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Housing Status and the Health of People Living with HIV/AIDS

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Abstract

Individuals who are homeless or living in marginal conditions have an elevated burden of infection with HIV. Existing research suggests the HIV/AIDS pandemic in resource-rich settings is increasingly concentrated among members of vulnerable and marginalized populations, including homeless/marginally-housed individuals, who have yet to benefit fully from recent advances in highly-active antiretroviral therapy (HAART). We reviewed the scientific evidence investigating the relationships between inferior housing and the health status, HAART access and adherence and HIV treatment outcomes of people living with HIV/AIDS (PLWHA.) Studies indicate being homeless/marginally-housed is common among PLWHA and associated with poorer levels of HAART access and sub-optimal treatment outcomes. Among homeless/marginally-housed PLWHA, determinants of poorer HAART access/adherence or treatment outcomes include depression, illicit drug use and medication insurance status. Future research should consider possible social- and structural-level determinants of HAART access and HV treatment outcomes that have been shown to increase vulnerability to HIV infection among homeless/marginally-housed individuals. As evidence indicates homeless/marginally-housed PLWHA with adequate levels of adherence can benefit from HAART at similar rates to housed PLWHA, and given the individual and community benefits of expanding HAART use, interventions to identify HIV-seropositive homeless/marginally-housed individuals and engage them in HIV care including comprehensive support for HAART adherence are urgently needed.

Keywords

HIV/AIDS; antiretroviral therapy; homelessness; People Living with HIV/AIDS (PLWHA); adherence; CD4+; plasma; HIV-1; RNA; viral load; highly-active antiretroviral therapy (HAART); behavior aspects of HIV/AIDS

INTRODUCTION

Individuals who are homeless, living in marginal conditions or lacking permanent access to safe, secure and private personal space suffer from a substantial burden of mental illness, physical disease and disability (1,2). Studies of homeless individuals, typically from urban settings in North America, have identified elevated levels of morbidity and mortality

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resulting from proximate conditions and exposures including psychosis, schizophrenia, depression and other affective disorders (1,3); cutaneous, respiratory and blood-borne infections (4–7); use of tobacco, alcohol and illicit drugs, often by injection (3,8,9); and abuse, accidents and violence (10,11). Although suffering from high rates of chronic and acute disease, homeless individuals have inferior contact with the healthcare system (12), and typically experience low rates of preventative and ambulatory care, while accounting for high levels of urgent care (13,14). In the United States, the most recent government estimates suggest 1 in 200 individuals, approximately 650,000 individuals, were sheltered or unsheltered homeless at any time in 2009 (15).

Strongly linked to poorer health status, homelessness has long been recognized as an important contributor of vulnerability to HIV infection (6,16–18). Seroprevalence of HIV in homeless/marginally-housed populations is estimated to range from 10 to 20%, or typically five to ten times higher than among housed populations (18). Although both sexual- and injection-related risk have been reported in studies among homeless/marginally-housed individuals, elevated HIV seroprevalence is driven by exposures less experienced by housed individuals, including engagement in the survival sex trade, incarceration, and poor access to health and HIV preventive services (19–22). Among individuals who use illicit drugs, being homeless/marginally-housed has been identified as independently associated with a shorter time to HIV seroconversion (17).

Although advances in the development and distribution of highly-active antiretroviral therapy (HAART) for HIV infection have resulted in substantial declines in HIV/AIDS-related morbidity and mortality in most regions of the globe (23,24), not all seropositive groups have benefitted equally from HIV treatment. There is a persistent and growing gap in HIV treatment outcomes even in well-resourced areas with access to antiretroviral medications (25). In many of these settings, the HIV/AIDS epidemic is increasingly entrenched among individuals belonging to interrelated marginalized communities including but not limited to illicit drug users, ethnic and racial minorities, sex trade workers, prisoners and the urban indigent (26). In light of the extreme HIV-related health inequalities experienced by homeless/marginally-housed individuals (6,27), this narrative review aims to synthesize the evidence, primarily from a North American context, examining the relationships between housing status and the health, HAART adherence patterns and HIV treatment outcomes of people living with HIV/AIDS (PLWHA.)

