# **AIDS and Behavior**

# Predictors of adult retention in HIV care: A systematic review --Manuscript Draft--

Manuscript Number:	AIBE-D-16-00586
Full Title:	Predictors of adult retention in HIV care: A systematic review
Article Type:	Substantive Review
Keywords:	Retention in care, HIV, predictors, adult, treatment cascade, developing countries, developed countries
Abstract:	Abstract Introduction: A systematic literature review was conducted to identify key predictors of poor adult retention in HIV medical care in developed and developing countries.  Methods: An electronic search was conducted with MEDLINE (OVID), PubMED, EBSCO, SCOPUS, and Cochrane databases, as well as manual searches. Inclusion and exclusion criteria were decided, and only original quantitative studies which identified predictors of retention in care were reported on.  Results and discussion: Of the two hundred and sixty-eight articles identified, twenty six were included in the review following an independent assessment by two raters. In developed countries, the most frequently cited predictor of poor retention in care was active substance use. In developing countries, demographic and medical factors were the most frequently cited factors associated with poor retention in care.  Conclusions: Psychosocial factors are important considerations when targeting interventions to improve retention rates. This review compares the results for developed versus developing countries, and suggests primary concerns for poor retention include substance use, demographic and medical factors.

#### **Abstract**

**Introduction:** A systematic literature review was conducted to identify key predictors of poor adult retention in HIV medical care in developed and developing countries.

**Methods:** An electronic search was conducted with MEDLINE (OVID), PubMED, EBSCO, SCOPUS, and Cochrane databases, as well as manual searches. Inclusion and exclusion criteria were decided, and only original quantitative studies which identified predictors of retention in care were reported on.

**Results and discussion:** Of the two hundred and sixty-eight articles identified, twenty six were included in the review following an independent assessment by two raters. In developed countries, the most frequently cited predictor of poor retention in care was active substance use. In developing countries, demographic and medical factors were the most frequently cited factors associated with poor retention in care.

**Conclusions:** Psychosocial factors are important considerations when targeting interventions to improve retention rates. This review compares the results for developed versus developing countries, and suggests primary concerns for poor retention include substance use, demographic and medical factors.

**Keywords:** Retention in care, HIV, predictors, adult, treatment cascade, developing countries, developed countries

#### Introduction

The Human Immunodeficiency Virus (HIV) Care and Treatment Cascade outlines the proportion of people living with HIV (PLWHIV) across a number of domains: living with HIV, linked to/engaged in care, retained in care, on treatment, and virologically suppressed [1]. The Centres for Disease Control and prevention [2] in the US estimates only 50% of PLWHIV receive regular medical care, compared to an estimate of 73% in Australia [3]. The World Health Organization (WHO) estimates that most PLWHIV are lost to follow up (LTFU) within the first few years of starting treatment. Their synthesis of the available data suggests that the average retention rate 12 months after initiating medication ranges from 64% to 94%, and can reach 60% at 60 months in resource-limited countries [1]. In the interest of providing holistic HIV care, understanding the role of psychosocial factors in managing engagement with and retention in medical care is important.

Since their inception in the 1990's, significant improvements have been made to Antiretroviral Therapy (ART), and subsequently developed Highly Active Antiretroviral Therapy (HAART), with respect to efficacy, dosage and how well they are tolerated. In developed countries HAART is widely available, in contrast to resource-limited countries where there are significantly fewer medication options. Early findings from a recent clinical trial, the Strategic Timing of AntiRetroviral Treatment (START), across 35 countries indicate that starting medication early and maintaining adherence is beneficial from an individual health perspective [4]. Maintaining medication adherence affords optimal suppression of the virus and ensures a functioning immune system, leaving individuals less vulnerable to other infections/illnesses. Recent evidence also points to a strong link between virological suppression and a decrease in the risk of HIV transmission [5], which is the basis for the WHO global public health initiative 'Treatment as Prevention' [1]. Thus, retaining HIV+ individuals in medical treatment/care to increase HAART adherence is key in the maintenance of individual health and the eradication of the new infections.

Multiple HIV treatment guidelines address adherence to treatment and retention in HIV care. The US Department of Health and Human Services recommends those who are newly diagnosed with HIV should immediately commence HAART, access medical care every three to four months, and continue this regime until they are virologically suppressed [6]. The US Health Resources and Services Administration (HRSA) defines successful retention in medical care as at least two visits (including blood collection to determine viral load) in a calendar year, spaced at least three months apart [6, 7]. This guideline is consistent with the European AIDS Clinical Society Guidelines [8]. More broadly, the WHO [1] has globally recommended that those who are stable on medication to be reviewed clinically every 3-6 months.

While the topic of retention in care has been broadly studied and reviewed, there lacks a synthesis of the literature to date to assist researchers and clinicians to identify and understand the key predictors of poor retention in HIV care. The overarching goal, regardless of country or resources available, is to improve adherence to medication to benefit both the individual and the wider public. The optimal way to achieve this is by retaining patients in care in order to address medical and psychological comorbidities, medication adherence, and other psychosocial factors which impact upon physical and mental health. In this way, developing our understanding of the key factors which are implicated in poor retention in care is required. The current review aims to address this gap in the literature.

#### Method

Systematic literature search

Search terms and associated synonyms reflecting predictors of retention in care for HIV+ populations were identified. Synonyms were identified for key themes of interest, and five databases (MEDLINE [OVID], PubMED, EBSCO, SCOPUS, and Cochrane) were searched using the following terms: (predict\* OR factor\* OR caus\* OR Component\* OR Correlat\*) – Title, AND (retention\* OR retain\* OR engage\* OR continuum OR treatment cascade) – Title, AND (HIV) – keyword. Manual searches through reference lists of relevant articles were also conducted. Duplicates were deleted, and articles were then screened by title, abstract and article content by two authors (SB and TNJ), with articles not meeting the agreed upon criteria removed. Figure 1 shows the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) [9] flowchart of the systematic literature search process.

