

Factors impacting on adherence of antiretroviral treatment for people living with HIV/AIDS in Asian developing countries: a systematic review

Reference:

Wasti SP, van Teijlingen E, Simkhada P, Randall JA, Baxter S, Kirkpatrick P, Vijay Singh Gc. (2012) Factors influencing adherence to antiretroviral treatment in Asian developing countries: a systematic review, *Tropical Medicine & International Health* **17**(1): 71-81

Abstract

Background

Patient adherence to prescribed antiretroviral medication is crucial to achieve optimum results from Human Immunodeficiency Virus (HIV) treatment. Poor adherence leads to treatment failure with many studies observing that numerous factors impact negatively or positively on adherence to antiretroviral treatment (ART).

Objectives

This study aims to systematically review the literature of factors affecting adherence to ART in Asian developing countries.

Methods

Database searches were conducted in Medline/Ovid, Cochrane library, CINAHL, Scopus and PsychINFO for studies published between 1996 and December 2010. The reference lists of included papers were also checked, with citation searching on key papers.

Results

A total of 437 studies were identified, and 18 articles met the inclusion criteria and were extracted and critically appraised, representing in 12 quantitative, four qualitative and two mixed-methods studies. Thirty-one individual themes, including financial difficulties, side-effects, access, stigma and discrimination, simply forgetting, and being too busy had a negative impact on adherence to ART, and 11 themes, including family support, self-efficacy, and desire to live longer had a positive impact.

Conclusion

Adherence to ART is a dynamic phenomenon which varies between individuals. We need to address the negatively impacting factors while positively impacting factors should be promoted to the wider population. Policy makers should develop targeted interventions, such as, financial support, better access points for refill medicine and consulting doctors for support with side-effects, social support, warm and caring relationships with care providers to promote and reinforce adherence.

Background

Antiretroviral treatment (ART) aims to provide relief to HIV-infected individuals by reducing the likelihood of opportunistic infections rather than curing the disease. Since 1996 the introduction of ART has significantly improved the life span and quality of life for people living with HIV (PLWH) (Amico *et al.*, 2005). Better ART has led to a reduction in disease progression, but around 25% of new HIV cases are regimen resistant (DoH, 2001). Hence, HIV is still a life threatening and lifelong infection.

Medication adherence is a crucial component for successful treatment as it has been associated with clinically significant viral load reduction (Lopez *et al.*, 2007). However, maintaining optimal levels of adherence over a lifetime is difficult (Cooper *et al.*, 2009). Obtaining the full benefits of ART is a complex individual behavioural process determined by many broader factors including patient attributes and health care systems. Human behaviours and beliefs, inadequate knowledge and negative attitudes toward ART, drug side-effects, financial constraints, service-related factors, stigma, discrimination, inability to disclose HIV status and various socio-cultural issues [pic](Nordqvist *et al.*, 2006, Kgatlwane *et al.*, 2005, Mills *et al.*, 2006b, Sanjobo *et al.*, 2009, Hendershot *et al.*, 2009, Murray *et al.*, 2009) may be significant impacting factors that prevents patients from seeking treatment as well as maintaining adherence. Although there was “a paucity of data to guide the implementation of adherence intervention in clinical settings” (Simoni *et al.*, 2006). Systematic reviews on aspects of adherence to ART have been conducted elsewhere [pic](Simoni *et al.*, 2006, Mills *et al.*, 2006a, Falagas *et al.*, 2008, DiMatteo, 2004, Hendershot *et al.*, 2009, Malta *et al.*, 2008, Mills *et al.*, 2006b); however, there appears to be no systematic review on factors impacting on adherence to ART in Asian developing countries. Therefore, this review of published articles on factors impacting on adherence to ART could have significant value in Asia as well as providing information for wider populations in order to achieve full benefits for ART patients and service providers.

Aims

The main aim is to systematically review the literature on factors impacting on adherence to ART in Asian developing countries.

Methods

This review considered qualitative, quantitative and mixed-method studies that examined factors impacting on adherence of ART for PLWH. Combining quantitative and qualitative studies in a systematic review may provide additional insights into links between theory and practice (Dixon-Woods *et al.*, 2005). Qualitative research may provide detailed information on delivery of interventions, which is not the focus of quantitative studies. Therefore, this review included qualitative data from individual interviews and focus group discussions together with quantitative survey data. It has been argued that including both qualitative and quantitative studies in a review may limit bias, improve reliability and enhance accuracy of recommendations (Mulrow, 1994).