SEARCH STRATEGY AND SELECTION CRITERIA

For this review, we identified and reviewed published studies from the indices of major academic databases (MEDLINE [via Pubmed], Science Citation Index [via Web of Science], Cochrane CENTRAL and Google Scholar) with no language or date specified in the search criteria. Key words used included HIV, AIDS, homeless, unstably housed, HAART; additional strategies were identified by examining citation lists from relevant articles.

HOUSING STATUS AMONG PLWHA AND RECEIPT OF HIV CARE

A substantial proportion of participants in many studies of PLWHA report outright homelessness or routinely living in marginal residential situations, including shelters and single-room occupancy (SRO) hotel rooms (12,28). In a representative sample of PLWHA in New York City, 33% were homeless/marginally-housed with 18% in unstable, temporary or transitional housing at the baseline interview and 15% homeless, defined as sleeping in the street, in a shelter, jail or halfway house (12). Further, 70% of participants reported some sort of housing need during the study, including being homeless or marginally housed, unable to pay rent, facing eviction or living in a situation marked by physical danger or violence (12). In a large behavioral surveillance survey of over 7,900 PLWHA from 19 sites

in the United States, 4% were living on the streets or in a shelter at the time of interview (28), a prevalence likely underestimated given the large number of eligible individuals unable to be contacted for recruitment.

Poorer housing status is linked to worse health status in a wealth of studies involving PLWHA (12,29–36). In a multi-site study in the United States, a significantly larger proportion of homeless individuals had CD4+ cell counts below 200 cells/mL (43% vs. 32%, p-value < 0.001) and detectable plasma HIV-1 RNA viral loads (PVL) (65% v 51%, p-value < 0.001) compared to non-homeless participants (32). This is in line with other studies that have found higher levels of unsuppressed PVL among homeless individuals (33,35,37). In a recent study among over 11,000 PLWHA individuals enrolled in a publicly-funded HIV care programme in Los Angeles County, 13% reported non-permanent housing or homelessness (35). In crude analyses, these individuals had a significantly elevated likelihood of unsuppressed PVL (Odds Ratio [OR] = 1.72, p-value < 0.001), however this association was rendered non-significant in a multivariate model adjusted for other factors including illicit drug use, income and incarceration. In addition to morbidity, homelessness has also been linked to higher rates of mortality among PLWHA (36,38–40). For example, in a case-control analysis of 129 deceased patients and 240 randomly selected patients at a public health HIV clinic in Florida, homeless individuals had almost ten times higher odds of death compared to those who were stably housed (Adjusted Odds Ratio [AOR] = 9.98, p-value < 0.01) (40).

Although some specific findings have differed (41,42), studies of healthcare access and utilization among PLWHA (30,43,44) have generally found that poorer housing status is correlated with not receiving optimal HIV care (12). In a representative sample of 1661 PLWHA in New York City, housing need was independently associated with lower likelihoods of receipt of appropriate HIV medical care and entry into any medical care (12). At the same time, individuals who received assistance with housing needs had significantly higher odds of receipt of any medical care for HIV, receipt of appropriate HIV medical care, entry into any medical care and entry into appropriate HIV care in separate multivariate models (12). Similarly, in a study of 333 PLWHA in Los Angeles county, the strongest factor independently associated with having any unmet needs was homelessness in the previous twelve months (AOR = 2.3, 95% Confidence Interval [CI]: 1.1 – 6.1) (45). In addition, studies of risk factors associated with seroconversion among homeless/marginally-housed individuals suggest that there are a number of barriers to identifying newly-infected individuals and engaging and retaining them in care, including high-intensity drug use, recent release from the correctional system and participation in the sex trade (17,46). Homelessness has also been linked to lower levels of exposure to ART (28,31,47) and poorer adherence patterns among persons who do initiate therapy (30,33,48). For example, a recent study conducted among 743 HIV-positive prisoners at ten sites in the United States (30) found that individuals homeless prior to arrest were less likely to have an HIV care provider or be exposed to ART compared to non-homeless prisoners. Among those ART-exposed, homeless persons were less likely to be optimally adherent in the seven days prior to incarceration (30).

