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A Systematic Review of Behavioral and Treatment Outcome Studies Among HIV-Infected Men Who Have Sex with Men Who Abuse Crystal Methamphetamine

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Abstract

Men who have sex with men (MSM) have the highest incidence of HIV infection in the United States. One of the contributing factors to HIV spread among this group is the use of crystal methamphetamine ("meth"). The objective was to review the behavioral impact of crystal meth use in HIV-infected MSM and potential treatment options. A systematic review of MEDLINE identified studies that evaluated the clinical effects of crystal meth on the HIV-infected MSM population. Search terms included HIV, methamphetamine, MSM, antiretroviral therapy, adherence, resistance, and treatment. U.S. citations in the English language in peer-reviewed journals until December 2010 were included. The primary author reviewed eligible articles, and relevant data including study design, sample, and outcomes were entered into an electronic data table. The 61 included studies highlight that HIV-infected MSM who use crystal meth are more likely to report high-risk sexual behaviors, incident sexually transmitted infections, and serodiscordant unprotected anal intercourse, compared to HIV-infected MSM who do not use crystal meth. Medication adherence in this population is notably low, which may contribute to transmission of resistant virus. No medications have proven effective in the treatment of crystal meth addiction, and the role of behavioral therapies, such as contingency management are still in question. HIV-infected MSM who abuse crystal meth have worse HIV-related health outcomes. Behavioral interventions have shown variable results in treating crystal meth addiction, and more investigation into rehabilitation options are needed. The results presented support efforts to develop and implement novel interventions to reduce crystal meth use in HIV-infected MSM.

Introduction

Fifty-three percent of new HIV infections in the United States in 2006 were among men who have sex with men (MSM).[1] The incidence of HIV has been climbing in this population since the 1990s, and MSM continue to bear a disproportionate burden of new HIV infections. Unprotected anal sex is a significant risk factor for HIV transmission and acquisition in this group of men, and is closely associated with substance use, particularly crystal methamphetamine ("meth") use.[2] In fact, the incidence of HIV in MSM who use crystal meth is more than double that of MSM who do not use crystal meth[3] and a relationship between increased intensity of crystal meth use and HIV risk has been observed.[4] While previous reviews have highlighted the growing problem of crystal meth use in HIV-uninfected MSM, the data on clinical outcomes and potential therapies among those who are infected with HIV are just emerging. HIV-infected MSM who use crystal meth can experience a broad range of destructive outcomes including failure to adhere to medications, decreased access to medical care, and increased sexual risk behavior.[5–15] Being diagnosed with HIV may have an impact on

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motivations surrounding crystal meth use, and success with treatment, compared to the HIV-uninfected population. In this review, we systematically examine crystal meth use in HIV-infected MSM with a specific focus on HIV-related behavioral health outcomes and potential treatment options.

Methods

Data sources and searches

We conducted a systematic search of MEDLINE using combinations of the keywords HIV, methamphetamine, MSM, antiretroviral therapy, adherence, resistance, and treatment to identify studies that evaluated the clinical effects of crystal meth on the HIV-infected MSM population. Our search was limited to English-language, human, original research published in peer-reviewed journals until December 2010. Only U.S. citations were included as the limited literature from Western Europe and Australia only points toward the association of crystal meth with high-risk behavior, without particular attention to HIV-related outcomes in MSM. The bibliographies from included articles were manually reviewed for additional relevant studies.

Study selection

Our search yielded 376 citations, which were screened at the abstract level for relevance to the HIV-infected, MSM population using crystal meth. Twenty-four additional articles were obtained from the manual review of bibliographies. Included were qualitative and quantitative studies reporting original data on sexual risk behaviors, medication adherence, and treatment outcomes of HIV-infected MSM who use crystal meth. We excluded abstracts that were not original research in a peer-reviewed journal or did not study the HIV-infected MSM population in the United States. As this is a review of the behavioral and treatment outcomes, basic science literature was excluded. A total of 100 abstracts were eligible for full article review and an additional 39 were excluded based on the above criteria. Full articles were reviewed to ascertain whether or not they were applicable to the HIV-infected, MSM, crystal meth-using population. Notably, there were a small number of publications that addressed stimulant use, where data from crystal meth use were combined with cocaine use. These articles addressing stimulant use were included to broaden the number of studies available for review. When a study combined stimulants, this was noted in the text. There were also a small number of articles that were not exclusively focused on HIV-infected MSM. These were included because the studies revealed information about HIV seroconversion or patterns of behavior that may be relevant to HIV-infected MSM. Furthermore, articles were included that cited treatment options for crystal meth-dependence in non-MSM or HIV-uninfected persons, as only one study exclusively examined the population of interest, and research among mixed samples may be applicable to this group. Ultimately, 61 articles met our eligibility criteria (Fig. 1). Thirty-nine studies describe sexual risk behavior, 6 relate to antiretroviral therapy adherence and/or drug resistance, and 16 pertain to treatment options. The primary author reviewed eligible articles, and relevant data including study design, sample, and outcomes were entered into an electronic data table. Given the early stage of research in this field, all studies were included regardless of methodological rigor. Methodological limitations are reported in the text where relevant.

Data synthesis

Results of the studies were synthesized qualitatively. Studies were grouped into 1 of 3 topics in electronic tables. Review topics include: sexual risk behavior, antiretroviral therapy adherence and/or drug resistance, and crystal meth treatment options. We also examined sexually transmitted infections (STI) and reasons for crystal meth use in HIV-infected MSM. Quantitative results were presented from each study, with specified odds ratios and 95% confidence intervals where available.

Results

HIV risk behavior

HIV-infected MSM who use crystal meth are more likely to engage in unprotected anal intercourse (UAI),[5,8,16,17] have group sex,[18] have multiple sex partners,[5,8,10,19] find sexual partners on the Internet,[8] have sex with an injection drug user,[5] and be high or intoxicated during sex[5,8] compared to MSM who do not use crystal meth, regardless of HIV status (Table 1). Furthermore, qualitative research of HIV-infected, crystal meth-using MSM indicates that crystal meth use is associated with high rates of anal sex, low rates of condom use, sexual marathons (i.e., sexual activities lasting hours or days with one or more partner), and sex with anonymous partners.[14] Another qualitative study of 27 HIV-infected MSM observed that UAI was related to substance use in general (8% used crystal meth), social environmental factors such as high-risk venues, engaging in sex work, and psychological factors such as increase in sexual drive, lack of inhibition, and a decrease in the desire for sexual intimacy.[20] Characteristics of one's sexual partner and unspoken beliefs about the partner's HIV status also had a role in determining whether to engage in high-risk sexual behaviors.

Compared to other drugs of abuse, crystal meth is a particularly strong predictor of UAI in this population.[6,21] Moreover, among HIV-infected MSM with a serodiscordant (HIV-uninfected or unknown HIV status) sexual partner, crystal meth use is significantly associated with UAI (insertive: odds ratio [OR] 1.9, 95% confidence interval [CI] 1.1–3.3; receptive: OR 1.6, 95% CI 0.9–3.1).[22] This has been corroborated by multiple studies.[23–25] There are subgroups within this community with variable patterns of crystal meth use that engage in behaviors that are at particularly high risk for HIV transmission and STI acquisition. These include crystal meth users who use sildenafil (Viagra®, Pfizer Inc., New York, NY)[6,21,25–27] or other illicit drugs during sex,[28,29] those who trade crystal meth for sex,[15] those who report high levels of sexual compulsivity,[25,30] those who engage in sexual encounters in public venues,[31,32] and those who report crystal meth binges.[33] Additionally, crystal meth use in MSM has been associated with a recent diagnosis of HIV infection (OR 3.02, 95% CI 2.30–3.99),[34] suggesting that new HIV infection may be the result of engaging in high-risk behaviors while under the influence of crystal meth.[3,6,18,35–44] A case-control study comparing 32 HIV-infected MSM cases to 110 HIV-uninfected MSM controls observed that crystal meth use during UAI was independently associated with recent HIV infection (adjusted