Inclusion and exclusion criteria

The population consisted of participants over the age of 18 years who had been prescribed ART. Similarly, data describing ART service providers were also included to provide a staff perspective regarding factors impacting on adherence to ART. The included studies considered populations from 24 Asian developing countries as defined by the World Bank (WorldBank., 2010) . Papers where the language was not English, published before 1996, review articles, policy documents, and adherence training manuals were excluded.

Search and selection methods

A systematic search of articles that focused on factors impacting on adherence to ART was undertaken in relevant databases. Searches were based only in English because of problems of analysing other languages. The following electronic databases were searched: Medline/Ovid, Cochrane library, CINAHL, Scopus, PsycINFO between 1996 to December 2010. The search strategy combined the following key words: *HIV or AIDS, antiretroviral or HAART or ARV, adherence or compliance, factor* or determin* or barrier*, facilitate* or motivate*, Asia*. In addition to the database searching, reference lists of included papers were checked and citation searching was carried out on key papers.

Study selection and data extraction

Two authors independently reviewed the retrieved studies at title and abstract level. Those articles meeting the inclusion criteria were critically appraised. A standard data extraction form was used which covered both quantitative and qualitative research. The data extraction form was developed using the Centre for Reviews and Dissemination guidance template (CRD, 2009). Standardised data extraction forms provide consistency of results that reduce bias, improve validity and reliability. This form records basic information first (authors, date, title of paper and journal details), then detailed information about each study (study design, study location, aims of the study, study population, sample size and major findings) and reviewers' comments. Data extraction was double-checked and, if necessary, amendments were made after discussion.

Quality appraisal and data synthesis

Included studies were assessed for quality and relevancy to understanding the strengths and weaknesses of the body of evidence (Pawson, 2008, CRD, 2009). Quality assessment was undertaken following Hawker and colleagues, since their tool is validated for both qualitative and quantitative methods systematic review in health care settings (Hawker *et al.*, 2002). This checklist consists of nine questions each with four subcategories (good, fair, poor and very poor) of methodological quality that ranges from nine (very poor) to 36 (good). All articles were

assessed to be of good methodological quality with scores ranging from 22 to 34. The included studies were read several times and findings were coded and organized in a tabulation form. Due to the heterogeneity of the data (quantitative and qualitative), meta-analysis was not appropriate. Therefore, a thematic synthesis was undertaken (Harden and Thomas, 2005) and the results were presented in table format (Dixon-Woods *et al.*, 2005).

Results

Figure 1 shows that 12 articles were selected from the database search and six emerged from reference lists. All studies were conducted between 2005 and 2009. Papers were excluded on the grounds of not covering Asian developing countries, wrong age range, non-English language and addressing effectiveness of treatment rather than adherence. Thirteen studies were quantitative, four were qualitative and two mixed methods. The sample size of the studies ranged from 27 to 1,366. Ten of the 18 studies were from India [pic](Akhila *et al.*, 2010, Cauldbeck *et al.*, 2009, Kumarasamy *et al.*, 2005, Sarna *et al.*, 2008, Shah *et al.*, 2007, Sharma *et al.*, 2007, Sogarwal and Bachani, 2009, Wanchu *et al.*, 2007, Venkatesh *et al.*, 2010, Safren *et al.*, 2005), four from China [pic](Sabin *et al.*, 2008, Starks *et al.*, 2008, Wang *et al.*, 2008b, Wang *et al.*, 2009), three from Thailand [pic](Li *et al.*, 2010, Ruanjahn *et al.*, 2010, Han *et al.*, 2009), and one from Cambodia [pic](Spire *et al.*, 2008b) (Table I). The 18 studies identified factors impacting (negatively and positively) on adherence (see Appendix I and II).