Among HIV-seropositive individuals who use illicit drugs, recent studies have highlighted the important role of housing on uptake and adherence to HAART (31,33,34,47). In a recent study among 807 active injection drug users (IDU) in a multi-site study in the United States assessing the individual, social and structural factors associated with HAART uptake, stable housing was associated with being on HAART after adjustment for education, age, illicit drug use, disease progression, health care insurance and engagement in HIV primary care (47). Similarly, homelessness was an independent barrier to being on HAART in a study of 350 hospitalized crack cocaine-using individuals in Miami and Atlanta (31). Homelessness

was also identified as a barrier to effective HIV treatment among 247 illicit drug users beginning HAART in British Columbia, Canada, a setting with universal access to HIV care including medications (33). In a multivariate survival model, homelessness was independently associated with lower rates of PVL suppression following ART initiation (AHR = 0.60, *p*-value = 0.003) (33), although this relationship was mediated by lower adherence to ART. In another study from the same observational cohort, homelessness was independently associated with lower levels of ART adherence in a model adjusted for heroin use, engagement in methadone maintenance therapy, and disease progression (34).

DETERMINANTS OF HIV-RELATED HEALTH AMONG HOMELESS/ MARGINALLY-HOUSED PLWHA

Despite the substantial levels of HIV/AIDS-related morbidity and mortality among homeless/marginally-housed PLWHA (35,49), there has been limited inquiry into the determinants of sub-optimal HIV treatment outcomes among this population. Table 1 presents a summary of relevant studies of health status, ART adherence and HIV treatment outcomes among homeless/marginally-housed PLWHA; Table 2 presents summaries of studies evaluating interventions aimed at improving the health of homeless/marginally-housed PLWHA; Table 3 contains a summary of barriers and facilitators of ART adherence.

As with a number of vulnerable groups at the beginning of the HAART era, concerns over possible non-adherence to medication led some to suggest combination therapy would be ineffective and drug-resistant viral subtypes would be generated (50). However, subsequent investigations have demonstrated that homeless individuals can benefit equally from ART given adequate levels of adherence to treatment (51). Among homeless PLWHA, a number of behavioral factors have been associated with lower levels of adherence to HIV treatment (52,53). In 2004, Moss and colleagues published the first observational study of adherence among a community-recruited group of homeless or marginally-housed PLWHA (52). The Research in Access to Care in the Homeless (REACH) cohort in San Francisco, California, is a representative sample of individuals from shelters, free meal programmes and SRO hotels in the impoverished Tenderloin district (52). Of 148 ART-exposed individuals included in the analysis of adherence, 46 (31%) discontinued treatment during the study. In a multivariate survival analysis of time to discontinuation, current IDU and individuals of African-American ethnicity exhibited significantly faster rates of discontinuation. Among those who did not discontinue, lower mean adherence was associated with crack cocaine use and African-American ethnicity. The association of illicit drug use on poorer adherence was echoed in a recent report from a study involving 602 homeless/marginally-housed PLWHA in Baltimore, Maryland; Chicago, Illinois and Los Angeles, California (53). In adjusted analyses, marijuana users (AOR = 2.08), crack cocaine users (AOR = 2.09) and alcohol users (AOR = 2.98) had elevated levels of self-reported non-adherence in the previous two days (53). More recently, two studies have identified how structural factors, specifically access to health insurance, is linked to ART exposure and adherence (54,55). Using a marginal structural modeling approach to account for selection effects associated with the exposure, Riley and colleagues found that among homeless/marginally-housed PLWHA, possessing both intermittent and continuous health insurance was associated with greater odds of receiving ambulatory care and exposure to ART compared to those who were uninsured (55). Further, changes to health insurance regulations, specifically increases in medication cost-sharing, were associated with self-reported ART interruptions (AOR = 7.50, *p*-value < 0.01) (54).

Depression, a common barrier to adherence among PLWHA, has also been associated with poorer health status and HIV treatment outcomes among homeless/marginally-housed PLWHA (56,57). In a study among homeless/marginally-housed PLWHA in San Francisco,

California, a validated measure of depression was independently associated with lower scores on every domain of the Short Form (SF)-36, a validated measure of physical and mental health status. In a related study, more half of the homeless/marginally-housed participants in the REACH cohort were found to be depressed, with a higher likelihood of depression among individuals of Caucasian race and those reporting more than 14 alcoholic drinks in the last week (56).