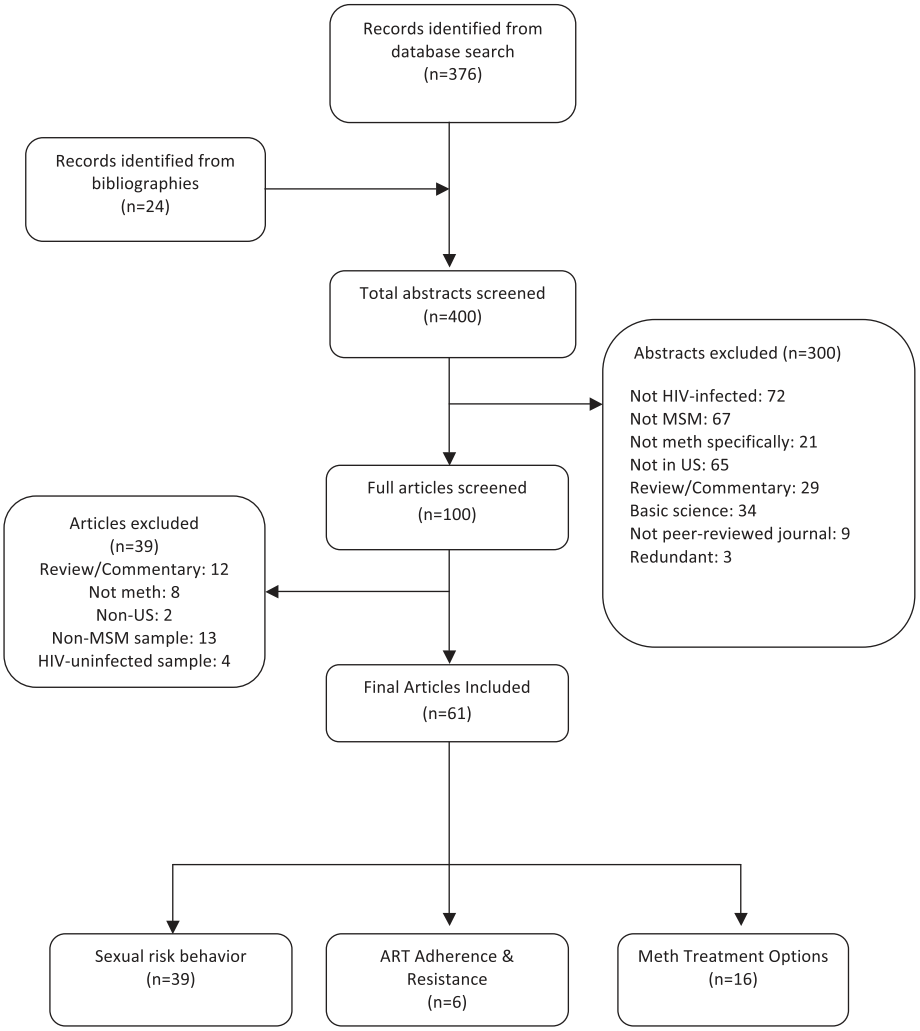

FIG. 1. Summary of study selection.

odds ratio [aOR] = 9.0, 95% CI 1.5–55.0).[43] Another study found that of 20 HIV-infected, crystal meth-using MSM, 50% did not consistently disclose their HIV status to sexual partners.[11] Together these findings highlight the strong association between crystal meth use, HIV risk behavior, and subsequent HIV infection.

Sexually transmitted infections

Given the increased frequency of high-risk sexual behavior associated with crystal meth use, it is not surprising that both HIV-infected and uninfected MSM who use crystal meth have a greater risk of STIs compared to MSM who do not use crystal meth.[8,34] Studies have shown that HIV-infected MSM who use crystal meth are more likely to report a history of STI,[6,41] specifically gonorrhea (59.5% versus 26.9%, $p < 0.01$), compared to HIV-uninfected MSM who use crystal meth.[45] Furthermore, HIV-infected MSM who have used crystal meth in the prior 3 months have a significantly higher odds of being diagnosed with an STI (gonorrhea, chlamydia, or syphilis) in the past year, compared to HIV-infected MSM who have not used crystal meth (OR = 3.37, 95% CI 1.67–6.81).[16]

With regard to STIs, another area of public health concern is the combination of crystal meth with sildenafil during sex. The use of sildenafil in MSM irrespective of substance use has been associated with higher rates of UAI.[46] With respect to crystal meth specifically, often crystal meth abusers use sildenafil to counteract the side effect of erectile dysfunction, a frequent side effect of stimulant use. One survey of 1318 MSM (both HIV-infected and uninfected) showed that risk factors for early syphilis included use of both crystal meth and sildenafil together (OR = 6.2, 95% CI 2.6–14.9) and crystal meth use alone (OR = 3.2, 95% CI 1.3–7.6), compared to MSM who had not used either drug.[26] Another cross-sectional study of 1976 MSM found that of those who used crystal meth with sildenafil, 57% were HIV infected.[22] Additionally, this group was significantly more likely to engage in serodiscordant UAI (OR = 4.0, 95% CI 2.2–7.5) and be diagnosed with an STI (OR = 3.0, 95% CI 1.6–5.5) compared to those who had not used crystal meth and sildenafil in the last year.

Reasons for crystal meth use

HIV-infected MSM are more likely to report crystal meth use compared to HIV-uninfected MSM.[8,23,32] In a study of 340 HIV-infected crystal meth-using MSM participants were asked to cite the reasons why they used crystal meth. Explanations included to experiment, to party, to enhance sexual pleasure, to get more energy, to escape, to meet sex partners, to feel more self-confident, to deal with grief, to

Table 1. Summary of Sexual Risk Behavior Associated with HIV-Infected, Meth-Dependent MSM

