Use specially designed condoms that do not restrict the top of the penis (for example, Inspiral, Xtra Pleasure).

Source: US Department of Health and Human Services Health Resources and Services Administration. Guide for HIV/AIDS Clinical Care. January 2011. <http://hab.hrsa.gov/deliverhivaidscares/clinicalguide11/>.

in different cultural settings.”²¹ WHO, Cochrane, and the CDC²⁷ all agree that findings to date do not support circumcision as an HIV prevention strategy for gay or bisexual men and that further research should address the potential role of circumcision among MSM who take the insertive role during anal intercourse.

Caution makes sense when weighing the potential role of circumcision in preventing HIV among gay men, regardless of whether they prefer being insertive “tops” or receptive “bottoms.” A retrospective CDC study of 4889 North American and

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European MSM enrolled in the VAXGen HIV vaccine trial underlines that point.²⁸ An analysis that controlled for demographics and risk behaviors determined that being uncircumcised did not raise the risk of picking up HIV even a tiny bit (adjusted hazards ratio [AHR] 0.97, CI 0.56 to 1.68). In study visits during which men reported unprotected insertive anal sex with a positive partner, HIV infection was reported in 3.16% of visits by circumcised men and 3.93% of visits by uncircumcised men (relative risk [RR] 0.80, CI 0.46 to 1.39).

Should uncircumcised HIV-negative heterosexual men in the United States and countries with similar HIV epidemics be encouraged to get circumcised to lower their HIV risk? In April 2007, after release of results from the three randomized African trials,²²⁻²⁴ the CDC held a 2-day powwow on circumcision to prevent HIV infection in the United States and summed up with this advice for heterosexuals:

“Sufficient evidence exists to propose that heterosexually active males be informed about the significant but partial efficacy of male circumcision in reducing risk for HIV acquisition and be provided with affordable access to voluntary, high-quality surgical and risk-reduction counseling services.”²⁷

Whether uncircumcised HIV-positive heterosexuals should be urged to get circumcised to curb chances of transmitting HIV to sex partners is another question entirely. Mathematical modeling suggests that male circumcision trims the risk of male-to-female HIV transmission more than first predicted.²⁹ Basing their analysis on HIV transmission rates in four randomized trials and

in observational studies of already circumcised men in stable partnerships, these investigators calculated that male circumcision eases the risk of male-to-female HIV transmission by 46%.

But it is probably naïve to imagine that many uncircumcised HIV-positive men—straight or gay—can be persuaded to shed their foreskin to protect sex partners. A confidential survey of 653 MSM recruited in London gyms found that only 10% of 464 uncircumcised men said they would sign up for a study of circumcision to prevent HIV infection.³⁰ Only one third of uncircumcised men thought circumcision has benefits, compared with two thirds of circumcised men. Similar proportions of these men (39% uncircumcised and 37% circumcised) reported unprotected anal sex in the past 3 months. One quarter of uncircumcised men had HIV infection.

On the other hand, about half of HIV-negative MSM in a 2006 US study claimed they would get circumcised if research showed the operation would trim their HIV risk.³¹ Researchers interviewed 780 men at gay pride events, all of them presumed to be HIV-negative and 133 of them (17%) uncircumcised. The gay pride events took place in Birmingham, Alabama, Anchorage, Alaska, Raleigh-Durham, North Carolina, Springdale, Utah, Charlotte, North Carolina, Chicago, and St. Louis.

Seventy-one of 133 uncircumcised men (53%) claimed they would consider circumcision, pending favorable research results. Black men, men who did not inject drugs, and men who believed circumcision would lower their risk of penile cancer were more likely to consider circumcision. The research summarized above suggests those

men are still waiting to see if circumcision will help keep them free of HIV. But physicians who care for HIV-negative gay men should be aware some may consider circumcision.

Does serosorting sort out HIV risk?

HIV clinicians heaved grateful sighs in the middle of the last decade when they learned that gay men had devised their own strategy to limit HIV transmission and that it seemed to work.^{32,33} Serosorting—having sex only with men of the same HIV status—appeared to explain why STI incidence rose from 1998 through 2004 in San Francisco MSM while HIV incidence peaked in 1999 then leveled off.³³ But even these early reports noted that HIV incidence remained high and cautioned that “a strategy of risk reduction by HIV serosorting can be severely limited by imperfect knowledge of one’s own and one’s partners’ serostatus.”³³

Analyzing data from 3 studies in developed countries, WHO figured that HIV-negative men who relied on serosorting rather than consistent condom use had a 79% higher risk of HIV acquisition (RR 1.79, 95% CI 1.2 to 2.65) and a 61% higher risk of getting a new STI (RR 1.61, 95% CI 1.43 to 1.81).²¹ Compared with no condom use, however, serosorting cut chances of HIV infection 53% (RR 0.47, 95% CI 0.26 to 0.84) and whittled STI risk by 14% (RR 0.86, 95% CI 0.78 to 0.93).