Two recent analyses of data from the REACH cohort (58,59) used marginal structural modeling and targeted variable importance approaches to estimate a ranked list of factors associated with overall physical and mental health. Among 129 homeless/marginally-housed HIV-seropositive women, unmet subsistence needs were found to have the largest effect on overall mental health, as measured by changes in SF-36 scores; crack use was found to have the largest effect on overall physical health (58). Unmet subsistence needs were estimated to have the largest effects on both overall mental and physical scores in an analysis of the SF-36 scores of 288 homeless/marginally-housed HIV-seropositive men (59).

INTERVENTIONS FOCUSED ON HOMELESS/MARGINALLY-HOUSED PLWHA

Interventions evaluated to improve the health, HAART adherence and HIV treatment outcomes of homeless/marginally-housed PLWHA include: individual-focused pharmacologic programmes (60,61); supportive housing and case management (62); housing assistance (28,63); directly-observed therapy (DOT) (64); outreach and case management (65); and a housing-first harm reduction-based programme (66). Among interventions evaluated using random assignment (28,62,63), modest (62) or no (63) effects on HIV-related measures were observed. In a trial of immediate rental assistance versus standard care involving 630 homeless and unstably housed PLWHA, no differences were seen after 18 months on the proportion exposed or adherent to HAART or with detectable viral load or CD4+ cell count above 200 cells (63). Although the authors suggest that the substantial decline in homelessness and unstable housing among the comparison group limited power in their intent-to-treat analyses, significant differences were seen in levels of depression and overall physical health (63). In a trial of immediate housing and intensive case management, a significantly greater proportion of individuals in the intervention arm reached the primary endpoint of survival with intact immunity (CD4+ $\geq$ 200 cells and PVL < 100,000) at 12 months (62). This difference was largely driven by differences in immunologic response as there were no significant differences in mortality or PVL between the two arms (62). More recently, two studies have investigated the impact of harm reduction-based approaches on HAART adherence (64) and viral loads among groups of homeless/marginally-housed PLWHA with a substantial proportion of illicit drug users. In Vancouver, British Columbia, engagement in a DOT-like programme was associated with higher odds of optimal HAART adherence (AOR = 4.76, p-value = 0.003) among unstably-housed individuals in the provincial HIV treatment registry (64). In Pittsburgh, Pennsylvania, a case study of 26 residents of a harm reduction-based housing service found that 69% achieved undetectable viral load. While both results are impressive, the findings should be considered in light of the lack of a comparison group, in one case (66), or adjustment for non-random assignment to the intervention in the other (64).

CONCLUSION

The evidence reviewed here indicates inferior housing status is a pervasive experience for PLWHA and is strongly correlated with lower rates of appropriate HIV care, access and adherence to HAART and optimal HIV treatment outcomes. However, the specific causal pathways from homelessness to HAART adherence and treatment outcomes are unclear.

Also unresolved is the relative contribution of homelessness and how it mediates more distal exposures. To date, research has focused on proximate individual-level behavioural and psychological determinants of HAART adherence and HIV treatment outcomes, such as depression and illicit drug use. While the management of PLWHA with co-occurring disorders including mental health comorbidities and active illicit drug use is complex (67), a growing collection of scientific evidence indicates that social- and structural-level exposures exacerbate these problems and further undermine HAART adherence and HIV treatment outcomes among members of vulnerable and marginalized populations (68–70). For example, among illicit drug users, the criminalization of drug use and resulting exposure to the criminal justice and correctional system has been shown to be strongly associated with HAART adherence independent of individual-level factors including drug use itself (71). Among homeless/marginally-housed PLWHA, the relationships of these social- and structural-level factors to HAART adherence and HIV treatment outcomes remain poorly understood and require further evaluation. Findings from the REACH study in San Francisco have provided initial indications of how changes to publicly-funded HIV care programmes have helped determine patterns of HAART access and adherence (54,55). Emerging research also suggests that, at least among HIV-seropositive illicit drug users, factors that contribute to vulnerability to HIV infection also play a role in blunting the effectiveness of HAART (69,72). Thus, future research could investigate how prevalent social- and structural-level exposures previously linked to HIV vulnerability among homeless/marginally-housed PLWHA, including engagement in the survival sex trade (73,74), incarceration (20,75), antecedent sexual and physical abuse (20) and low socioeconomic position (21), drive poorer HIV treatment outcomes.