Author, year (reference) *Study design*	*Sample measures*	*Summary of findings*
1. Bousman, 2009[5]	175 nonmonogamous MSM. Divided into 4 groups: Meth+/HIV+, Meth−/HIV+, Meth+/HIV−, Meth−/HIV−	Meth+/HIV+ reported condom use less than 25%, more likely to engage in intoxicated sex, or have sex with an injection drug user compared to Meth−/HIV+ and Meth−/HIV− Meth+/HIV+ was associated with higher depression and confusion scores. Meth−/HIV+ reported condom use 51–75% of time
Cross-sectional study	Self-reported sexual behavior. Beck Depression Inventory and Profile of Moods States questionnaire	
2. Brewer, 2006[36]	311 MSM; 14% HIV-infected	In HIV-uninfected, strongest correlates of HIV exposure were STIs (OR 5.8), recent sex at bathhouse (OR 9.1), recent use of sildenafil (OR 4.4), or meth use (**OR 8.0**)
Cross-sectional study, telephone survey	Self-reported UAI with a man of opposite or unknown serostatus in the past year	
3. Buchacz, 2005[3]	2991 MSM; 290 were amphetamine users	HIV incidence among amphetamine users was 6.3% per year (95% CI 1.9–10.6%). HIV incidence among nonamphetamine users was 2.1% per year (95% CI 1.3–2.9%)
Cross-sectional study	Self-reported amphetamine use, sexual risk behavior and HIV status	
4. Carey, 2009[6]	111 recently HIV-infected MSM (cases); 333 HIV-uninfected MSM (controls)	HIV-infected MSM had more UAI, more frequently used meth, sildenafil, and poppers during UAI, more likely to have a history of STI. Recent HIV seroconversion associated with UAI with an HIV-infected person (aOR 3.01, 95% CI 1.14–7.92). Meth use during UAI and sildenafil use during UAI lost statistical significance after adjusting for other variables
Case-control study	HIV serostatus as documented at clinic. Self-reported sexual behaviors and drug use	
5. Drumright, 2007[37]	207 MSM with recent HIV infection within the past 12 months	Before HIV diagnosis, UAI was associated with meth use (**OR 7.12, 95% CI 1.8–28.6**). After HIV diagnosis, UAI was associated with other substances, but not meth use
Cross-sectional study, computer-based interviews	HIV status extracted from medical records. Self-reported sexual behavior and substance use with last 3 sexual partners	
6. Forrest, 2010[8]	946 MSM in Florida; 18% report using meth. 17% reported being HIV-infected	HIV-infected MSM more likely to report using meth compared to HIV-uninfected MSM (**32% vs. 15%, $p < 0.0001$**). HIV-infected meth users reported higher rate of UAI compared to HIV-infected non-meth users. Meth users (both HIV-infected and uninfected) were more likely to be intoxicated during sex, use sildenafil during sex, find sex partners over the Internet, and have an STI compared to non-meth users
Cross-sectional study, questionnaire and interviews	Self-reported meth use and sexual behavior	
7. Frosch, 1996[38]	16 Meth-using MSM	62.5% reported UAI, and 56.3% reported having sex with an HIV-infected partner in the prior 12 months
Cross-sectional study, survey	Self-reported HIV risk behaviors	
8. Halkitis, 2009[21]	232 MSM who reported using club drugs (ecstasy, GHB, meth, cocaine, or ketamine); 37.5% HIV-infected	Meth use associated with UAI with casual partners who are HIV-infected or of unknown status
Prospective cohort over 12 months	Self-reported sexual behavior and drug use	
9. Halkitis, 2005[48]	48 meth-using, MSM; 56% HIV-infected	68% of participants used meth for its sexual effects. HIV-infected participants more likely to use meth for sexual reasons (85.2% in HIV+ vs. 50% in HIV−), as opposed to HIV-uninfected who often used meth for social reasons
Cross-sectional study, qualitative interviews	Self-reported reasons for meth use and sexual risk behaviors	

(*continued*)

Table 1. (Continued)

Author, year (reference) *Study design*	*Sample measures*	*Summary of findings*
10. Halkitis, 2005[18]	49 meth-using, MSM; 57% HIV-infected	More frequent UAI in HIV-infected as compared to HIV-uninfected
Cross-sectional study, interviews	Self-reported reasons for meth use and sexual risk behaviors	
11. Hatfield, 2009[27]	675 HIV-infected MSM living in 6 U.S. cities	27% of white MSM were using methamphetamine. Serodiscordant UAI associated with poor self-efficacy with a condom
Cross-sectional study, questionnaire	Self-reported meth use and sexual behavior	
12. Mansergh, 2006[17]	388 MSM, of which, 155 HIV-infected	Meth use associated with sildenafil use (aOR = 4.00, 95% CI 1.45–11.09) and HIV positive serostatus (**aOR=2.86, 95% CI 1.41–5.84**)
Cross-sectional study, survey	Self-reported HIV status and sexual behavior during most recent sexual encounter	
13. Mayer, 2010[16]	398 HIV-infected MSM; 22.9% had used meth in the last 3 months	Meth use was significantly associated with having been diagnosed with an STI in the past year (**OR=3.37, 95% CI 1.67–6.81**). Meth use was significantly associated with serodiscordant UAI (**OR=4.25, 95% CI 2.45–7.38**)
Retrospective cohort, chart review	Tested for gonorrhea, syphilis, and chlamydia. Self-reported serodiscordant UAI	
35. Menza, 2009[39]	1903 HIV-uninfected MSM	Developed a prediction model for HIV acquisition in MSM. Model includes use of meth in the prior 6 months, serodiscordant UAI, 10 or more male sex partners in the past year, and history of STI
Retrospective cohort, chart review	Self-reported substance use, STD, history and sexual behavior	
15. Mimiaga, 2008[11]	20 HIV-infected, meth-using MSM	Meth use resulted in weight loss, depression, and anxiety, and compromised social relationships. Participants described high risk sexual behaviors while high on meth. 50% did not consistently disclose their HIV status to sexual partners
Qualitative study, open-ended semistructured interviews	Self-reported sexual behaviors, patterns of drug use, consequences of drug use	
16. Molitor, 1998[35]	258567 men and women; 12.5% MSM; 1.1% HIV-infected	Meth users less likely to use condoms, more likely to have sex with IDU, and more likely to have an STI. Meth users who were MSM were more likely to have HIV compared to MSM who did not used meth
Cross-sectional study	Self-reported sexual behaviors and drug use	
17. Morin, 2007[12]	4016 HIV-infected patients; 2109 were MSM	MSM were more than twice as likely to have UAI with a serodiscordant partner compared to heterosexual men (**OR 2.35, 95% CI 1.84–3.00**). MSM were more likely to use meth compared to heterosexual men and women (8% vs. 2% and 3%)
Cross-sectional study, computer interviews	Self-reported sexual behavior and drug use	
18. Morin, 2005[40]	1910 HIV-infected MSM	Predictors of HIV transmission with a steady male partner included meth use (**OR 2.1, 95% CI 1.0–4.39**). Predictors of transmission with a casual partner included meth use (**OR 1.76, 95% CI 1.16–2.86**)
Cross-sectional study, computer interviews	Conducted psychological measures and self-reported sexual behaviors with 5 most recent partners	
19. Nakamura, 2009[47]	340 HIV-infected, meth-using MSM	Reasons for initiating meth use: to experiment (73%), to party (67%), to get high (59%), for sexual pleasure (49%), to increase energy (45%), to cope with mood (32%), to meet sex partners (31%), to feel self-confident (27%), to deal with grief (21%), to cope with HIV-related symptoms (15%)
Cross-sectional study, interview	Self-reported meth use and sexual behavior	
20. Patterson, 2005[28]	261 HIV-infected, meth-using, MSM	64% used meth with cocaine, heroin, hallucinogens, or ketamine. This group had significantly more serodiscordant sex partners and reported UAI, was more impulsive, and had negative self-perceptions compared to those who used meth alone or used meth with marijuana or poppers
Cross-sectional study, interviews	Self-reported drug use and sexual behaviors	

(*continued*)

Table 1. (Continued)