#### Eligibility criteria

Searches were limited to adult populations, published articles post-1995 (to identify those written in the medication era), and those in English. Articles related to medication adherence, focusing on linkage as opposed to retention in care, and focusing on measuring retention or interventions to improve retention were all excluded from the analysis. Specific samples based on systemic factors which may impact results were also excluded; for example, forensic populations where clients were mandated to attend appointments. Articles relating to a range of adult populations were included, on the basis that they could offer insight into retention issues from a broader context.

Original quantitative articles only (retrospective and prospective studies) were included while reviews were not, and studies which focused on psychosocial, demographic, medical and welfare issues were included to provide a breadth of knowledge and understanding regarding all possible predictors of retention.

## Study appraisal and selection

The inclusion/exclusion criteria were defined by SB and TNJ. The first 10 articles were jointly reviewed to establish consistency, with the following 96 reviewed separately and then compared.

Inter-rater reliability of 89.6% was achieved and, through consultation, agreement was reached regarding the remaining articles. In this context, the semantics associated with articles required clear definition, such that both raters were certain about the differences between articles focusing on access vs. linkage vs. engagement vs. retention to/in care. A total of 26 articles were included in the review (see Figure 1).

#### Data extraction and review

Data were extracted from the articles by the primary author (SB) using the PRISMA-P protocol. This standardised method of extracting data obtained information regarding the quality of the study (appropriate use of measures and analyses, internal and external validity, any ethical concerns, minimisation of any bias), and confirmed the research met the inclusion criteria agreed upon by SB and TNJ.

#### **Results**

The database and manual searches yielded a total of 268 articles, with 26 retained for final review (see Figure 1 for a full appraisal of the article selection process). Of the 26 remaining, all listed retention in care as a dependent/outcome variable. One study [10] operationalized retention in care as the duration of episodes on or off HARRT as defined by pharmacy dispensing records. While this is associated with medication, it does not relate to adherence per se but instead explores medication dispensing which is consistent with other measures of retention. In most other studies, attendance to medical appointments, including phlebotomy, was used to measure retention in care.

There were stark differences between the predictors identified for developing versus developed countries, which speaks to inherent access differences and different priorities; developed countries offer comparatively greater access to medical care than their developing counterparts. Table I provides a broad overview of the studies retained for analysis, including the setting, design, participants and primary outcomes (predictors of retention identified). Table II and Table III identify the predictors for developed and developing countries respectively. There were fifteen articles which focused on developed countries, and eleven which targeted developing countries, as defined by the United Nations World Economic Situation and Prospects [11]. The predictors of retention in care have been categorised under the broad banners of developed and developing countries, and are presented from higher to lower frequency in the articles included in the review. Results are also divided, where relevant, into predictors of poor retention followed by predictors of retention.

#### **Developed Countries**

# Substance Use

Substance use was, by far, the most cited predictor of poor retention in the literature in developed nations, and was referred to in 50% of the studies examined. [12] theorised a model of predisposing and needs factors in a sample of detainees recently released from jail, but not mandated to attend HIV treatment. This study used viral load (VL) testing as a proxy for retention in care, a practice used by other researchers in this field. They also utilised the Behavioural Model for Vulnerable Populations to suggest that predisposing (for example, demographics, mental health, substance use) and needs factors (including medical comorbidity, addiction severity and psychiatric severity) interact with other factors (for example, jail and community services) to influence health behaviours; in this instance, medication adherence and retention in care. Using logistic regression, the authors concluded that substance use, among other factors, was significantly associated with poorer sustained retention in care.

Other studies which identified a relationship between active substance use and poor retention include [13], who reviewed a cohort of US Veterans; [14], who reported the greatest attrition rate from medical care among their substance using population above all others; [10], who noted that intravenous drug use (IVDU) in particular was associated with poor retention; [15], who noted that those within the IVDU HIV transmission risk group were more likely, than their non-IVDU counterparts, to dropout of care; and [16], who identified that those classified as receiving "no care" (i.e. those who did not see a doctor for their HIV after diagnosis, or had not seen an HIV specialist within the past 6 months) were more likely to report binge drinking or illicit drug use in the previous 30 days.

#### Psychiatric Co-Morbidities

Psychiatric illness, besides substance use, has been identified in a number of the studies reviewed as being a significant predictor of poor retention in care. [16] noted that subjects with poorer mental health scores were less likely to be retained in care. [17] further noted that active psychiatric illness at the last clinical visit was associated with not returning for care. Conversely, [18] noted in their study that those who reported at least 14 "mentally unhealthy" days per month were more likely to remain retained in care.

#### **Demographics**

Various demographic characteristics were also identified as strong predictors of retention in care.

Those factors associated with poorer retention in care included male sex [19], female sex [10, 12, 14, 15], having young children [18], younger age [10, 13, 14, 19, 20], and being from an ethnic minority [15, 18]. [10] further identified aboriginality was a predictor of poor retention in their Canadian study. Conversely, [19] found that certain ethnic minorities (e.g. Latinos) were more likely to be retained than others (e.g. African Americans, or Anglo Americans).

## HIV-Disease Progression and Medical Co-Morbidities

Some authors identified that medical, rather than psychosocial, factors were pertinent to a person's capacity to remain engaged in care. [13] identified that those with Hepatitis C (HCV) coinfection and with higher CD4 counts ( $>350 \times 10^6$ /L) were less likely to be retained in care. Those with HCV coinfection were also more likely to present with active substance use, which would likely have further interfered in retention. It is possible that a higher CD4 count is also related to health beliefs (e.g. "feeling well") and therefore a perception of not requiring medical care [10, 20]. Conversely, [7] identified that those with lower baseline CD4 counts were less likely to be retained in care.