Figure 1: Review of studies for inclusion [pic]

Table I: Basic characteristics of the study

Author/year	Study conducted year	Location & setting	Study design	Sample size & sampling methods	Mode of information collection
Akhila et al. 2010	2006- 2007	India/ hospital	Quantitative / survey	313/ (sampling procedure unclear)	Not clear
Cauldbeck et al. 2009	2006	India/ hospital	Quantitative / survey	60/ (sampling procedure unclear)	Self-administered anonymous questionnaire survey
Han et al. 2009	2009	Thailand/ hospital	Qualitative/ in-depth interview	27/purposive convenience sampling	In-depth interview
Kumarasamy et al. 2005	Not stated	India/ private ARV treatment centre	Qualitative	60 (sampling procedure unclear)	Semi structured in-depth interview
Li et al. 2010	2007	Thailand/ hospital	Quantitative / survey	507/ ARV (sampling procedure unclear)	Interview with structured questionnaire
Ruanjaha et al. 2010	2006	Thailand/ home/ clinic	Mixed approach	32/ purposive or judgmental sampling	Pre-tested self reported adherence survey and semi structured interview
Sabin et al. 2008	2005 - 2006	China/ hospital	Qualitative	36 (sampling procedure unclear)	Semi structured in-depth interview and FGD
Safren et al. 2005	Not stated	India/ clinic	Quantitative / Survey	304 (sampling procedure unclear)	Self -reported questionnaire
Sarna et al. 2008	2004	India/ health facilities	Quantitative / survey	310 /(sampling procedure unclear)	Semi-structured interview with pre-tested questionnaire
Shah et al. 2007	2004 -2005	India/ 3 private outpatients clinics	Quantitative / survey	279/ convenience sampling	Structured interview with pre-tested questionnaire
Sharma et al. 2007	November 2004 -2005	India/ hospital	Mixed approach	226/ purposive sampling (snow ball sampling)	Semi structure questionnaire survey/ interview
Sogarwal & Bachani 2009	2007	India/ 27 ARV centres	Quantitative / survey	1366 / (sampling procedure unclear)	Face to face interview
Spire et al. 2008	2004 -2005	Cambodia/ hospital	Quantitative / survey	346 (sampling procedure unclear)	Individual face to face pretested standardizes questionnaire interview
Starks et al. 2008	Not stated	China/ hospital	Qualitative/ in-depth interview	29/ (sampling procedure unclear)	Semi structured in-depth interview

Wanchu et al. 2007	2004 -2005	India/ clinic	Quantitative / survey	200/(sampling procedure unclear)	Self-reported questionnaire sur
Wang et al. 2008	2006	China/ 7 ART centres	Quantitative / survey	308 (sampling procedure unclear)	Structured face t face survey
Wang & Wu 2007	2005	China/ rural areas	Quantitative / Survey	181/ (sampling procedure unclear)	Interviewer administered pre-tested questionnaire
Venkatesh et. al 2010	Not stated	India/ clinic	Quantitative / survey	198/ (sampling procedure unclear)	Structured interviewer administered questionnaire

Factors impacting on adherence to ART

Twenty-two individual themes regarding factors impacting negatively on adherence were identified from the 18 studies, encompassing patient-related factors, socio-cultural factors, and beliefs about medication, financial, health-system and drugs-related factors (see Appendix I).

Patient-related factors: Eighteen studies described individual factors impacting on adherence encompassing personal trust, beliefs, and motivation to take pills. Individual factors relating to non-adherence to treatment were: forgetting to take medication on time (8 studies) [pic](Li *et al.*, 2010, Cauldbeck *et al.*, 2009, Sarna *et al.*, 2008, Wanchu *et al.*, 2007, Wang and Wu, 2007, Shah *et al.*, 2007, Wang *et al.*, 2008a, Starks *et al.*, 2008), being too busy with other things (7 studies) [pic](Shah *et al.*, 2007, Wang and Wu, 2007, Sarna *et al.*, 2008, Li *et al.*, 2010, Wang *et al.*, 2008b, Han *et al.*, 2009, Safren *et al.*, 2005), being away from home (6 studies) [pic](Safren *et al.*, 2005, Sarna *et al.*, 2008, Wanchu *et al.*, 2007, Shah *et al.*, 2007, Wang *et al.*, 2008a, Starks *et al.*, 2008), not understanding treatment (5 studies) [pic](Han *et al.*, 2009, Wanchu *et al.*, 2007, Wang *et al.*, 2008a, Starks *et al.*, 2008, Li *et al.*, 2010), feeling depressed or overwhelmed (5 studies) [pic](Safren *et al.*, 2005, Sarna *et al.*, 2008, Sabin *et al.*, 2008, Akhila *et al.*, 2010, Sogarwal and Bachani, 2009), concurrent substance misuse (including alcohol & drug, 4 studies) [pic](Safren *et al.*, 2005, Wang *et al.*, 2008a, Venkatesh *et al.*, 2010, Sharma *et al.*, 2007), wanting to be pills free (2 studies) [pic](Wang *et al.*, 2008a, Starks *et al.*, 2008). Furthermore, one study each identified sleeping in (Wang and Wu, 2007), lack of motivation (Akhila *et al.*, 2010), stopping pills after feeling better [pic](Starks *et al.*, 2008), involvement in socio-community activities (Wang and Wu, 2007) and personal problem at home (Safren *et al.*, 2005) .