Author, year (reference) *Study design*	*Sample measures*	*Summary of findings*
21. Peck, 2005[41] Cross-sectional study, interviews	162 meth-dependent, MSM; 61% HIV-infected Self-reported sexual behavior and drug use	HIV-infection associated with meth dependence, UAI, and history of STIs
22. Plankey, 2007[42] Prospective cohort	4003 HIV-uninfected MSM Measured time to HIV seroconversion via HIV testing at baseline and follow-ups. Self-reported drug use and sexual risk behavior	HIV seroconversion was associated with meth use (**aOR 1.46; 95% CI 1.12–1.92**)
23. Rudy, 2009[34] Cross-sectional study	6435 MSM at an STI/HIV clinic. 13% reported meth use Self-reported meth use, other drug use, no drug use, and sexual behavior	Meth use associated with new HIV-infection (**OR 3.02, 95% CI 2.30–3.99**), gonorrhea (OR 2.16, 95% CI 1.30–3.58), sex for drugs or money (OR 2.83, 95% CI 2.02–3.96), and sex with an injection drug user (OR 12.1, 95% CI 7.73–18.8)
24. Schwarcz, 2007[23] Cross-sectional, telephone survey	1976 MSM; 25% HIV-infected Self-reported sexual behaviors and drug use	HIV-infected MSM were more likely to use meth than HIV-uninfected MSM. 26% of HIV-infected men had used meth in the prior year. In HIV-infected MSM, UAI with a serodiscordant partner was associated with using sildenafil (**aOR 2.34, 95% CI 1.1–5.0**), and using meth (**aOR 2.76, 95% CI 1.3–5.7**)
25. Semple, 2010[15] Cross-sectional study, interviews	155 HIV-infected, meth-using MSM Self-reported sexual behaviors, and patterns of meth use	43% reported trading sex for meth in the prior 2 months. Trading sex for meth associated with UAI (**OR 4.0, 95% CI 1.53–10.45**), meth binges (**OR 2.62, 95% CI 1.22–5.60**), homelessness (OR 4.68, 95% CI 1.63–13.50)
26. Semple, 2010[31] Cross-sectional study, interviews	321 HIV-infected, meth-using MSM Self-reported sexual behaviors, and context of meth use	Men who reported sex in public venues used significantly more meth than those who had sex in commercial or private venues. Men who reported sex in public or commercial venues were more likely to have UAI or a serodiscordant partner compared to those who had sex in private venues
27. Semple, 2009[30] Cross-sectional study, questionnaire, interview	341 HIV-infected, meth-using MSM. 65% reported meth coadministration (with other drugs) in the past 2 months Self-reported use of meth, other drugs and sexual risk	Meth coadministration significantly associated with unprotected sex, casual, anonymous, and paid partners compared to men who used meth alone. Meth coadministered with either marijuana, sildenafil, poppers, GHB, ketamine, cocaine
28. Semple, 2009[29] Retrospective cohort	341 HIV-infected, meth-using MSM Self-reported sexual behavior, drug use behavior	84% reported engaging in sexual marathons while high on meth. Those who engaged in sexual marathons used significantly more illicit drugs, and were more likely to use sildenafil
29. Semple, 2006[24] Cross-sectional study, interviews	132 HIV-infected, meth-using, MSM who had serodiscordant (HIV-uninfected or of unknown status) and seroconcordant (HIV-infected) partners Self-reported sexual behaviors and drug use with respect to partner serostatus	HIV-infected, meth-using MSM had twice as many HIV-uninfected or partners of unknown serostatus, as compared to HIV-infected partners. UAI was high among both serodiscordant and seroconcordant partners
30. Semple, 2006[25] Cross-sectional study, interviews	217 HIV-infected, meth-using MSM Assessed sexual compulsivity via self-report	Higher sexual compulsivity scores were associated with meth use during or before sex, finding partners on the street or at sex clubs, and greater number of serodiscordant partners

(*continued*)

Table 1. (Continued)

Author, year (reference) *Study design*	*Sample measures*	*Summary of findings*
31. Semple, 2002[14]	25 HIV-infected, meth-using MSM	Meth use associated with high rates of UAI, low condom use, anonymous sex.
Cross-sectional study, interviews	Self-reported sexual behaviors and reasons for meth use	Motivations included sexual enhancement and to cope with HIV status
32. Semple, 2003[33]	90 HIV-infected meth-using MSM	46% identified themselves as binge users. Binge meth-users reported more high-risk sexual behaviors, more mental and physical health problems, more social difficulties compared to those who did not identify themselves as binge meth-users
Cross-sectional study	Assessed social and behavioral characteristics of those who binge on meth via self-report	
33. Shoptaw, 2001[45]	68 MSM seeking treatment for meth dependence	HIV-infected MSM meth users were more likely to have medical problems, a history of gonorrhea, inject meth, and have more UAI, with more sexual partners compared to HIV-uninfected MSM meth users
Cross-sectional study, interviews	HIV status, self-reported sexual behaviors, drug use	
34. Spindler, 2007[22]	1976 MSM; 25% HIV-infected	Of MSM who used sildenafil with meth, 57% were HIV-infected. Sildenafil use with meth was associated with serodiscordant UAI, and recent STI (**OR 3.0, 95% CI 1.6–5.5**)
Cross-sectional, telephone survey	Self-reported sexual behavior and drug use	
35. Taylor, 2007[44]	1904 MSM with diagnosis of early syphilis; 1113 HIV-infected (59%)	167 patients reported meth use (9%). 68% of them were HIV-infected. Meth use associated with having multiple partners (OR 2.2; 95% CI 1.2–4.3), not using condom (OR 3.2; 95% CI 1.4–7.2), recent incarceration (OR 10.5; 95% CI 3.6–30.4), and meeting sex partners at bathhouses (OR 2.6; 95% CI 1.3–5.2)
Retrospective cohort	Self-reported sexual behavior and drug use	
36. Thiede, 2009[43]	142 MSM; 32 HIV-infected	Recent HIV infection was associated with meth use during UAI **(aOR=9.0, 95% CI 1.5–55.0)**; UAI with an HIV-negative casual partners (aOR=4.3, 95% CI 1.3–13.9); meeting partners at bathhouses or sex clubs (aOR=11.5; 95% CI 1.7–77.2), bars or dance clubs, (aOR=8.2; 95% CI 1.5–45.7), or online (aOR=6.7; 95% 1.6–27.7)
Case-control study	HIV status (as referred), self-reported sexual behaviors, drug use and partner characteristics (3 most recent partners)	
37. Whittington, 2002[32]	959 MSM in Seattle, WA; 35.6% HIV infected	Compared to HIV-uninfected men, HIV-infected participants more frequently reported having used meth (**19.9 vs. 12.3; $p < 0.02$**) and amyl nitrates with sex (54.2 vs. 37.6; $p < 0.001$). Gonorrhea, chlamydia, or syphilis was diagnosed in 12% of HIV-infected and 13% of HIV-uninfected MSM. No difference in rates of STIs between men with HIV-concordant and discordant partnerships
Cross-sectional study, interviews	HIV status (as referred) and self-report and/or testing for STIs, and self-reported sexual behavior and drug use	
38. Wohl, 2008[19]	455 HIV-infected MSM and 228 HIV-infected non-MSM	Lifetime meth use was 35% for MSM. 11% of MSM had used meth in the prior year. Compared to nonusers, MSM meth users were more likely to be white (OR 4.1, 95% CI 2.5–6.6) or black (OR 2.1, 95% CI 1.2–3.8) than Latinos, and have 10+ sexual partners in the prior year (OR 3.1, 95% CI 1.7–5.6)
Cross-sectional study, questionnaire	Self-reported sexual behaviors and drug use	
39. Wong, 2005[25]	1318 MSM; 18% HIV-infected	Early syphilis diagnosed in 4%. Early syphilis diagnosis associated with HIV-infection (**OR 3.9, 95% CI 2.0–7.7**), using meth+sildenafil in the prior month (**OR 6.2, 95% CI 2.6–14.9**), and meth use alone (**OR 3.2, 95% CI 1.3–7.6**) compared to men who did not use meth
Cross-sectional study, survey	Self-reported sexual behavior and drug use	

MSM, men who have sex with men; UAI, unprotected anal intercourse; IDU, injection drug user; STI, sexually transmitted infection; OR, odds ratio; CI, confidence interval; a OR, adjusted odds ratio.

feel more attractive, and to cope with HIV-related symptoms.[47] Another study of 48 crystal meth-using MSM (56% HIV infected) found that HIV-infected MSM were more likely to use crystal meth for sexual reasons compared to HIV-uninfected MSM (85.2% versus 50%, $p = 0.009$).[48] Participants described the sexual enhancement while using crystal meth as prolonging sexual encounters and enhancing sexual feelings and attitudes toward sex. Another study found that HIV-infected MSM not only used crystal meth for sexual reasons, but also to cope with their HIV diagnosis, either by making them feel more physically energetic, helping them to view their situation in a more positive light, or by providing an escape from social rejection and depression.[14]