#### Social/Welfare

In their study of retention among a US cohort of women of colour, [18] identified that those who had dependent children <18 years old and those living in institutional facilities were less likely to remain retained in care. [7] noted that patients who were publicly insured were less likely to be retained in care. [21] also identified that cost (e.g. lack of insurance) was a significant barrier to them continuously accessing care despite, as the authors noted, the study being conducted in a US state with universal access to care.

Miscellaneous (health beliefs, support, domestic violence, practical factors)

Other factors have also been identified as predictors of poor retention in care. Health beliefs appear to play an important role, and include feeling hopeless about treatment for HIV [18]; feeling well and being too busy [17]; perceiving 'wellness' as a barrier to seeking treatment, not trusting the medical system or not 'bothering' because there is no cure [16]. In addition, [22] identified that intimate partner violence could have a role, such that patients who feel threatened by their partner are less likely to remain retained in care.

Practical factors (e.g. access to transport to attend appointments, ease of obtaining an appointment with an HIV specialist) were also identified as barriers to patients remaining in care [21]. These authors found that this was more of an obstacle than other psychosocial issues such as depression and substance use, despite these being highly prevalent.

#### **Predictors of Retention**

Even though most studies have focused on barriers to retention, some have focused on predictors to retention in care. A number of authors have also looked at the role of certain factors in improving retention rates; for example, social and/or professional support. [16] noted that professional support (such as case management from HIV and/or mental health services) was associated with

greater retention in care. [12] also noted that access to case management was an important factor to improve retention in their population of recently released inmates. [23] also identified that social support mediates the relationship between cognitive impairment and retention in care, such that those who are cognitively impaired and have some support are more likely to be retained in care. Conversely, [24] noted in their study of newly diagnosed patients that social support did not significantly predict retention in care.

#### **Developing Countries**

#### Demographic

Demographic factors were identified in eight of the 11 articles which focused on resource-limited countries, suggesting it is a key predictor of poor retention in developing populations. Factors such as sex, age, and education level were frequently cited in these articles. For example, a number of articles noted that male sex was associated with an increased risk of attrition from care [25-29], as was younger age [30, 31], and lower levels of education [26, 32, 33].

#### HIV-Disease Progression and Medical Co-Morbidities

HIV-disease progression [26-31, 33], and lower body mass index (BMI) [25, 27, 28, 31, 34] were also cited in eight of the 11 articles in developing countries. Lower baseline CD4 counts or higher WHO stage of the disease was usually associated with higher rates of attrition, however in a number of articles, the authors noted that higher CD4 counts were related to poorer retention in care [30, 33]. [31] found that those with a poorer level of functionality (e.g. those who were bedridden) were also less likely to remain retained in medical care. [26] also noted that those with either low or high baseline CD4 counts were more likely to be lost to follow-up (LTFU). It is possible that, for some people, having the health belief of "feeling well", as well as "feeling unwell" for others, is a risk factor for not attending appointments.

Miscellaneous (Process/Clinic Factors, Mental Health)

Other factors associated with poor retention in care were cited far less frequently than those already mentioned in the literature reviewed in resource-limited countries. [30] notes that those patient who commenced medication as an inpatient or when pregnant were at greater risk of LTFU. The authors suggest this may be because patients were required to commence medication at a faster rate than usual, and perhaps before they were psychologically ready, thereby limiting their capacity to effectively prepare for it. [32] also noted that patients who had not received medication adherence counseling at baseline were less likely to remain engaged in regular medical care, and that those who commenced medication later in the study period were more likely to become LTFU. This finding was replicated by [34], and likewise [31] found that retention rates decreased as the number of years the clinic had been in operation increased. [32] suggested this may be due to increased workload within the clinic in the absence of any increase in resources. Likewise, [29] noted that clinics with part-time (compared to full-time) nursing and medical staff demonstrated poorer retention rates. [27] also note that those initiating medication at primary healthcare facilities (compared to district hospitals) were more likely to remain retained, and the authors suggest this is likely because rural patients would travel to urban hospitals to initiate treatment under medical specialists and then likely transfer back to rural facilities.

Only one study in developing countries included in the review investigated the potential role of mental health, and found that mental health concerns were a factor in retention rates in developing countries. [35] found that depression was significantly associated with LTFU rates, and that this effect was not mediated by suboptimal medication adherence as hypothesised.

#### Discussion

The 26 articles included in this systematic review highlight both the complexity of the issues surrounding retention in care, and the paucity of knowledge regarding consistent factors which reliably predict it. The differences associated with retention rates, and the factors with which they are related, between developed and developing countries is also evident. This issue is not unique to HIV and is well documented throughout the chronic disease literature; however there are factors specific to the HIV+ population which require particular attention.

The primary predictor of poor retention identified in developed countries in this review is active substance use [10, 12-16]. We already know that active substance use impacts the frontal cortex, among other structures, which is responsible for a person's capacity to plan and make decisions [36]. The limbic system (the 'reward center') is also implicated in substance use, meaning intoxicated individuals not only experience a heightened sense of reward and pleasure, but also potentially lack the capacity to effectively care for themselves in the short, medium and long-term, depending on the severity of their use [36]. Disorganisation, impulsivity, lack of stable housing, and other medical and social problems associated with substance use are also likely to contribute to poor retention in care. In the context of retention, it is clear that treating substance use in order to alter the effects of substances on the brain could better equip a person to make decisions and manage their healthcare. Active substance use can also impact certain populations more than others. In many developed countries (for example, Australia) the prevalence of HIV in MSM populations is higher than the general population, and substance use is common within the community, in part due to its (often positive) impact on the frequency and intensity sexual experiences [37], as well as management of perceived stigma and potential discrimination [38]. Developing our knowledge about or treatment of substance use in this particular context may positively impact retention rates. A goal for future research might be to ascertain the level of variance accounted for by substance use in a regression model of multiple predictors on retention in care.