Recent studies involving injection drug users (76) and HIV-serodiscordant couples (77) have revealed the important influence of plasma HIV-1 RNA viral load, at both the individual and community levels, on HIV transmission patterns. Confirming the potential of HIV treatment to prevent new infections, these studies have sparked new interventions designed to seek out individuals at risk, test them for infection and engage and retain them in evidence-based medical care including HAART. To date, the effect of so-called seek, test, treat and retain (STTR) strategies has not been specifically evaluated among homeless/marginally-housed individuals. Clearly there are steep barriers to implementing an STTR strategy among homeless/marginally-housed individuals. These including the competing needs of homeless/marginally-housed individuals, a high prevalence of co-occurring mental and physical disorders, suboptimal contact with the healthcare system and, finally, limited public funds, in many jurisdictions, for HIV care for members of marginalized populations. However, more than a decade since a high-profile review argued in favour of not denying homeless individuals access to then-novel protease inhibitors (50), studies have demonstrated that homeless/marginally-housed individuals can benefit from HAART given adequate levels of adherence to treatment (33,78). Thus, to reduce elevated levels of preventable HIV/AIDS-related morbidity and mortality and to address secondary HIV transmission from homeless/marginally-housed PLWHA to their sexual and drug-using partners, interventions to identify HIV-seropositive individuals and engage them in care including HAART adherence support should be piloted immediately. As previous interventions have demonstrated modest effects on HAART adherence and HIV treatment outcomes, comprehensive programmes including directly-observed treatment delivered free-of-charge within a housing-first and harm reduction environment may be most effective.

There are various limitations of this review to consider. First, no standard definition of housing status was used by all studies included in the review. Some studies focused on outright homelessness while others involved those who lived in unstable conditions, such as single-room occupancy hotels and shelters. In order to best investigate the relationships of housing status on the health of PLWHA, all relevant studies were included. Details of the

definition of housing status have been included in all cases where relevant. Second, although the impact of socioeconomic status is seen in all aspects of the global HIV/AIDS pandemic, our review has focused on the impact of housing status in North America. In addition, a substantial proportion of the research has been generated by the REACH cohort in San Francisco, California. However, the study is a large and longitudinal observational cohort recruited using rigorous sampling techniques that is believed to be representative of the homeless/marginally-housed population the area. Finally, there are some methodologic issues and limitations common to many studies, including difficulty retaining homeless/marginally-housed individuals in intervention studies, the impossibility of conducting blinded studies and need to allow for cross-over. Future research should endeavor to employ developing statistical modeling techniques, including marginal structural causal models, to address these weaknesses.

To conclude, we reviewed the scientific evidence on the relationship of housing status on the health status, HAART adherence and HIV treatment outcomes of PLWHA. Inferior housing, including homelessness and living in marginal conditions, is common among PLWHA and strongly associated with poorer health, lower rates of exposure and adherence to HAART and sub-optimal HIV treatment outcomes. However, the barriers to HAART access and adherence still have yet to be completely described and the impact of social- and structural-level exposures has not been well evaluated. Although future research should address these uncertainties, there is a clear need to immediately implement innovative and comprehensive HIV treatment interventions realize the public health benefits of HAART as well as address the substantial HIV-related health disparities among homeless/marginally-housed PLWHA.

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TABLE 1

Factors associated with health status, HIV treatment outcomes or ART adherence among homeless/marginally-housed PLWHA