HIV medication adherence

Prior studies have clearly shown that active substance abuse is associated with significantly decreased medication adherence, higher viral loads, opportunistic infections, and increased mortality in HIV-infected persons.[49–52] However, these studies were primarily conducted in heterosexual users of cocaine, crack, or opiates. The literature specifically investigating medication adherence in HIV-infected MSM who use crystal meth is limited (Table 2). One cross-sectional study of HIV-infected patients (39% MSM) showed that crystal meth use in the prior 4 weeks was associated with poor antiretroviral therapy (ART) adherence (27% versus 13%, 95% CI: 1.3–3.5, $p < 0.05$).[10] Additionally, crystal meth users were less likely to be on ART than non-crystal meth users (57.5% versus 70%, 95% CI 0.6–0.9, $p < 0.02$). In a prospective cohort of highly active antiretroviral therapy (HAART) adherence, 102-HIV-infected drug users (i.e., tested positive for opioids, crystal meth, benzoylecgonine, tetrahydrocannabinol, phencyclidine, and/or barbiturates) were compared to 48 HIV-infected drug-free participants.[53] Investigators used medication event monitoring system (MEMS) caps to assess medication adherence. Poor adherence was defined as taking less than 90% of prescribed doses of HAART. Notably, more than half (65%) of the study population identified as MSM and 70% of drug-positive participants were stimulant users (27% tested positive for cocaine only; 70% tested positive for cocaine and crystal meth; and 3% tested positive for crystal meth only). The study observed that HAART adherence was poorest among active stimulant users compared to users of other drugs ($p = 0.001$). Moreover, active stimulant users were 7 times more likely to have poor adherence compared to drug-free participants (OR 7.0, 95% CI 1.8–9.3, $p < 0.01$). While the study did not include analyses for crystal meth users alone, researchers found that those who used crystal meth and cocaine together had a trend toward poorer adherence compared to those who used cocaine alone (54.5% versus 68.1%, $p = 0.06$).

Few studies have investigated the reasons for poor adherence in HIV-infected MSM who use crystal meth. A qualitative study of 20 HIV-infected MSM who believed that they had seroconverted in the context of crystal meth use revealed that crystal meth intoxication compromised one's ability to care for one's self by eating correctly, sleeping regularly, taking medications as prescribed, visiting the doctor regularly, paying bills, and going to work.[11] Many participants had lost jobs in the context of crystal meth abuse, had become socially estranged from family and friends, were homeless, and chronically depressed—outcomes that may have significant implications for HIV medication adherence. Moreover, some former users reported long-term cognitive impairment, where despite having ceased crystal meth use individuals were still unable to remember to take their HIV medications appropriately. In a different qualitative study of 23 HIV-infected, crystal meth-abusing MSM all participants acknowledged that crystal meth use interfered with HIV medication adherence.[13] Nonadherence was divided into planned and unplanned adherence. Planned nonadherence was used by participants as a way to regain control over their lives after being diagnosed with HIV and included taking medication vacations and avoiding the mixing of drugs. Unplanned nonadherence was closely tied to crystal meth intoxication and included the inability to maintain a schedule, and difficulty with regular eating and sleeping patterns. A cross-sectional study of 122 HIV-infected, crystal meth-using MSM (94%) or transgendered individuals on ART found that positive affect was significantly associated with the increased likelihood of reporting perfect (aOR = 1.79, 95% CI 1.06–3.02, $p < 0.05$) or near perfect ($\leq 90\%$; (aOR = 1.63, 95% CI 1.00–2.65, $p = 0.05$) ART adherence in the past month.[7] Conversely, negative affect was associated with weekly crystal meth use (aOR = 1.76, 95% CI 1.02–3.03). These findings suggest that both crystal meth use and medication adherence may be highly tied to mood, and crystal meth use may be a means of coping with negative affect relating to one's HIV diagnosis.

HIV resistance

Crystal meth use in HIV-infected individuals has been associated with significantly increased viral loads in the age of HAART.[54] Antiretroviral medications suppress viral replication only when drug concentrations are maintained at specific levels. Thus, poor adherence to antiretroviral drugs is thought to contribute to drug resistance because of decreased inhibition of viral replication. Two studies specifically address HAART resistance in HIV-infected MSM who use crystal meth. A cross-sectional study of 300 recently HIV-infected MSM crystal meth users showed that weekly crystal meth use was associated with primary drug resistance to non-nucleoside reverse transcriptase inhibitors (NNRTI; OR = 3.5, 95% CI 1.2–10.8, $p = 0.03$), even after controlling for multiple sex partners, race/ethnicity, other illicit drug use, and previous use of antiretroviral drugs.[55] However, no association was found between frequent crystal meth use and resistance to NRTIs or protease inhibitors. A retrospective study of 117 MSM with recent HIV infection (diagnosed within the prior 12 months) who were HAART-naïve examined HAART resistance in the context of substance abuse.[9] Overall, crystal meth was the most commonly used drug during sex with 34% of participants having used crystal meth during sexual activity with their last three sexual partners. Among crystal meth users specifically, more than half had evidence of resistant virus (57% genotypic; 56% phenotypic), compared to nonusers (30% genotypic; 31% phenotypic). Meth users were four times more likely to develop phenotypic resistance (aOR = 4.00, 95% CI 1.19–13.38), compared to participants who did not use crystal meth. Given that the study population was HAART naïve, these findings suggests that phenotypic resistance may be transmitted through sexual contact, which

Table 2. Summary of HIV Medication Adherence and HIV Resistance in the HIV-Infected MSM, Meth-Dependent Population

Author, year (reference) *Study design*	*Sample measures*	*Summary of findings*
1. Carrico, 2010[7]	122 HIV-infected MSM, meth users on ART	Negative affect was independently associated with weekly meth use (aOR = 1.76, $p < 0.05$). Those with positive affect were less likely to report injection drug use in the prior month (aOR = 0.62, $p < 0.05$). Positive affect independently associated with perfect ART adherence in the past month (aOR = 1.79, $p < 0.05$)
Cross-sectional, face-to-face interview	Self-reported ART adherence, frequency of meth binges, recent stimulant use (cocaine, crack, meth). Positive and negative affect measured by PANAS	
2. Colfax, 2007[55]	300 recently HIV-infected MSM meth users	Frequent meth use (at least weekly) was associated with NNRTI resistance (**OR 3.5; 95% CI 1.2–10.8**), but not with protease inhibitor resistance or NRTI resistance
Cross-sectional study	Self-reported meth use. Serum samples for genotypic testing	
3. Gorbach, 2008[9]	117 recently HIV-infected MSM; 51% reported substance abuse during sexual activity in prior year	Meth use during sexual activity associated with 4 times greater odds of phenotypic drug resistance (**aOR 4.0; 95% CI 1.19–13.38**)
Retrospective cohort	Serum samples tested for genotypic and phenotypic resistance. Self-reported sexual risk behavior and meth use	
4. Hinkin, 2007[53]	150 HIV-infected drug users on ART; 65% MSM	Stimulant users (cocaine or meth) were associated with 7 times greater risk of poor ART adherence compared non drug users (**OR=7.0; 95% CI=1.8–9.3**). Those who used cocaine and meth had a trend toward poorer adherence compared to those who used cocaine alone ($p = 0.06$)
Prospective cohort	Urine drug screen. MEMS caps to assess medication adherence over 6 months	
5. Marquez, 2009[10]	653 HIV-infected patients seeking care at outpatient HIV clinic in San Francisco; 67% MSM	39% on HIV-infected MSM reported meth use in prior 4 weeks. Meth use in prior 4 weeks was associated with poor ART adherence (**27% vs. 13%, $p<0.05$**). Meth users in the prior 12 months were less likely to be on ART (57.5% vs. 70%, $p < 0.02$, RR = 0.7, 95% CI: 0.6–0.9)
Cross-sectional, one page anonymous survey	Self-reported meth use and ART adherence	
6. Reback, 2003[13]	23 HIV-infected MSM meth abusers	Barriers to adherence included: 1. Planned nonadherence: as a way to escape from or get control over their disease 2. Unplanned nonadherence: secondary to behavioral disruption while using meth
Qualitative, semistructured interview	Self-reported ART adherence and patterns of meth use	

PANAS, positive and negative affect schedule; MEMS, medication event monitoring system; ART, antiretroviral therapy; NNRTI, non-nucleoside reverse transcriptase inhibitor; aOR, adjusted odds ratio; MSM, men who have sex with men; CI, confidence interval; RR, relative risk.

may have implications on the choice of initial HAART regimen for this subpopulation.