Demographic factors were also highly predictive of retention rates in the literature surveyed, both in developed and resource-constrained countries. In particular, sex, age, education level and ethnicity all appear to play a large role in retention rates, across the board. Health beliefs such as self-efficacy/locus of control were important, and may moderate relationships with other variables. For example, younger people may not fully appreciate the necessity for ongoing medical care or feel unable to 'commit'; conversely, older people may feel as though there is "no point" in managing their care. Further research is required to explore these relationships.

Medical factors, including how unwell a person was, were also highly correlated with retention in care. Studies identifying competing results have been reviewed here, such that some authors [7, 28] noted that those with lower baseline CD4 counts were less likely to be retained, while others [20, 30] found the opposite to be true. It is evident that these mixed findings are apparent in both developed and developing countries. Clearly further research is warranted to explore these discrepancies, with a number of potentially influential factors including health beliefs, level of social support and other demographic variables requiring examination.

Other key predictors of retention identified in this review were health beliefs, psychiatric illness, support, social/welfare issues, clinic factors, and others. The prevalence of psychiatric illness, especially mood disorders, in an HIV+ population is well documents [39], as is the impact this can have on self-care including attendance to medical appointments and medication adherence [35]. Health beliefs in particular appear to have strong correlations (e.g. feeling too well or too busy) [17]. In addition, professional support in the form of case management appeared to positively assist vulnerable populations (e.g. forensic) [12] to remain engaged in care. Other practical factors, including the ease with which patients can attend appointments [21], and clinic factors (e.g. the number of patients enrolled in a clinic and associated staff workloads) [29]; the availability of

medication adherence counselling prior to initiation [32] were also noted. These point to the subtle interplay between psychological and social factors impacting retention, and acknowledge the role of both in researching this area.

In resource-limited countries, compared to developed countries, it appears that fundamental factors such as weight, disease progression, and education level are the key factors which impact upon retention in care, whereas in developed countries other factors such as psychiatric illness and active substance use are the primary factors which interfere in optimal retention in care. This points to inherent differences between developed and developing countries with respect to access to adequate care and medication, and the overall differences between patient needs in both contexts.

Of interest is the absence of quantification of the role of perceived stigma and/or discrimination in impacting an individual's capacity or willingness to remain retained in medical HIV care. This is despite numerous findings regarding the importance of stigma and/or discrimination in HIV [e.g. 40], including its impact on self-efficacy and perceived capacity to manage one's own health [41]. While attitudes and understanding about HIV and its transmission in developed countries have greatly improved over the past 30 years, stigma and/or discrimination regarding HIV remains an issue for some, and it was therefore expected to have been identified as a predictor. Despite this, none of the studies included in this review explicitly investigated the potential role of stigma in retention in care. Likewise, it was not identified as a retention-interfering factor in the developing countries literature, which is perhaps even more surprising. In their study, [27] noted that those HIV-infected patients in rural settings were more likely to travel to urban areas for their medical treatment, and it is possible this is related (at least in part) to concerns around stigma and/or discrimination.

A large proportion of the studies included in this review employed a retrospective cohort design; this was especially true in developing countries, and is likely due to limitations in conducting prospective

studies. An issue with retrospective studies is the risk that key variables are missed as the analysis depends wholly on data routinely collected) (for example, it is unlikely that perceived stigma and/or discrimination would have been routinely collected). A further limitation is that many of the studies reviewed discuss correlates versus predictors of retention in care). It is possible this is an issue of semantics, where the terms are used interchangeably. It is also possible that some of the studies lacked the statistical design necessary to identify predictors as distinct from correlates. Future research could attempt to cohesively measure predictors of retention, for the purposes of identifying those 'at-risk' of dropping out and intervening as early as possible.

A key issue with the data reviewed involves definitional terms; there appears to be a lack of consistency regarding the terminology in this area. For example, the terms 'engagement in care' and 'retention in care' are often ill-defined and used interchangeably, and this impacted the search strategy and the analysis of the articles to ensure authors' definition of retention in care matched our own. Likewise, definitions of retention in care varied slightly between studies, despite there being clear guidelines stipulated by the HRSA and EACS [7, 8] in developed countries. It seems there are no/limited guidelines specifically related to developing countries, which may in itself be an issue, in addition to the varied definitions of LTFU which were employed by studies.

There are (limitations with some of the specific studies reviewed), the most common of which relates to the definition and means of measuring retention in care. Inconsistencies were noted in the ways in which retention was measures; some used viral load tests as a proxy for retention [e.g. 12, 15], while others [e.g. 18] measured attendance to HIV medical appointments. [16] used self-reported use of medical services as the outcome variable in their analysis, perhaps not the most rigorous test of this variable and open to subjective bias. The definition of LTFU also needs to be carefully considered; for example, [33] noted that patients who had transferred their care to another clinic

were counted as LTFU, suggesting their retention rates may be underestimated. A reliable way of measuring retention would likely be useful in standardising conclusions.

Inherent in this investigation into predictors of retention is the necessity to focus/direct interventions appropriately so as to maximise retention rates. A thorough understanding of these factors is therefore necessary in order to fully achieve this goal. Furthermore, given the bulk of the literature in developed countries is from the US/Canada, it would be important to conduct studies in other developed countries to ascertain whether there are any differences, given the different nature of the epidemic across the globe, and fundamental differences in access to medical care and medication. There were no articles included from Europe, for example, which satisfied all eligibility criteria. This may point to a gap in our knowledge, or that HIV retention research in developed countries is concentrated on the United States and Canada.