HEALTH STATUS					
Study	**Setting**	**Sample**	**Analysis**	**Outcome**	**Significant associations**
Riley et al., 2003 (57)	San Francisco, California, USA. July 1996 to December 1997 and January 1999 to May 2000	330 respondents (83% male, 43% African-American) in representative sample of homeless and marginally housed individuals (HMH)	Multivariate linear regression of cross-sectional survey data	Score on SF-36, a self-reported generic measure of health status, ranging from 0 to 100. Mean physical health composite score = 44; mental health composite score = 43	Independent negative associations between depression, injection drug use and female gender in multiple areas of physical and mental health status
Weiser et al., 2006 (56)	San Francisco, California, USA. June 1999 to October 2000	239 HMH respondents (43% Caucasian, mean age 41.6 years, > 75% history of illicit drug use, 74% history of incarceration	Multivariate logistic regression of cross-sectional survey data	Beck Depression Inventory score > 13, indicating mild-to-moderate or severe depression. 101 (42%) mild-to-moderate, 33 (14%) severe	Caucasian race (Adjusted Odds Ratio [AOR] = 2.22); having a representative payee (OR 2.37); missed medical appointments within 90 days (AOR 2.57); heavy alcohol consumption (> 14 drinks/week) (AOR 4.70)
Tsui et al., 2007 (79)	San Francisco, California, USA. Study period not reported	216 HMH respondents (17% female, median age 41.) Hepatitis C virus (HCV) seropositivity detected by enzyme immunoassay: 142 (66%) HCV- seropositive; 120 (84%) with detectable virus.	Multivariate linear regression of cross-sectional survey data	Score on SF-36	HCV seropositivity associated with lower Physical Component Score ($p < 0.01$) but not Mental Component Score ($\beta = -2.07$, $p = 0.24$)
Hansen et al., 2011 (80)	San Francisco, California, USA. September 2007 to June 2008	270 HMH respondents (64% male, 42% African American) reporting pain or analgesic use in the past 7d	Contingency tables	Score on Brief Pain Inventory. Moderate to Severe Pain (248, 92%)	More likely to be female (30% v 5%, $p = 0.01$); prescribed opioid analgesic past 90d (96% v 4%, $p < 0.01$); chronic pain lasting at least six months (92% v 72%, $p < 0.01$); moderate/severe depression (98% v 2%, $p < 0.01$)
HEALTH STATUS					
Study	**Setting**	**Sample**	**Analysis**	**Outcome**	**Significant associations**
Riley et al., 2011 (81)	San Francisco, California, USA. July 2002 to September 2008.	129 HMH female respondents (median age 44, 52% African-American, 33% crack cocaine use)	Marginal structural models with targeted variable importance (tVIM) of longitudinal survey data	Scores on mental and physical components of SF-36. Median physical score = 43/100; median mental score = 46/100	Mental health: Unmet subsistence needs ($\beta = -5.4$); ≥90% ART adherence ($\beta = 5.1$); has close friend ($\beta = 3.2$) Physical health: Crack use ($\beta = -3.6$); any drug use ($\beta = -3.1$); unmet subsistence ($\beta = -2.9$)
Riley et al., 2012 (59)	San Francisco, California, USA. July 2002 to September 2008	288 HMH male respondents (< 40% high school graduates, 23% recent crack cocaine use)	Marginal structural models tVIM of longitudinal survey data	Scores on mental and physical components of SF-36. Median physical score = 43/100; median mental score = 46/100	Mental health: Unmet subsistence needs ($\beta = -3.5$); has a close friend ($\beta = 3.2$) Physical health: Unmet subsistence ($\beta = -3.8$)
HIV TREATMENT OUTCOMES					
Study	**Setting**	**Sample**	**Analysis**	**Outcome**	**Significant associations**
Riley et al., 2005 (78)	San Francisco, California, USA.	330 HMH respondents (43% Caucasian, 16% female) in representative sample of homeless and marginally housed. Median	Survival analysis using longitudinal survey data	Time to death, all- cause. 57 deaths/ 330 participants (5.29 per 100 person-years [PY]) Causes of death: AIDS (63%); overdose (17%);	Uninsured (Adjusted Hazard Ratio [AHR] = 0.35); baseline CD4+ cell count (AHR 0.80); ART last six months vs. no treatment (AHR 0.38)

HEALTH STATUS					
Study	**Setting**	**Sample**	**Analysis**	**Outcome**	**Significant associations**
	July 1996 to May 2002	CD4+ cell count at baseline = 349 cells/μL; 85% on ART during study		cardiac complications (17%); liver disease (11%)	
Weiser et al., 2009 (49)	San Francisco, California, USA. 2006	104 HMH respondents (33% Caucasian, mean age 46.5) on ART and unannounced pill count adherence monitoring. 49% food insecure	Multivariate logistic regression of cross-sectional survey data	Plasma HIV-1 RNA viral load (PVL) suppression (< 50 copies/mL) 56%	Severely food insecure (AOR 0.23); months on HAART (AOR 1.08 per 3 months); nadir CD4+ cells (AOR 1.27 per 50 cells); ART adherence > 80% (OR 5.94)