WHO concluded that “serosorting may be a potential harm reduction strategy for [MSM] who choose not to use condoms, but it should not be promoted as an alternative strategy for HIV prevention. Consistent condom use is a more effective method to prevent HIV infection.”²¹ These

experts advise frequent HIV and STI screening for MSM who rely solely on serosorting to shield themselves from sexually transmitted intruders.

CDC positive-prevention guidelines stress that condom-free serosorting does not protect men from picking up new STIs or another HIV.³ Although the clinical hazards of superinfection with a second HIV remain open to question, a few case reports suggest a second HIV may be much nastier than the first,³⁴⁻³⁶ and a superinfecting HIV could bear resistance mutations.

HIV providers should be aware that HIV-negative serosorters may believe they have a lower risk of getting infected, may indulge in unprotected sex as a result, and may get tested for HIV less than once yearly, as the CDC recommends.³⁷

Advice on working with IDUs and other drug abusers

Although injection drug users (IDUs) accounted for only 10% of new HIV infections in the United States in recent years, that rate did not budge from 2006 through 2009, the most recent years for CDC calculations.³⁸ That plateau implies that IDUs continue to infect their partners at a steady pace.

There’s no secret about how to cut HIV transmissions in drug injectors—get them to quit shooting up by referring them to opioid-substitution programs.³ And if that doesn’t work, urge them to use clean injection equipment and never to reuse or share that equipment.³ Providers should not neglect counseling IDUs about *sexual* transmission of HIV, which accounts for more transmissions in this group than equipment sharing.

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The CDC's 2003 positive-prevention guidelines suggest a thoughtful approach to asking IDUs about their needle-sharing habits and encouraging them to stop completely if they haven't already (**Figure 2** in CDC guidelines³). An HIV provider might get the ball rolling by asking, "How often do you borrow or share a needle or works?" If the patient answers sometimes or always, the provider could ask, "What do you plan to do about sharing needles in the future?" If the person has no plans, possible follow-up questions may be "Have you heard that HIV can survive in the cotton and rinse water?" or "Can you tell me something about sharing needles?" If the person does have a plan, the clinician might ask, "How do you think your friends will deal with you when you don't share needles or works?"

The CDC stresses that giving up injecting "is the only reliable way to eliminate the risk of injection-associated HIV transmission."³ These guidelines cite more than a dozen studies showing that substance abuse treatment—particularly opioid substitution—can reduce risky injection habits, risky sex, and HIV incidence. For IDUs who can't or won't quit shooting, the CDC favors "once-only use of sterile syringes" because "it is difficult to reliably disinfect syringes" and because studies show disinfecting is not as safe as using a new sterile syringe.

The Midwest AIDS Training + Education Center offers a useful patient-level flier on avoiding needle sharing and keeping needles clean at <http://www.uic.edu/depts/matec/Drug/Safer.htm> (accessed November 5, 2011). Providers can download the flier and print it on two pages.

As research summarized in the first article in this issue shows, noninjection drug use also inflates the risk of HIV transmission. HIV providers should talk to patients about drug use and should refer those who need help getting a handle on their habit.

Behavioral interventions can trim transmission risk

One might assume that getting people on anti-retrovirals, getting their viral load under 50, and screening for and treating other STIs will prevent HIV transmission so effectively that providers needn't bother with costly, time-consuming, hit-or-miss behavioral interventions.

But some new behavioral tactics are inexpensive, require little or no provider time, and proved effective in randomized trials.

So ignoring this option may deprive some HIV-positive people of an approach that fits their needs best. For example, behavioral interventions may be a good bet for healthy people who want to put off antiretroviral therapy, those on treatment who can't reach an undetectable viral load, people with continuing high-risk behavior despite regular counseling, patients who like to take charge of their own health, and people inclined to try group programs or who have an amicable provider relationship that makes one-on-one interventions a natural fit.

In 2006 CDC investigators ran a meta-analysis of interventions designed to quell risk behaviors



in HIV-positive people to see what worked and what predicted success.³⁹ They considered only studies that used randomization or assignment with minimal bias, relied on statistical analysis, and assessed behavioral or biologic outcomes at least 3 months after the intervention. Together the interventions cut the risk of unprotected sex almost 40% (OR 0.57, 95% CI 0.40 to 0.82) and clipped STI incidence 80% (OR 0.20, 95% CI 0.05 to 0.73). Among the traits of successful programs were delivery by providers or counselors, delivery in settings where HIV-positive people receive routine services or medical care, and a design based on behavioral theory. (See the interview with the CDC's Nicole Crepaz in this issue for details of this meta-analysis.)