Socio-cultural factors: Factors having a negative impact on adherence to ART were: stigma and discrimination, fear of being recognized, fear of disclosure of status to community, and fear of stigma from family (7 studies) [pic](Wang and Wu, 2007, Wang *et al.*, 2008b, Akhila *et al.*, 2010, Sabin *et al.*, 2008, Starks *et al.*, 2008, Kumarasamy *et al.*, 2005, Li *et al.*, 2010). This review shows that to prevent unwanted disclosure, participants hid their medications which in turn led to either delayed or missed medications. Similarly, four studies reported that lack of family support led to non-adherence [pic](Wang *et al.*, 2008b, Akhila *et al.*, 2010, Kumarasamy *et al.*, 2005, Wanchu *et al.*, 2007).

Beliefs about medication: Two studies reported that patients did not think pills were needed [pic](Wang *et al.*, 2008b, Starks *et al.*, 2008), one that pills were a burden (Wang and Wu, 2007) and one that taking pills over a long period could lead to non-adherence (Venkatesh *et al.*, 2010).

Financial factors: Thirteen studies reported non-adherence due to financial difficulties [pic](Cauldbeck *et al.*, 2009, Sarna *et al.*, 2008, Akhila *et al.*, 2010, Han *et al.*, 2009, Wang and Wu, 2007, Sharma *et al.*, 2007, Kumarasamy *et al.*, 2005, Ruanjahn *et al.*, 2010, Spire *et al.*, 2008b, Safren *et al.*, 2005, Sogarwal and Bachani, 2009, Sabin *et al.*, 2008, Starks *et al.*, 2008). Transport, prescription charges, food costs and hospital diagnostic costs, were also prominent as reasons for patients failing to access their medication.

Health-system factors: This included accessibility of services and the relationship between service providers. Some health care delivery systems made it difficult to seek regular treatment.

Eight studies reported that distance from home to health services caused problems with access [pic](Starks *et al.*, 2008, Sarna *et al.*, 2008, Li *et al.*, 2010, Wang and Wu, 2007, Sogarwal and Bachani, 2009, Sharma *et al.*, 2007, Wanchu *et al.*, 2007, Cauldbeck *et al.*, 2009) and two studies found that inadequate counselling services (limited instruction provided) [pic](Starks *et al.*, 2008, Wang and Wu, 2007) prevented adherence.

Drug-related factors: Ten studies reported that drug side-effects were an important reason for non-adherence [pic](Sarna *et al.*, 2008, Wang and Wu, 2007, Sharma *et al.*, 2007, Li *et al.*, 2010, Kumarasamy *et al.*, 2005, Ruanjahn *et al.*, 2010, Spire *et al.*, 2008b, Safren *et al.*, 2005, Shah *et al.*, 2007, Wanchu *et al.*, 2007). Whilst two studies reported that the complexities of the medication regimens [pic](Wang and Wu, 2007, Ruanjahn *et al.*, 2010) had an impact on adherence to ART.

Factors positively impacting on adherence

Eleven themes were identified from the 18 studies as factors impacting positively (facilitators or motivators) on adherence to ART (Appendix III). Among them, four studies mentioned that social support [pic](Ruanjahn *et al.*, 2010, Kumarasamy *et al.*, 2005, Starks *et al.*, 2008, Akhila *et al.*, 2010), predominantly partners, children and friends played a significant role in increasing adherence. Similarly, three studies reported that self-efficacy [pic](Kumarasamy *et al.*, 2005, Starks *et al.*, 2008, Akhila *et al.*, 2010) and willingness to live longer [pic](Kumarasamy *et al.*, 2005, Starks *et al.*, 2008, Ruanjahn *et al.*, 2010) positively influenced adherence. Two studies noted that improved overall health [pic](Kumarasamy *et al.*, 2005, Starks *et al.*, 2008), getting financial assistance [pic](Kumarasamy *et al.*, 2005, Ruanjahn *et al.*, 2010) and being in higher income groups [pic](Ruanjahn *et al.*, 2010, Li *et al.*, 2010) resulted in better adherence. Moreover, the use of electronic reminders [pic](Starks *et al.*, 2008), obligation to live for family [pic](Starks *et al.*, 2008), good relationship with care providers [pic](Starks *et al.*, 2008), status disclosure [pic](Spire *et al.*, 2008a) and worries regarding a fear of drug resistance [pic](Starks *et al.*, 2008) were found to have a positive influence on adherence.