#### **Conclusions**

As treatments improve we have an ageing HIV+ population, which is accompanied by an increase in comorbidities and amplifies the need for often complex monitoring and retention in care.

Concentrating on medical aspects alone can fail to account for the broader range of factors which impact an individual's life. In this way, expanding this focus to retention in HIV care (versus medication adherence alone) offers a more holistic view of HIV management and moves away from the pure medical model to account for psychological and physical comorbidities, and other psychosocial issues in conjunction with medication adherence.

The literature reviewed here points to a collection of factors which appear to predict retention in medical HIV care, both across developed and developing countries. However, it is also clear that further research is required to quantify some of the constructs identified (e.g. stigma and/or discrimination), and to do so with other samples not previously reported in the literature. While we

have a sound knowledge regarding the factors that contribute to poor retention, little remains understood regarding the complexity of interrelationships between these, and whether intervening in one part of the system will ultimately impact the outcome.

#### **Conflict of Interest**

The authors declare that they have no conflict of interest.

# Acknowledgements and funding

Nil

#### References

- [1] World Health Organization. (2016). Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach.

  Available from <a href="http://apps.who.int/iris/bitstream/10665/208825/1/9789241549684">http://apps.who.int/iris/bitstream/10665/208825/1/9789241549684</a> eng.pdf?ua=1

  Accessed on 4<sup>th</sup> August 2016.
- [2] Centers for Disease Control and Prevention. (2011). Vital signs: HIV prevention through care and treatment United States. CDC: December 2, 2011/60(47); 1618-1623. Available from: <a href="http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6047a4.htm">http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6047a4.htm</a>. Accessed 12<sup>th</sup> March 2016.
- [3] The Kirby Institute. HIV, viral hepatitis and sexually transmissible infections in Australia Annual Surveillance Report 2015. The Kirby Institute, UNSW Australia, Sydney NSW 2052.
  - [4] National Institutes of Health. (2015). Starting antiretroviral treatment early improves outcomes for HIV-infected individuals. Retrieved from <a href="https://www.nih.gov/news-events/news-releases/starting-antiretroviral-treatment-early-improves-outcomes-hiv-infected-individuals">https://www.nih.gov/news-events/news-releases/starting-antiretroviral-treatment-early-improves-outcomes-hiv-infected-individuals</a>.

    Accessed 30 May 2016.
  - [5] Charania, M. R., Marshall, K. J., Lyles, C. M., Crepaz, N., Kay, L. S., Koenig, L. J. et al. (2014). Identification of evidence-based interventions for promoting HIV medication adherence: Findings from a systematic review of US-based studies, 1996–2011. *AIDS Behav*, 18(4), 646-660.
  - [6] Young, B. The importance of retention in HIV care. *Medscape*. Sep. 10, 2014. Available from: <a href="http://www.medscape.com/viewarticle/831324">http://www.medscape.com/viewarticle/831324</a>. Accessed: April 28 2015.
  - [7] Tedaldi, E. M., Richardson, J. T., Debes, R., Young, B., Chmiel, J. S., Durham, M. D. et al. (2014). Retention in care within 1 year of initial HIV care visit in a multisite US cohort: who's in and who's out? *J Int Assoc Provid AIDS Care*, *13*, 232-241.

[8] European AIDS Clinical Society. EACS European Guidelines for treatment of HIV infected adults in Europe. Available from: <a href="http://www.eacsociety.org/Guidelines.aspx">http://www.eacsociety.org/Guidelines.aspx</a> Accessed: April 28 2015.

[9] Moher, D., Shamseer, L., Clarke, D., Ghersi, D., Liberati, A., Petticrew, M. et al. (2015).

Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015

Statement. *BMJ* 2015;349:g7647.

[10] Nosyk, B., Lourenço, L., Min, J. E., Shopin, D., Lima, V. D., Montaner, J. S. et al. (2015). Characterizing retention in HAART as a recurrent event process: insights into 'cascade churn'. *AIDS*, 29(13), 1681-1689.

[11] The United Nations. World economic situation and prospects (2014). Available from <a href="http://www.un.org/en/development/desa/policy/wesp/wesp current/2014wesp country classification.pdf">http://www.un.org/en/development/desa/policy/wesp/wesp current/2014wesp country classification.pdf</a>. Accessed: 7<sup>th</sup> December 2015.

[12] Althoff, A. L., Zelenev, A., Meyer, J. P., Fu, J., Brown, S. E., Vagenas, P. et al. (2013).

Correlates of retention in HIV care after release from jail: results from a multi-site study. *AIDS Behav*, 17 Suppl 2, S156-170.

[13] Giordano, T. P., Hartman, C., Gifford, A. L., Backus, L. I., & Morgan, R. O. (2009).

Predictors of retention in HIV care among a national cohort of US veterans. *HIV Clin Trials*, *10*(5), 299-305.

[14] Lourenço, L., Colley, G., Nosyk, B., Shopin, D., Montaner, J. S. G., & Lima, V. D. (2014). High levels of heterogeneity in the HIV cascade of care across different population subgroups in British Columbia, Canada. *PloS one*, *9*, e115277.

[15] Rebeiro, P., Althoff, K. N., Buchacz, K., Gill, J., Horberg, M., Krentz, H. et al. (2013).

Retention among North American HIV-infected persons in clinical care, 2000-2008. *JAIDS (1999), 62*, 356-362.