The Cochrane group analyzed 44 studies of behavioral interventions involving 18,585 MSM with or without HIV.⁴⁰ These studies, published or presented from 1988 through 2007, included 26 small-group interventions, 21 individual-level interventions, and 11 community-level interventions. Overall, these programs cut the risk of unprotected sex or partner numbers by 15% to 27%, depending upon study type. The Cochrane experts concluded that "HIV prevention for this population can work and should be supported."⁴⁰

Besides conducting the just-cited meta-analysis,³⁹ the CDC's Prevention Research Synthesis (PRS) team reviews and vets mountains of evidence on HIV prevention interventions and distills it all on

Web pages devoted to "promising-evidence interventions" that can rein in sex- or drug-related risk behaviors, curb rates of new HIV and other STIs, or bolster HIV-protective behaviors.⁴¹ The 28 programs identified to date meet PRS efficacy criteria and are judged scientifically sound.

Four of these interventions target HIV-positive people: Options/Opciones Project, Partnership for Health, Together Learning Choices (TLC), and Women Involved in Life Learning With Other Women (WILLOW). Options/Opciones and Partnership for Health are one-on-one interventions delivered by the HIV provider. TLC is a small-group intervention aimed at teens and young adults, and WILLOW is a small-group program for HIV-positive women. **Table 4** describes these four programs and provides links for further information.

Innovative interventions discussed by Stephen Morin in the interview in this issue let patients screen themselves for transmission risk behaviors on laptops or handheld devices while waiting for their appointment. If the patient signals some risk on these self-administered surveys, a red flag waves in the clinic's electronic medical records, alerting the provider before the patient visit and allowing the provider to take appropriate action. The table between the two interviews in this issue describes four patient self-administered programs.

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Table 4. Four effective risk-reducing behavioral programs for people with HIV

Options/Opciones Project

Options/Opciones is an individual-level, clinician-delivered HIV risk reduction intervention for HIV-positive persons during their routine clinical care visits and repeated at each visit. The intervention consists of a brief, patient-centered discussion (5-10 minutes) between clinician and patient at each clinic visit. Based on motivational interviewing techniques, clinicians evaluate sexual and drug-use behaviors of HIV-positive patients, assess the patient's readiness to change risky (or maintain safer) behaviors, and elicit various methods from patients for moving toward change or maintaining safer behaviors. Clinician and patient then negotiate an individually tailored behavior change goal or plan of action, which is written on a prescription pad, for the participant to achieve by the next visit.

For more information:

<http://www.cdc.gov/hiv/topics/research/prs/resources/factsheets/options.htm>

Partnership for Health

The Partnership for Health (PfH) loss-frame intervention is a one-on-one, brief provider-administered safer sex intervention for HIV-positive persons in care. The intervention emphasizes the importance of the patient-provider relationship to promote patients' healthful behavior. At each clinic visit, the provider delivers a brief counseling session (3-5 minutes) with messages that focus on self-protection, partner protection, and disclosure. Loss-framed messages are framed in a way that emphasizes the risks or negative consequences of risky behavior. The provider also uses brochures, informational flyers, and posters with the loss-framed messages to facilitate counseling and works with the patient to identify goals for the patient to work on.

For more information:

<http://www.cdc.gov/hiv/topics/research/prs/resources/factsheets/PfH.htm>

Together Learning Choices (TLC)

TLC (Together Learning Choices, previously referred to as Teens Linked to Care) is a small-group intervention designed for youth and young adults living with HIV. TLC consists of 2 modules: Stay Healthy and Act Safe. The Stay Healthy module consists of 12 sessions to

promote positive health behaviors. Intervention sessions are focused on coping with learning one's seropositive status, addressing issues of disclosure, and helping youth to implement new daily routines to stay healthy and actively participate in health care decisions. The Act Safe module consists of 11 sessions to increase self-protection and other-protection motivation to change behavior and to reduce substance use and unprotected sex acts. . . . Group discussions, role-play, video, exercises, and goal setting encourage the ability to effectively reach goals, solve problems, and effectively respond to stressful situations.

For more information:

<http://www.cdc.gov/hiv/topics/research/prs/resources/factsheets/TLC.htm>

Women Involved in Life Learning With Other Women (WiLLOW)

The WiLLOW intervention is a small group, skill-training intervention for women living with HIV. Through interactive discussions within groups of 8 to 10 women, the intervention emphasizes gender pride and informs women how to identify and maintain supportive people in their social networks. The intervention enhances awareness of HIV transmission risk behaviors, discredits myths regarding HIV prevention for people living with HIV, teaches communication skills for negotiating safer sex, and reinforces the benefits of consistent condom use. WiLLOW also teaches women how to distinguish between healthy and unhealthy relationships, discusses the impact of abusive partners on safer sex, and provides information about local shelters for women in abusive relationships.