Discussion

In this review, findings of a mixture of studies on adherence to ART were analysed for experiences of patients who are prescribed ART and health service providers underlying the factors impacting on adherence. This review integrated results of both quantitative and qualitative studies reporting views of patients and healthcare providers and found that adherence is a dynamic phenomenon, but ART is also a lifelong commitment for PLWH and for maximum benefits of ART, adherence should be a priority.

The review revealed that individual personal factors such as simply forgetting, being too busy or depressed and substance misuse were common reasons impacting on non-adherence [pic](Wang *et al.*, 2008b, Wang *et al.*, 2009, Starks *et al.*, 2008, Sabin *et al.*, 2008, Sogarwal and Bachani, 2009, Sarna *et al.*, 2008, Sharma *et al.*, 2007, Shah *et al.*, 2007, Li *et al.*, 2010, Wanchu *et al.*, 2007, Venkatesh *et al.*, 2010, Cauldbeck *et al.*, 2009, Kumarasamy *et al.*, 2005). Regular patient follow-up and health carers giving attention during follow-up might help improve adherence. Patient specific and appropriate information and counselling may lead to better knowledge and, in turn

can help to promote adherence. Asking individual patients to describe their daily behaviour may be helpful and care providers could repeat instructions during follow-up appointments. Health care providers should provide personal support (reminders) or directly observe treatment to improve adherence rates. At the same time, substance misuse was a determinant of non-adherence. There is a need for those patients with concurrent substance misuse to have direct observed therapy. Patients who are depressed could be advised to undergo psychological treatment before initiating ART. Patients' self-efficacy, their desire to live longer and improve their overall health due to ART were all positive influence on adherence [pic](Ruanjahn *et al.*, 2010, Starks *et al.*, 2008, Akhila *et al.*, 2010, Kumarasamy *et al.*, 2005). This indicates that individual perceptions of ART effectiveness or visible signs that medications work are helpful to reinforce continuing adherence practices (Adam *et al.*, 2003).

Similarly, complexity of regimens such as fitting the regimens into daily life, and experience of side-effects were seen as important reasons for non-adherence in this review. ART drugs have toxicities and adverse side-effects (varying from mild to severe and from acute to chronic) can prevent adherence [pic](Catz *et al.*, 2000). One study reported that 92% of its study population were non-adherent due to the ART side-effects (Altice *et al.*, 2001). According to Wilson *et al.* illness ideology (representing someone's belief about treatment) was described as a factor influencing adherence choices based on either trust or distrust (Wilson *et al.*, 2002). Similarly, the primary reason for medication discontinuation often was regimen intolerance (Melbourne *et al.*, 1998). This suggests the importance of providing educational or counselling interventions as well as instructions on how to cope with these side-effects (Lewis *et al.*, 2006). Trust in ART medication, self-awareness of their health, and knowledge of the consequences of adherence and non-adherence are an important basis of both trust, and belief that can reinforce adherence despite ART side-effects. It is worth noting that the included papers are from narrow time span (2004 - 2009), during this time there was no significant variation in available regimens and patients were mostly prescribed first line ART.

Many studies identified financial difficulties (cost) as a factor affecting non-adherence. Two-thirds of the studies (n=12) stated that due to financial difficulties patients failed to adhere to their medication. Studies in other resource-limited settings also concluded that ART associated costs acted as a barrier to adherence to ART [pic](Tuller *et al.*, 2009, Konkle-Parker *et al.*, 2008, Mills *et al.*, 2006c, Naik *et al.*, 2009, Bartlett and Shao, 2009). Having a higher income and better access points for repeat prescriptions as well as obtaining financial support or support with travel costs generally improves adherence. [pic](Li *et al.*, 2010, Kumarasamy *et al.*, 2005, Ruanjahn *et al.*, 2010). Addressing the issue of non-adherence in Asian developing countries may therefore require a somewhat different approach to solutions applied in developed countries where financial issues are not such a major concern. The countries included in this study varied in the range of governmental and non-governmental support available for ART treatment. This will have impacted on issues of adherence.