[16] Tobias, C. R., Cunningham, W., Cabral, H. D., Cunningham, C. O., Eldred, L., Naar-King, S. et al. (2007). Living with HIV but without medical care: barriers to engagement. *AIDS Patient Care STDs*, *21*, 426-434.

[17] McMahon, J. H., Moore, R., Eu, B., Tee, B.-K., Chen, M., El-Hayek, C. et al. (2015). Clinic Network Collaboration and Patient Tracing to Maximize Retention in HIV Care. *PloS one, 10*, e0127726.

[18] Blank, A. E., Fletcher, J., Verdecias, N., Garcia, I., Blackstock, O., & Cunningham, C. (2015). Factors associated with retention and viral suppression among a cohort of HIV+ women of color. *AIDS Patient Care STDS*, *29 Suppl 1*, S27-35.

[19] Horberg, M. A., Hurley, L. B., Klein, D. B., Towner, W. J., Kadlecik, P., Antoniskis, D. et al. (2015). The HIV Care Cascade Measured Over Time and by Age, Sex, and Race in a Large National Integrated Care System. *AIDS Patient Care STDs*, *29*(11), 582-590.

[20] Richey, L. E., Halperin, J., Pathmanathan, I., Van Sickels, N., & Seal, P. S. (2014). From diagnosis to engagement in HIV care: assessment and predictors of linkage and retention in care among patients diagnosed by emergency department based testing in an urban public hospital. *AIDS Patient Care STDs*, 28(6), 277-279.

[21] Dombrowski, J. C., Simoni, J. M., Katz, D. A., & Golden, M. R. (2015). Barriers to HIV Care and Treatment Among Participants in a Public Health HIV Care Relinkage Program. *AIDS Patient Care STDs*, 29, 279-287.

[22] Schafer, K. R., Brant, J., Gupta, S., Thorpe, J., Winstead-Derlega, C., Pinkerton, R. et al. (2012). Intimate partner violence: a predictor of worse HIV outcomes and engagement in care. *AIDS Patient Care STDs*, *26*(6), 356-365.

[23] Waldrop-Valverde, D., Guo, Y., Ownby, R. L., Rodriguez, A., & Jones, D. L. (2014). Risk and protective factors for retention in HIV care. *AIDS Behav*, *18*(8), 1483-1491.

[24] Kelly, J. D., Hartman, C., Graham, J., Kallen, M. A., & Giordano, T. P. (2014). Social support as a predictor of early diagnosis, linkage, retention, and adherence to HIV care: results from the steps study. *J Assoc Nurses AIDS Care*, *25*(5), 405-413.

[25] Allam, R.R., Murhekar, M.V., Bhatnagar, T., Uthappa, C.K., Chava, N., Rewari, B.B. et al. (2014). Survival probability and predictors of mortality and retention in care among patients enrolled for first-line antiretroviral therapy, Andhra Pradesh, India, 2008-2011. *Trans R Soc Trop Med Hyg,* 108, 198-205.

[26] Charurat, M., Oyegunle, M., Benjamin, R., Habib, A., Eze, E., Ele, P. et al. (2010). Patient retention and adherence to antiretrovirals in a large antiretroviral therapy program in Nigeria: a longitudinal analysis for risk factors. *PLoS One*, *5*(5), e10584.

[27] Mutasa-Apollo, T., Shiraishi, R. W., Takarinda, K. C., Dzangare, J., Mugurungi, O., Murungu, J. et al. (2014). Patient retention, clinical outcomes and attrition-associated factors of HIV-infected patients enrolled in Zimbabwe's National Antiretroviral Therapy Programme, 2007–2010. *PLoS One, 9*(1), e86305.

[28] Thida, A., Tun, S. T. T., Zaw, S. K. K., Lover, A. A., Cavailler, P., Chunn, J. et al. (2014). Retention and risk factors for attrition in a large public health ART program in Myanmar: a retrospective cohort analysis. *PloS one*, *9*(9), e108615.

[29] Vella, V., Govender, T., Dlamini, S., Taylor, M., Moodley, I., David, V. et al. (2010).

Retrospective study on the critical factors for retaining patients on antiretroviral therapy in KwaZulu-Natal, South Africa. *JAIDS*, 55(1), 109-116.

[30] Boyles, T.H., Wilkinson, L.S., Leisegang, R., & Maartens, G. (2011). Factors influencing retention in care after starting antiretroviral therapy in a rural South African programme. *PloS One,* 6(5), e19201.

[31] Koole, O., Tsui, S., Wabwire-Mangen, F., Kwesigabo, G., Menten, J., Mulenga, M. et al. (2014). Retention and risk factors for attrition among adults in antiretroviral treatment programmes in Tanzania, Uganda and Zambia. *Trop Med Int Health*, *19*(12), 1397-1410.

[32] Vuylsteke, B., Semdé, G., Auld, A. F., Sabatier, J., Kouakou, J., Ettiègne-Traoré, V. et al. (2015). Retention and risk factors for loss to follow-up of female and male sex workers on antiretroviral treatment in Ivory Coast: a retrospective cohort analysis. *JAIDS*, 68, S99-S106.

[33] Yang, G. L., Yan, J., Liu, Y., Huang, Z. L., & Long, S. (2015). Retention in care and factors affecting it among people living with HIV/AIDS in Changsha city, China. Asia-Pacific *J Public Health*, *27*(2 suppl), 86S-92S.

[34] Palombi, L., Marazzi, M. C., Guidotti, G., Germano, P., Buonomo, E., Scarcella, P. et al. (2009). Incidence and predictors of death, retention, and switch to second-line regimens in antiretroviral-treated patients in sub-Saharan African Sites with comprehensive monitoring availability. *Clin Infect Dis, 48*(1), 115-122.