For more information:

<http://www.cdc.gov/hiv/topics/research/prs/resources/factsheets/WiLLOW.htm>.

Source: CDC Promising-Evidence Interventions.⁴¹

<http://www.cdc.gov/hiv/topics/research/prs/promising-evidence-interventions.htm>.

Not content with merely parsing and rating HIV risk-reduction programs, the CDC collaborates with Danya International to train providers, health departments, and community groups in science-based HIV-prevention interventions.⁴² A comprehensive Web site offers complete explanations of programs and a city-by-city calendar of free courses: go to the Diffusion of Effective Behavioral Interventions (DEBI) site at <http://www.effectiveinterventions.org/en/home.aspx>. The top of the home page offers a link to a 20-minute online DEBI overview.

Reviewing findings from trials done largely in high-income countries, WHO recommends behavioral interventions for HIV prevention in MSM, including individual interventions, community-level interventions, targeted Internet-based information, social marketing strategies, and sex venue-based outreach.²¹

WHO analyzed studies of two Internet-based strategies, one that aimed to temper risk behavior in US MSM with HIV (21%) or without HIV⁴³

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and one in Peru to increase HIV testing in seronegative MSM.⁴⁴ Among men who practiced unprotected anal intercourse when the US study began, after 3 months those randomized to the Internet program reported a marginally lower number of men with whom they had risky sex than did men in the control arm (risk reduction 15.6%, 95% CI 0.704 to 1.013, $P = 0.068$ in an adjusted analysis).⁴³

WHO observed that “Internet-based HIV prevention interventions make it easier for MSM with Internet access to obtain relevant HIV prevention messages in an anonymous fashion, at a convenient time and in private.”²¹ Prevention instruction and counseling via the Internet may be particularly appropriate for rural residents, who have to travel far to their HIV clinic or behavioral intervention sites, or for people uncomfortable with group interventions. One study of 475 rural US MSM found that one such program reduced anal sex and increased condom use.⁴⁵ But so far the CDC lists no Internet-based prevention programs for HIV-positive people.

Clinicians who don't know how their patients use digital media should start learning. How many providers who care for gay men know that many of them favor a smart-phone app,

GRINDR, that melds social networking with GPS to help men find friends—and sex partners—*fast*? A study of 375 young gay men who use GRINDR in Los Angeles found that 153 men (43%) reported unprotected receptive anal intercourse in the past month, 163 (47%) reported unprotected insertive anal intercourse, and 181 (48%) had sex under the influence of alcohol or drugs.⁴⁶ More than half of these men, 56%, found a sex partner via GRINDR. And when using GRINDR, fewer HIV-positive than negative men asked their potential partner's HIV status, a finding suggesting some of these positive men don't bother serosorting.

Limited clinic time and other strictures may sometimes frustrate clinicians who set their mind on one of the 3- to 10-minute positive-prevention exchanges recommended by the CDC (**Table 4**, Options/Opciones Project and Partnership for Health). But interventions self-administered by patients (summarized between the two interviews in this issue) take little or no provider time. And it takes about 5 seconds to ask office staff to copy the Prevention Pointers sheet that follows this article in *RITA!* and about 4 seconds to pull it out of a drawer and hand it to an HIV-positive patient at every visit.

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Prevention pointers for people with HIV: How to avoid passing your virus to someone else*

- The easiest ways to pass HIV to someone else are in blood or sexual fluids.
- Having sex without a condom or sharing drug-injection works can infect a partner with your HIV.
- If you inject drugs, you can stop with a drug-substitution program (for example, with methadone).
- If you continue to inject drugs, always use clean injecting equipment and never share injecting equipment with partners.
- Always use a condom during anal or vaginal sex.
- Use enough lubrication with a condom to avoid causing minor cuts in your partner's anus or vagina.
- Don't rely on a sex partner to tell you accurately (or truthfully) if he or she has HIV.
- Using drugs or alcohol before sex raises the chance you will forget to use a condom or won't bother to use one.
- If you haven't started antiretroviral therapy, consider starting as a way to limit chances you will infect a partner.
- If you're taking antiretrovirals, take your drugs as directed to make sure you reach and maintain an undetectable viral load.
- If you reach an undetectable viral load, your virus may become detectable again if you miss antiretroviral doses or get another sexually transmitted infection.
- Tell your HIV provider immediately if you have signs of a sexually transmitted infection, such as genital sores.
- Don't donate blood, plasma, tissue, organs, or semen because they can transmit HIV.
- Don't share toothbrushes, razors, douche equipment, or sex toys.

*Pointers based primarily on US Department of Health and Human Services Health Resources and Services Administration. Guide for HIV/AIDS Clinical Care. January 2011. <http://hab.hrsa.gov/deliverhivaidscares/clinicalguide11/>.



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