This review shows that patients were embarrassed to take medication in front of others and concerned about their privacy when collecting repeat prescriptions; these worries inhibited adherence. Patients who had not disclosed their HIV status, did not have support, or were unable to disclose their status to others were more likely to be non-adherent [pic](Wang and Wu, 2007, Kumarasamy *et al.*, 2005, Rao *et al.*, 2007, Ferguson *et al.*, 2002). It was described in one study that PLWHs were unwilling to seek treatment at the nearest health institution because of fear of stigmatization (Adeneye *et al.*, 2006). Negative community myths and beliefs about HIV were barriers to ART adherence elsewhere too (Irwin *et al.*, 2003).

Understanding the cultural issues regarding adherence is an important aspect to develop evidence-based

interventions targeted at individuals with suboptimal adherence. Support from family members, including children, medication reminders and disclosing the ART status to others (family members, peers, and society) had a positive influence on adherence [pic](Spire *et al.*, 2008b). Governments should encourage a supportive environment where PLWHs do not have to worry about stigma and discrimination, but talk openly to try to enhance adherence. This review argues that care and support, both emotional and medical, can help PLWHs to lead a fulfilling life.

Good relationships and trust with care providers are essential to build open communication and support for adherence. The review found that good relationships with their care provider enabled patients to have better information about the importance of adhering to their regimes [pic](Starks *et al.*, 2008), which is also fostered if patients have a strong relationship with their health service provider (Lewis *et al.*, 2006).

The literature supports the view that care providers spending time explaining to patients encourages positivity and perhaps time spent talking to significant influencing groups would also help to reinforce adherence [pic](Aspeling and van Wyk, 2008, Coetzee *et al.*, 2004). Service providers should promote optimal adherence by giving clear instructions about taking their medication, medical follow-up, possible side-effects and how to handle the side-effects if they occur, all this would help to reinforce adherence. The review shows that acceptance, open communication, spending adequate time, cooperation and trust of health care providers enhanced adherence [pic](Falagas *et al.*, 2008, Ickovics and Meade, 2002b, Ickovics and Meade, 2002a). Thus, the locus of responsibilities and commitments for adherence to medication shifts from the individual ART-prescribed patient to the service providers and to treatment teams as a whole.

Conclusion

Adherence to ART is a dynamic phenomenon that varies over time and between individuals. Many factors negatively impacted while a few positively on adherence to ART in the Asian developing communities. Financial difficulties, stigma and discrimination, simply forgetting, being too busy, concurrent substance abuse, and side-effects were identified as factors negatively impacting on adherence. Similarly, self-efficacy, family supports and financial assistances were reported as factors impacting positively on adherence and those should be promoted to the wider population. Due to the fear of exclusion from their family and society, patients skipped medication if they had to take it in front of others. To avoid this, patients should be taught strategies on how to handle taking pills in secret to increase adhere to their medication. Similarly, health care providers should give clear instructions and proper counselling to the patients about how to manage ART if side-effects occur. Efforts must be made to understand and subsequently develop targeted interventions (e.g. supporting with travel costs, better access points for repeat prescription and consulting doctors for side-effects, improving relationship with care providers) to promote and reinforce adherence.

Addressing the issue of non-adherence in Asian developing countries may therefore require somewhat different approaches to those practised in the developed countries or elsewhere.

This review did not perform a meta-analysis and simply enumerated the impacting factors because of heterogeneity of the data (mixed studies). Drawing coherent conclusions in this review was hampered by limited data and methodological limitations because there is a scarcity of comparative studies. It is as yet unclear whether the behavioural, educational, bio-medical, drug treatments with fewer side-effects or financial supports are more or less powerful in enhancing adherence. This needs to be assessed in future studies.

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• Medline	=	73
• CINAHL	=	146
• Cochrane	=	84
• Scopus	=	71
• Psyc INFO	=	63
Total	=	437

Duplicates excluded = 43

Number of records after duplicates removed = 394

After title shifting and identified potential relevant rerecords = 315

Excluded at title level/irrelevant title = 79

Potential relevant records after abstract shifting = 46

Excluded at abstract level not original number, did not examine barriers, affecting factors, facilitators, motivators, were not focused on adherence to antiretroviral number, geographic range (outside study areas) = 269

Excluded after full text design due to geographic range, population (children), insufficient information regarding adherence, different language = 34

Total studies included in review = 12

Included
Identification

Eligibility

Screening

Citation search paper = 6

Total = 18