Treatment

Drawing on the success of pharmacologic treatments for other substance dependencies (e.g., cocaine and nicotine), researchers have increasingly studied the utility of medications in treating crystal meth dependence (Table 3). Galloway et al.[56] conducted a randomized controlled trial testing the efficacy of Imipramine, a tricyclic antidepressant, in treating crystal meth dependence. The intervention (150 mg/day), which was conducted among 32 crystal meth users (31% MSM, 28% HIV-infected), was not successful in reducing crystal meth use, affective status, or cravings, and no differences were seen between the intervention group (150 mg/day) and the control group (10 mg/day). Similarly, Shoptaw et al.[57,58] tested the effects of selective serotonin reuptake inhibitors (SSRI) antidepressants in treating crystal meth dependence. In two separate, randomized controlled trials bupropion and sertraline were found to be no more effective than placebo in treating crystal meth dependence. However, *post hoc* analyses indicated that bupropion was effective in reducing crystal meth use among light users (0–2 crystal meth-positive urine samples during the 2-week baseline phase) versus heavy users (3–6 crystal meth-positive urine samples during the 2-week baseline phase), warranting further evaluation of the drug in treating light crystal meth users. Modafinil, a wakefulness medication successfully used to treat cocaine dependence, was also evaluated for its efficacy in treating crystal

Table 3. Summary of Studies on Treatment of Meth Dependence Among Mixed (e.g., HIV-Uninfected and/or Non-MSM) and HIV-Infected MSM Samples

Author, year (reference) *Study design*	*Sample measures*	*Summary of findings*
1. Galloway, 1996[56]	32 meth-dependent; 28% HIV-infected, 30% MSM	No significant differences between groups regarding meth use, cravings, or depression
Double-blinded randomized controlled trial of 150 mg imipramine vs. 10 mg imipramine (control) daily over 6 months	Urine tested for meth, self-reported meth use, and craving. Assessed depression using the Beck Depression Inventory	
2. Jaffe, 2007[71]	145 MSM with meth dependence; 60% HIV infected	Control group reported the most meth use over the 16 weeks Decline in meth use was associated with reduction in depression and sexual risk-taking. GCBT group showed a more rapidly decreasing rate of meth use
Randomized controlled trial comparing (1) CBT (2) CM (3) CBT + CM (4) GBCT culturally tailored CBT for gay and bisexual men over 16 weeks	Urine drug screens three times weekly. Assessed depression and sexual risk overtime	
3. Mausbach, 2007[62]	341 HIV-infected, meth-dependent MSM	Those randomized to safe-sex intervention had significantly more protected sex acts at 8 months (**$p=0.034$**) and 12 months (**$p=0.007$**) compared to control group
Randomized controlled trial comparing safe-sex behavioral intervention vs. diet and exercise control	Assessed changes in self-reported safer-sex behaviors over 12 months	
4. McElhiney, 2009[59]	10 HIV-infected, meth-dependent MSM	Six of the 10 participants who completed the study reported reduced meth use of over 50%
Single-blinded pilot study of modafanil + CBT over 16 weeks	Biweekly urine drug screens and self-reported meth use. Assessed depression using the Beck Depression Inventory	
5. Menza, 2010[63]	127 meth-using MSM from Seattle, WA; 55% HIV infected	During intervention treatment and control groups were equally likely to have meth + urine (aRR 1.09, 95% CI 0.71–1.56), and to report non concordant UAI (0.80, 95% CI 0.47–1.35)
Randomized controlled trail of CM vs. placebo (referral to community resources) over 12 weeks	Self-reported nonconcordant unprotected anal intercourse (UAI) in the prior 6 weeks. Self-reported -meth use, urine tested for meth twice weekly	Post-intervention CM group more likely to have meth + urine though not statistically significant (aRR = 1.21; 95% CI: 0.95, 1.54, $p=0.11$)
6. Mimiaga, 2010[72a]	10 meth-dependent MSM. HIV uninfected	After 3 months, participants had less unprotected anal intercourse, less meth use, decreased number of sexual partners while using meth, and less depressive symptoms
Prospective pilot study assessing effect of Behavioral Activation Therapy (BAT) in 10 individuals. Individuals received 10 sessions of BAT and were followed up at 3 months	Self-reported sexual risk taking, meth use, and depression	
7. Peck, 2005[64]	162 MSM with meth dependence; 60% HIV infected	All participants in treatment groups had significant reduction in meth use and depression scores over 52 weeks of follow up, regardless of treatment group or HIV status. Meth use for up to 5 days prior to BDI score, had a strong association with depression ($p<0.0001$). Whereas, BDI scores had no association with subsequent meth use
Randomized controlled trial where participants are randomly assigned to CBT, CM, CBT + CM, Gay specific CBT, or placebo for 16 weeks	Self-reported meth use plus urine drug screens 3 times per week. Assessed depression weekly via Beck Depression Inventory, compared to baseline at enrollment	

(*continued*)

Table 3. (Continued)

Author, year (reference) *Study design*	*Sample measures*	*Summary of findings*
8. Rawson, 2004[61a] Randomized controlled trial comparing Matrix Model to treatment as usual over a course of 16 weeks	978 meth-dependent men and women; did not report # of MSM or HIV-infected participants Assessed session attendance and meth use via weekly urine drug screens	Those assigned to the Matrix treatment attended more sessions, stayed in treatment longer, provided more meth-free urine samples, and had longer periods of abstinence from meth. Effect was lost at follow-up
9. Rawson, 2006[70a] Randomized clinical trial comparing CM vs. CBT vs. combined CM/CBT over the course of 16 weeks	177 stimulant users (90% cocaine and 10% meth); did not report # of MSM or HIV-infected participants Stimulant use tested via urine samples 3 times per week	CM procedures (CM or CM/CBT) produced better retention and lower rates of stimulant use than CBT alone. No additive effect when the two treatments were combined. Self-reported stimulant use was reduced from baseline levels at all follow-up points, however differences between groups were lost
10. Reback, 2004[65] Randomized controlled trial, CBT, CM, CBT+CM, gay-specific CBT with qualitative interviews before and after interventions	162 MSM in treatment for meth abuse; 60% HIV-infected Urine drug screens 2 times weekly. Sexual risk behavior assessed at baseline, posttreatment at 16 weeks, 6 months, and 1 year follow-up	Before treatment: Avg 8.6 partners in the past 30 days. After treatment: Avg 2.9 partners in the past 30 days. After treatment: Less UAI, and increased sense of responsibility to disclose HIV status. At 1-year evaluations, associated behaviors of meth use and sexual risk behaviors were lessened
11. Reback, 2010[66] Randomized controlled trial of CM vs. placebo over 24 weeks	131 homeless, substance-dependent MSM; 63% meth-dependent; 28% HIV-infected Measured reductions in alcohol use, stimulant use, and meth use and health-promoting behaviors. Meth use assessed via urine samples	Those who participated in CM had greater reductions in meth use than those who did not and increased healthy behaviors. Reductions in meth use maintained over 12 month follow up period
12. Roll, 2006[67a] Randomized controlled trial comparing CM+CBT vs. CBT alone over 12 weeks	113 meth-dependent men and women; did not report # of MSM or HIV-infected participants Urine drug screens 2 times per week	Participants of CM+CBT group had significantly more negative urine samples and were abstinent for a longer period of time compared to those who only received CBT
13. Shoptaw, 2008[57a] Double-blinded randomized controlled trial comparing bupropion vs. placebo for treatment of meth dependence	73 meth-dependent men and women; did not report # of MSM or HIV-infected participants Urine samples tested for meth 3 times per week over 12 weeks	Bupropion was no more effective than placebo in meth-free urine samples, retention, drug cravings, and depressive symptoms
14. Shoptaw, 2006[58a] Double-blinded randomized controlled trial comparing sertraline vs. placebo for treatment of meth dependence	229 meth-dependent individuals; did not report # of MSM or HIV-infected participants Urine samples tested for meth 3 times weekly over 12 weeks. Retention, drug cravings, depressive symptoms were measured via observation and self-report	Sertraline was no more effective than placebo in meth-free urine samples, retention, drug cravings, or depressive symptoms. Sertraline resulted in significantly more adverse events compared to placebo (nausea, GI, sexual side effects)