[35] Krumme, A.A., Kaigamba, F., Binagwaho, A., Murray, M.B., Rich, M.L., & Franke, M.F. (2014). Depression, adherence and attrition from care in HIV-infected adults receiving antiretroviral therapy. *J Epidemiol Community Health*, *69*: 284-289.

[36] National Institute on Drug Abuse. Drugs, Brain and Behavior: The Science of addiction.

Available from <a href="https://www.drugabuse.gov/publications/drugs-brains-behavior-science-">https://www.drugabuse.gov/publications/drugs-brains-behavior-science-</a>
addiction/drugs-brain. Accessed 20 March 2016.

[37] Hull, P., Mao, L., Kao, S.-C., Edwards, B., Prestage, G., Zablotska, I. et al. (2014). Gay Community Periodic Survey: Sydney 2013. Sydney: National Centre in HIV Social Research, University of New South Wales.

[38] Hatzenbuehler, M. L. (2009). How does sexual minority stigma "get under the skin"? A psychological mediation framework. *Psychol Bull*, *135*(5), 707.

[39] Springer, S. A., Dushaj, A., & Azar, M. M. (2012). The impact of DSM-IV mental disorders on adherence to combination antiretroviral therapy among adult persons living with HIV/AIDS: a systematic review. *AIDS Behav*, *16*(8), 2119-2143.

[40] Sayles, J. N., Wong, M. D., Kinsler, J. J., Martins, D., & Cunningham, W. E. (2009). The Association of Stigma with Self-Reported Access to Medical Care and Antiretroviral Therapy Adherence in Persons Living with HIV/AIDS. *J Gen Intern Med, 24*(10), 1101-1108.

[41] Johnson, M. O., Neilands, T. B., Dilworth, S. E., Morin, S. F., Remien, R. H., & Chesney, M. A. (2007). The role of self-efficacy in HIV treatment adherence: validation of the HIV Treatment Adherence Self-Efficacy Scale (HIV-ASES). *J Behav Med*, *30*(5), 359-370.

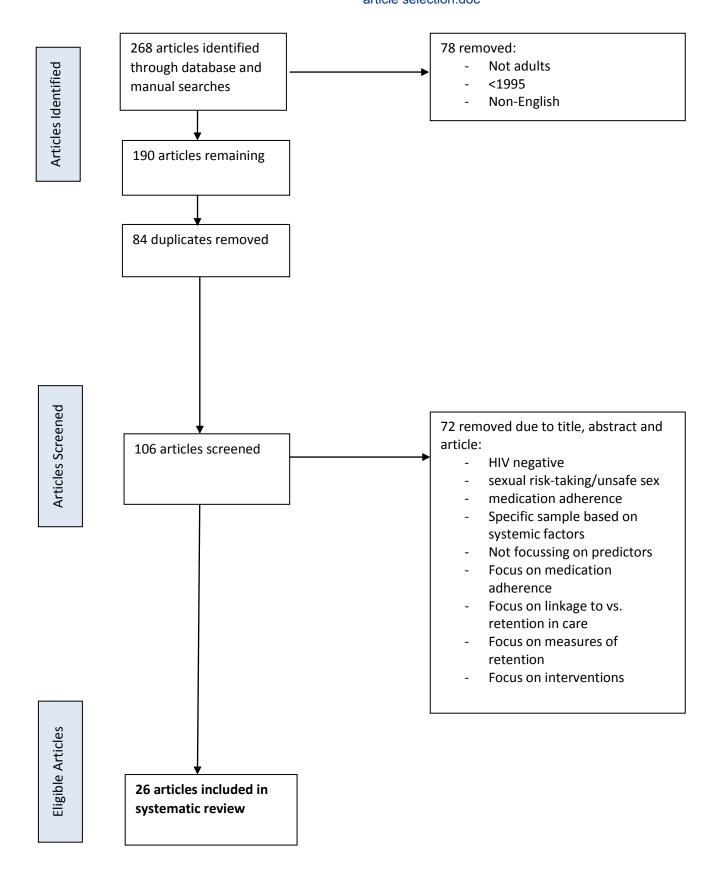


Figure 1. PRISMA-P flowchart of article selection

# Table I. Predictors of retention in HIV care – Developed and developing countries

First author (year) [article number]	Study dates	Country/Setting	Study design	Participants (N)	Predictors of retention
Allam (2014) [25]	January - December 2008	India/high caseload HIV clinics	Prospective cohort study	PLWHIV (≥ 15 years of age) initiated on ART during the study period (1690)	Demographics; Medical
Althoff (2013) [12]	January 2008 - March 2011	US/prisoners recently released	Prospective cohort study	PLWHIV prisoners recently released (867)	Demographics; Substance use; Support
Blank (2015) [18]	Unspecified	US/eight clinical services	Prospective cohort study	PLWHIV women of colour (921)	Demographics; Health Beliefs; Medical; Mental Health; Social/welfare
Boyles (2011) [30]	June 2005 – May 2009	South Africa/patients of a rural ART program	Prospective cohort study	PLWHIV initiated on ART during the study period (1803)	Demographics; Medical
Charurat (2010) [26]	March 2005 – July 2006	Nigeria/five health facilities	Prospective cohort study	PLWHIV initiated on ART during the study period (5760)	Demographics; Medical
Dombrowski (2015) [21]	April 2013 –April 2014	US/public health facility	Prospective cohort study	Diagnosed with HIV for ≥ 6 months with either (a) no CD4 count or VL results for ≥ 12 months, or (b) VL > 500 copies/mL (247)	Mental health; Substance use
Giordano (2009) [13]	1997 - 1998	US/Database of veterans with HIV	Retrospective cohort study	PLWHIV veterans (2,619)	Demographics; Medical; Substance use
Horberg (2015) [19]	2010 - 2012	US/HIV multi-site clinic	Retrospective cohort study	PLWHIV (>23,000)	Demographics
Kelly (2014) [24]	January 2006 - September 2007	US (Texas)/outpatient HIV clinic	Prospective observational	Diagnosed with HIV in previous 90 days and not yet have completed an outpatient visit with a care provider (168)	Social support (not significant)
Koole (2014) [31]	2003 - 2010	Tanzania, Uganda, Zambia/ART clinics	Retrospective cohort study	PLWHIV initiated on ART during the study period (4147)	Demographics; Medical
Krumme (2014) [35]	July 2006 – August 2008	Rwanda/ART clinics	Prospective cohort study	PLWHIV initiated on ART during the study period (610)	Mental health
Lourenço (2014) [14]	2011	Canada (BC)/database including residents diagnosed with HIV	Retrospective cohort study	PLWHIV (7621)	Substance use
McMahon (2015) [17]	February 2011 - June 2013	Australia (VIC)/ HIV clinics	Retrospective cohort study	PLWHIV (4966)	Health beliefs; Mental health; Time
Mutasa- Apollo (2014) [27]	2007 - 2009	Zimbabwe/multi-site clinics	Retrospective cohort study	PLWHIV initiated on ART during the study period (3919)	Demographics; Medical