HIV TREATMENT OUTCOMES					
Study	**Setting**	**Sample**	**Analysis**	**Outcome**	**Significant associations**
Tsai et al., 2010 (61)	San Francisco, California, USA. April 2002 to August 2007	158 HMH respondents (71% female.) 58% on ART at baseline, 75% received an antidepressant medication (84% serotonin selective reuptake inhibitor [SSRI])	Marginal structural model of longitudinal survey data	PVL suppression (< 50 copies/mL)	Receiving antidepressant medication (OR 1.55, AOR 1.58, weighted OR 2.03)
ADHERENCE TO ART					
Study	**Setting**	**Sample**	**Analysis**	**ART adherence**	**Significant associations**
Bangsberg et al., 2000 (51)	San Francisco, California, USA. January 1998 to July 1998	34 HMH participants (85% male, median age 42 years, 18% IDU) on protease inhibitor (PI)-based HAART	Unadjusted tests of difference	Last three days self- report (median adherence = 89%); unannounced pill count (median adherence = 73%); electronic medication monitoring cap (67%)	Adherence associated with concurrent PVL ($p < 0.001$)
Moss et al., 2004 (52)	San Francisco, California, USA. April 1996 to December 1997 and April 1999 to April 2000	148 HMH participants (85% male, 38% African-American) on ART and unannounced pill count adherence monitoring	Proportional hazards survival modeling (time to discontinuation); multivariate linear random effects modeling of months receiving therapy (mean adherence)	Time to ART discontinuation (46, 31%); mean adherence to treatment (67%)	Discontinuation: ≤50% adherence in first three months (AHR 6.1); ever hospitalized for mental health (AHR 2.1); current IDU (AHR 2.1) Adherence: Mental health inpatient history (83 v 71%, p = 0.02); baseline crack cocaine (64 v 77%, p = 0.01)
Kushel et al., 2006 (82)	San Francisco, California, USA. April 1996 to December 1997, April 1999 to April 2000	219 HMH respondents on ART with CD4+ nadir < 350 cells/mL	Multivariate linear regression od cross-sectional survey data	Adherence as measured by client self-report	Case management (moderate v rare/none [Adjusted β = 0.13])

ADHERENCE TO ART					
Study	**Setting**	**Sample**	**Analysis**	**ART adherence**	**Significant associations**
Das-Douglas et al., 2009 (54)	San Francisco, California, USA.	125 HMH participants (70% male, 40% African-American) on ART with pharmaceutical coverage (35% Medicare Part D)	Multivariate logistic regression analysis of cross-sectional survey data	ART interruptions, self- report (11%)	Medicare Part D pharmaceutical coverage (AOR 7.50); Beck depression inventory score (AOR 1.08 per point)

ADHERENCE TO ART					
Study	**Setting**	**Sample**	**Analysis**	**ART adherence**	**Significant associations**
Friedman et al., 2009 (53)	Baltimore, Maryland; Los Angeles, California; Chicago, Illinois, USA	602 homeless/at-risk of homeless participants (79% African American, 31% female, 45% CD4+ = 200 – 499 cells	Multivariate logistic regression analysis of cross-sectional survey data	≥ 1 missed dose in previous 2 days, self report	Any illicit drug (82 v 73%, $p < 0.05$); alcohol (87 v 70%, $p < 0.01$)
Bangsberg et al., 2010 (60)	San Francisco, California, USA.	118 respondents (73% male, 63% ever injection drug user [IDU]) on HAART and unannounced pill count adherence monitoring. 40% on single-tablet regimen (STR)	Multivariate generalized estimating equation analysis of cross sectional survey data	Proportion of doses taken calculated from unannounced pill counts. Mean adherence to STR = 86%; mean adherence to non-STR = 73% ($p = 0.001$)	Treatment (STR v non- STR, $z = 2.75$, $p = 0.006$); nadir CD4+ (per cell/ml, $z = 3.34$, $p = 0.001$)
Parashar et al., 2011 (64)	British Columbia, Canada. July 2007 to January 2010	212 unstably housed PLWHA (68% male, 44% current IDU) on HAART in a HIV treatment registry	Multivariate logistic regression of factors associated with ≥ 95% adherence	Pharmacy refill data	Older age (AOR = 1.07 per year); incarcerated (AOR = 0.20); current illicit drug use (AOR = 0.40); enrolled in MAT programme (AOR = 4.76)
Riley et al., 2011 (81)	San Francisco, California, USA. July 2002 to September 2006	330 HMH participants (19% female, 54% used crack cocaine, 28% employed)	Marginal structural model of longitudinal survey data	Exposure to ART in past three months, self-report	Continuously insured, 12 mos v uninsured (AOR 3.34)