(*continued*)

Table 3. (Continued)

Author, year (reference) *Study design*	*Sample measures*	*Summary of findings*
15. Shoptaw, 2006[68] Prospective cohort to implement CM over 12 weeks	111 meth-using MSM in San Francisco, CA; 77% HIV-infected Urine tested for meth three times per week	30% retention at the end of 12 weeks. Average of 5 weeks of negative urine samples. 52% achieved meth-free urine samples at 4 weeks, 17% had meth-free urine samples at 8 weeks, and 8% had meth-free urine samples at 12 weeks
16. Shoptaw, 2005[69] Randomized controlled trial comparing (1) CBT (2) CM (3) CBT+CM (4) culturally tailored CBT over 16 weeks	162 meth-dependent gay and bisexual men in Los Angeles; 60% HIV-infected. Urine drug screens three times weekly, and sexual risk behaviors monthly over 16 weeks. Follow-up assessments at 12 months	CM and CBT+CM showed better retention and more consecutive negative urine samples for meth. Culturally-tailored CBT significantly reduced unprotected receptive anal intercourse after 4 weeks ($\chi^2=6.75$; $p<0.01$). At 1-year follow-up, these differences were no longer apparent

[a]Mixed sample (e.g., not MSM and/or HIV-uninfected).
CM, contingency management; CBT, cognitive behavioral therapy; UAI, unprotected anal intercourse; BDI, Beck Depression Inventory; MSM, men who have sex with men; aRR, adjusted relative risk; GI, gastrointestinal.

meth dependence in a sample of HIV-infected MSM. In a small single blinded study, McElhiney and colleagues[59] tested the efficacy of modafinil combined with cognitive behavioral therapy (CBT), a psychotherapy often used to prevent substance use relapse. Among the 10 who completed treatment, 6 reduced their crystal meth use by more than 50%; however, the study was underpowered to draw any meaningful conclusions. The trial also lacked a control group, so it is not possible to determine whether preliminary efficacy was the result of modafinil or the behavioral therapy.

Given the lack of effective pharmacologic treatments, researchers have studied the effects of behavioral interventions such as CBT in treating crystal meth dependence, yet minimal research has been conducted in HIV-infected MSM specifically. CBT approaches for substance dependence target the motivations for use, and aid dependent persons in developing behavioral and cognitive skills to abstain and prevent relapse. While many variations of CBT exist, the fundamental elements include understanding the internal triggers (e.g., cravings, depression, anxiety) and external triggers (e.g., exposure to drug using environment) of drug use, and developing coping skills to aid individuals in overcoming theses triggers.[60] A randomized controlled trial of 978 crystal meth-dependent men and women in treatment tested the efficacy of the "Matrix Model" compared to treatment as usual (TAU; the treatment participants were already receiving) over the course of 16 weeks.[61] The Matrix Model consisted of intensive CBT (36 sessions), social support groups (4 sessions), family education (12 sessions), and individual counseling (4 sessions). While both groups had more crystal meth-free urine samples at the end of treatment, at 6-month follow-up the Matrix group attended more clinical sessions, stayed in treatment longer, produced more drug-free urine samples, and had longer periods of abstinence during treatment than the TAU group. However, significant differences between the Matrix and the TAU groups were lost postintervention. Moreover, the study was conducted in a mixed sample of HIV-infected and uninfected crystal meth users and did not demonstrate efficacy in crystal meth-dependent MSM specifically.

Only one treatment study has focused on the *HIV-infected* crystal meth-dependent MSM population, and the outcome of this study was a reduction in high-risk behaviors, not a reduction in crystal meth use. This randomized controlled trial was conducted in a group of 341 HIV-infected MSM who had used crystal meth in the prior 2 months, and compared safe-sex behavioral counseling versus diet and exercise counseling as a control.[62] Participants in both arms received eight 90-min sessions of individual therapy, during which time counseling took place. The intervention arm received training in condom use, safer sex practices in the context of crystal meth use, disclosure of HIV status to partners, and enhancement of positive social supports. The modes of education during these sessions included observation, role modeling, motivational interviewing, and rehearsing various scenarios. Primary outcomes included the total number of protected sex acts and the total number of unprotected sex acts. At 12-month follow-up those randomized to the safe-sex behavioral intervention reported significantly more protected sex acts compared to the control group (25.8% versus 18.7%, $p=0.038$).

Contingency management (CM) interventions have also been used to treat crystal meth abuse[63–69]; however, there is conflicting evidence regarding CM's efficacy. CM is a psychotherapy that provides rewards (e.g., cash or vouchers exchangeable for goods) for the achievement of specific treatment goals (e.g., abstinence from drug use or treatment session attendance). CM is grounded on the principles of operant conditioning, which posits that individuals are more likely to repeat behaviors that are followed by positive outcomes. In response to increases in crystal meth-related STIs and HIV infection among MSM, the San Francisco Department of Public Health established a CM field program for crystal meth-using MSM.[68] Of the 143 participants who enrolled at baseline, 77% were HIV-infected and 111 returned to participate in the 12-week CM treatment program. Participants were drug tested via

urine samples 3 times per week. Participants with a crystal meth-free urine sample received a voucher that could be exchanged for goods and services that promoted a healthy, drug-free lifestyle. During the 12-week study period, 52% of participants had 12 crystal meth-free urine samples, 17% had 24 crystal meth-free samples, and only 8% had 36 crystal meth-free samples. On average, participants produced 15 of 36 (42%) crystal meth-free urine samples over the course of the study. In a similar study, CM was implemented in a community HIV prevention setting in a sample of 131 homeless, substance-dependent MSM (28% HIV-infected).[66] Over the course of the 24-week intervention, both the control and the CM group received points for participating in HIV adherence activities. However, the CM arm also received points for crystal meth abstinence and health-promoting behaviors. Health-promoting behaviors included making appointments with health care providers and social workers, enrolling in educational programs, and getting and keeping a job. Points could be redeemed for goods at an onsite store. Goods most purchased were gift cards for grocery stores and restaurants. At the completion of the study, the CM group reported significantly more healthy behaviors and less crystal meth use (69% crystal meth-free urine versus 48%, $p < 0.05$) compared to the control group. Reductions in substance use were maintained at 9- and 12-month postintervention follow-up.

Contrary to the efficacy seen in the previously reported studies, a recent randomized controlled trial of 127 crystal meth-dependent MSM (55% HIV-infected) in Seattle, WA did not show significant differences between the CM intervention and the control (referral to community resources) in reducing crystal meth use.[63] The CM intervention was implemented over a 12-week period, and vouchers were provided for consecutive drug-free urine samples. Vouchers were redeemable for gift cards, goods, and services. The primary outcome was serodiscordant UAI in the prior 6 weeks. Secondary outcomes included crystal meth-free urine samples, self-reported crystal meth use, and number of serodiscordant partners. Comparing consecutive study visits, non-concordant UAI declined significantly in both study arms, with no significant differences seen between groups. Both groups were likely to provide crystal meth positive urine samples during the intervention. However, the CM group was slightly more likely to provide urine samples containing crystal meth post-intervention. Findings suggest that crystal meth dependent MSM may not benefit from stand alone CM interventions conducted outside of drug treatment.