First author (year) [article number]	Study dates	Country/Setting	Study design	Participants (N)	Predictors of retention
Noysk (2015) [10]	July 1996 - June 2012	Canada (BC)/database including residents living with HIV	Retrospective cohort study	PLWHIV (6152)	Demographics; Medical; Substance use
Palombi (2009) [34]		Mozambique, Milawi, Guinea- Conakry/public sector HIV clinics	Retrospective cohort study	PLWHIV initiated on ART during the study period (3749)	Medical
Rebeiro (2013) [15]	2000 - 2008	US and Canada/epidemiological database	Retrospective	PLWHIV ≥18 yo, receiving care in US or Canada with ≥ 1 CD4 or VL result (61,438)	Demographics; Social/welfare; Substance use
Richey (2014) [20]	Unspecified	US/public health facility	Prospective study	PLWHIV newly diagnosed by a public health ED (99)	Demographics; Linkage to care; Medical
Schafer (2012) [22]	April 2010 -April 2011	US/HIV clinic	Cross-sectional cohort study	PLWHIV (251)	Domestic violence
Tedaldi (2014) [7]	2000 - 2011	US/HIV clinics	Prospective observational cohort study	PLWHIV (1441)	Medical; Social/welfare
Thida (2014) [28]	June 2005 – October 2011	Myanmar/Integrated HIV Care Program	Retrospective cohort study	PLWHIV (5718)	Demographics; Medical
Tobias (2007) [16]	October 2003 - July 2005	US/Multi-site HIV clinics	Prospective, semi- structured interviews and review of blood results	PLWHIV (1000)	Health beliefs; Mental health; Substance use; Support
Vella (2010) [29]	March 2004 – May 2006	South Africa/public HIV clinics	Retrospective cohort study	PLWHIV initiated on ART during the study period (2835)	Demographics; Medical; Process/Clinic factors
Vuylsteke (2015) [32]	January – December 2010	Ivory Coast/HIV clinics	Retrospective cohort study	PLWHIV sex workers (414)	Demographics; process/Clinic factors
Waldrop- Valverde (2014) [23]	August 2009 - May 2011	US/HIV clinics in Florida	Prospective cohort study	Outpatient PLWHIV (210)	Cognitive impairment; Support
Yang (2015) [33]	Until June 2013	China	Retrospective cohort study	PLWHIV (822)	Demographics; Medical

Table II. Summary of predictors of retention in care, and associated articles – Developed Countries

Predictor(s) of retention in care	Number of articles in which predictor(s) is/are cited	Referenced in [First author (year)]
Substance use	7	Althoff (2013); Dombrowski (2015); Giordano (2009); Lourenço (2014); Noysk (2015); Rebeiro (2013); Tobias (2007)
Demographic	7	Althoff (2013); Blank (2015); Giordano (2009); Horberg (2015); Noysk (2015); Rebeiro (2013); Richey (2014)
Medical	5	Blank (2015); Giordano (2009); Noysk (2015); Richey (2014); Tedaldi (2014)
Mental health	4	Blank (2015); Dombrowski (2015); McMahon (2015); Tobias (2007)
Support	4	Althoff (2013); Kelly (2014); Tobias (2007); Waldrop-Valverde (2014)
Health beliefs	3	Blank (2015); McMahon (2015); Tobias (2007)
Social/welfare	3	Blank (2015); Rebeiro (2013); Tedaldi (2014)
<b>Cognitive impairment</b>	1	Waldrop-Valverde (2014)
Domestic violence	1	Schafer (2012)
Linkage to care	1	Richey (2014)
Time	1	McMahon (2015)

# Table III. Summary of predictors of retention in care, and associated articles – Developing Countries

Predictor(s) of retention in care	Number of articles in which predictor(s) is/are cited	Referenced in [First author (year)]
Demographic	8	Allam (2014); Boyles (2011); Charurat (2010); Koole (2014); Mutasa-Apollo (2014); Thida (2014); Vella (2010); Vuylsteke (2015); Yang (2015)
Medical	8	Allam (2014); Boyles (2011); Charurat (2010); Koole (2014); Mutasa-Apollo (2014); Palombi (2009); Thida (2014); Vella (2010); Yang (2015)
<b>Process/Clinic Factors</b>	4	Koole (2014); Mutasa-Apollo (2014); Vella (2010); Vuylsteke (2015)
Mental health	1	Krumme (2014)