TABLE 2

Interventions to improve the health of homeless/marginally-housed PLWHA

Study	Setting	Sample	Design	Intervention	Findings
Bansberg et al., 2010 (60)	San Francisco, California, USA	118 HMH participants (61% non-white, 73% men, 63% lifetime injection drug use) drawn from REACH cohort	Observational study of adherence among participants on single tablet HAART regimen versus historical controls	Single tablet HAART regimen (STR) containing efavirenz, emtricibine and tenofovir disoproxil fumarate	Higher levels of adherence observed among STR participants compared to non-one-pill-daily participants after adjustment for confounders
Buchanan et al., 2009 (62)	Chicago, Illinois, USA	105 HMH participants recruited from in-patient services	Participants randomized to care-as-usual or intervention. Primary outcome was survival with CD4+ ≥ 200 and PVL < 100,000	Permanent housing including intensive case management	55% of participants in intervention arm vs. 34% in control arm reached outcome (p = 0.04.)
Cameron et al., 2009 (65)	London, England, UK	27 HMH individuals recruited through social service agency	Case study	Housing referral with case management	Twelve (44%) individuals received temporary or permanent housing; all registered with GP
Hawk and Davis, 2012 (66)	Pittsburgh, Pennsylvania, USA	26 residents of low-barrier shelter, 96% use illicit drugs or alcohol	Observational study of residents comparing individuals with undetectable vs. detectable PVL	Exposure to Housing First, harm reduction-based shelter with case management in a 14-unit apartment building	69% of residents achieved undetectable viral loads
Parashar et al., 2011 (64)	British Columbia, Canada	212 unstably housed participants drawn from HAART treatment registry	Observational study of HAART adherence among participants in maximally-assisted treatment versus other	Exposure to a maximally-assisted treatment including observed therapy	Participation in MAT independently associated with higher likelihood of adherence (AOR 4.76, p = 0.003)
Tsai et al., 2010 (61)	San Francisco, California, USA	158 HMH participants drawn from REACH cohort with Beck Depression Inventory Score II > 13	Marginal structural modeling of observational study of effect of antidepressant medication on PVL suppression	Exposure to antidepressant medication (84% serotonin selective reuptake inhibitor)	Participants on antidepressants had 2.03 greater odds of viral suppression
Wolitski et al., 2010 (63)	Baltimore, Maryland; Chicago, Illinois; Los Angeles, California, USA	630 HMH individuals	Participants randomized to rental assistance or standard of care. Outcomes included CD4+ cell count, PVL, health status and healthcare usage	Immediate rental assistance though Housing Opportunities for People with AIDS (HOPWA) and case management	Decrease in depression (p = 0.043); improvements in physical health (p = 0.006); no change in HAART access or adherence, CD4

TABLE 3

Barriers and facilitators of HIV treatment outcomes and antiretroviral therapy access and adherence among homeless/marginally-housed PLWHA, 2000 to 2010

HIV treatment outcomes	
Barriers	**Facilitators**
Food insecurity (83)	Exposure to housing-first/harm reduction intervention (66)
No health insurance (78)	Exposure to supportive housing with integrated case management (62)
	Exposure to case management (82)
	HAART access/adherence (33,49,51,78)
	Uninterrupted health insurance (55)
	Medication for depression (84)
	Single-tablet HAART regimen (60)
Access/adherence to antiretroviral therapy	
Barriers	Facilitators
Depression (52,54)	Exposure to case management
Injection drug use (52)	Mental health in-patient admission (52)
Crack cocaine use (52,53)	Single-table HAART regimen (60)
Medication insurance status (54)	Exposure to maximally-assisted HIV treatment programme (64)
Alcohol use (53)	
Marijuana use (53)	
Any illicit drug use (53)	