Research comparing the efficacy of CM to CBT has been conducted among mixed samples of crystal meth users, although no trials to-date explore these interventions in an exclusively HIV-infected sample of MSM. In a randomized controlled trial of 113 crystal meth-abusing or crystal meth-dependent participants, Roll et al.[67] compared the efficacy of treatment as usual (CBT control group) to treatment as usual plus CM (CM + CBT) over the course of 12 weeks. Participants were recruited from treatment clinics where participants were receiving some form of CBT therapy (e.g., the Matrix Model). The proportion of HIV-infected MSM in the sample was not commented on in this study. Those randomly assigned to the CM plus treatment as usual arm received plastic chips for every drug-free urine sample provided. These chips could be exchanged for goods and services. After 12 weeks of treatment, those in the CM + CBT group had significantly more drug free urine samples and a longer period of abstinence compared to the CBT (treatment as usual) group. Similarly, a randomized clinical trial comparing CM to CBT to CM + CBT combined was conducted in a sample of stimulant users (90% cocaine users; 10% crystal meth users) over the course of 16 weeks.[70] The study did not report the number of HIV-infected or MSM participants in the sample. Stimulant use was tested three times per week via urine samples. The CM group could win vouchers for crystal meth-free urine samples worth up to $1200 over the course of the study. The CBT group received group sessions three times per week and the combined CM + CBT group received both the sessions and the vouchers. Reductions in stimulant use were observed for all groups. However, the CM groups (CM or CM + CBT) produced significantly greater retention and stimulant use reductions. At follow-up, reduced stimulant use was still observed, although differences between groups were lost. Another randomized controlled trial of 162 crystal meth-dependent MSM (60% HIV-infected), compared 4 combination treatments over the course of 16 weeks: (1) CBT alone, (2) CM alone, (3) CBT + CM, and (4) GCBT, a culturally tailored intervention for gay and bisexual crystal meth-dependent men.[41,64,65,69,71] Those assigned to CBT Matrix Model met three times per week for a group session, which provided education on drug use triggers, stages of recovery, and coping strategies to avoid specific triggers. The CM group received vouchers for each drug-free urine sample, and could exchange these vouchers for goods and services. On average, participants earned $415. Participants in the CM + CBT arm received all elements of the CM and CBT interventions. The GCBT arm integrated core components of the CBT intervention with the goal of reducing HIV-related risk behaviors. Results from the study were provided across multiple articles.[41,64,65,69,71] Shoptaw et al.[69] reported on several crystal meth-specific outcomes and found that the groups containing the CM intervention (CM only and CM + CBT) demonstrated the most crystal meth-free urine samples, increased treatment retention, increased treatment effectiveness scores, and fewer missed urine screens. In addition, the GCBT group demonstrated the fastest reduction rate in reported unprotected receptive anal sex during treatment compared to the CBT only group. Reductions in crystal meth use and HIV risk behavior were sustained at 1-year postintervention follow-up. Jaffe et al.[71] reported on crystal meth use reduction rates, indicating that the GCBT group showed the greatest rate of decline in crystal meth use compared to other groups.

New behavioral therapies, such as behavioral activation therapy (BAT) are also being explored in the treatment of crystal meth dependence. BAT is an evidence-based treatment for improving mood and increasing activity. BAT involves gradually learning how to reengage in life by identifying and actively engaging in pleasurable activities. A recent pilot study provided HIV-uninfected, crystal meth-using MSM with 10 sessions of BAT alongside HIV risk reduction counseling in order to reduce HIV-related risk behaviors and crystal meth.[72] At 3-month follow-up there was significant reduction in UAI, crystal meth use, and depressive symptoms. While results are promising, this potential intervention requires more rigorous testing in the context of a randomized controlled trial.

Discussion

HIV-infected, MSM who use crystal meth are a unique population. They are more likely to have high risk sexual

behaviors, STIs, and serodiscordant UAI compared to HIV-infected MSM who do not use crystal meth, and also relative to HIV-uninfected, crystal meth-using MSM. Their reasons for use may in part relate to their HIV diagnosis, whether they use crystal meth for sexual enhancement, to escape social isolation, or to feel more physically energetic. Medication adherence in this population is also notably low, which may contribute to the transmission of resistant virus that has been seen in newly infected MSM who use crystal meth. Given the lack of effective treatment options, providers may not have the tools to adequately address this issue, especially in the primary care setting.

The treatment studies, although well-designed, have failed to show a sustained impact in decreasing crystal meth use; no medications have proven effective in this population. A phase 2 clinical trial is currently underway evaluating the role of extended release naltrexone (Vivitrol®, Alkermes, Waltham, MA) in crystal meth-dependent individuals.[73] Early animal models suggest that there may be a role of varenicline (Chantix®, Pfizer, New York, NY) in the treatment of crystal meth abuse.[74] Meanwhile, the role of behavioral therapies is still in question. Some studies have demonstrated the potential benefit of contingency management for the treatment of crystal meth dependence. However, key limitations of CM include failure of the intervention to adequately address participants' mental health needs or work with participants to develop relapse prevention plans postintervention. Interventions testing the efficacy of CM alongside other therapies such as CBT have proven modestly effective in reducing crystal meth dependence,[61,66–68] however, these have not been routinely adopted into clinical practice due to cost[75] and required infrastructure. Some studies have focused on decreasing UAI as the primary outcome. Reducing UAI is not only meaningful in reducing transmission of resistant HIV, but also has been easier to achieve in prior studies as opposed to reductions in crystal meth use.

When looking at these treatment studies it is important to recognize that many behavioral therapy trials were not exclusively in an HIV-infected MSM population.[56–58,61,67,70] The HIV-infected population may have different relationships with medical providers and variable attitudes regarding adherence and healthy behaviors compared to the HIV-uninfected population. Thus, their response to behavioral counseling and treatment may be different than those that are uninfected. When focusing on HIV-infected individuals, poor health-related outcomes such as increased viral loads, increased transmission or resistant HIV, and decreased CD4 counts must be emphasized. Future studies that focus on behavioral interventions for HIV-infected individuals will need to explore these motivators in more detail.

The limitations of the current review mostly pertain to the methodological quality of the available studies. Many studies regarding risk behavior and adherence were cross-sectional or retrospective studies. Thus, causation cannot truly be determined. Furthermore, substance use, medication adherence, and sexual behaviors were often determined through self-report rather than more objective means such as toxicology screens and STI testing. Only one study used MEMS caps as a reliable marker of adherence.[53] Given the sensitive nature of these behaviors, participants may have under-reported their sexual and crystal meth-using behaviors.

Finally, there is much geographic variation in patterns of crystal meth use. Many studies in this review were performed in California, although some in Seattle and other locations. As a result, it may be difficult to generalize or apply them to different geographic regions. We limited our search to English-language studies based in the United States to account for this geographic variation, which would likely have been even more prominent international studies were included.

The treatment of HIV-infected MSM who use crystal meth must remain a priority among health care providers. By reducing crystal meth use, we can have an impact on individual HIV-related outcomes, and subsequently reduce HIV transmission rates on a population level. At this time, there is no clear treatment guidance regarding the best ways to reduce crystal meth use. As such, we must continue with research efforts that develop and test novel strategies. In the short term, however, the available data suggest that we continue to focus our efforts on decreasing high-risk behaviors in this population. Furthermore, among providers, it is critical that we continue to assess our patients' substance use. Even though there are no clear treatment options, adherence, risk reduction counseling, and linkage to care should remain an important focus in caring for this vulnerable population.

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