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

Reference:

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 (Nordqvist et al., 2006, Kgotlwane 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 (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, PsychINFO 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 (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 (Sabin et al., 2008, Starks et al., 2008, Wang et al., 2008b, Wang et al., 2009), three from Thailand (Li et al., 2010, Ruanjahn et al., 2010, Han et al., 2009), and one from Cambodia (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>
<thead>
<tr>
<th>Author/year</th>
<th>Study conducted year</th>
<th>Location &amp; setting</th>
<th>Study design</th>
<th>Sample size &amp; sampling methods</th>
<th>Mode of information collection</th>
</tr>
</thead>
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<tr>
<td>Akhila et al. 2010</td>
<td>2006-2007</td>
<td>India/ hospital</td>
<td>Quantitative</td>
<td>313/ (sampling procedure unclear)</td>
<td>Not clear</td>
</tr>
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<tr>
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<td>Qualitative/ interview</td>
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<tr>
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<td>Quantitative</td>
<td>507/ ARV (sampling procedure unclear)</td>
<td>Interview with structured questionnaire</td>
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<td>Thailand/ home/ clinic</td>
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<td>32/ purposive or sampling</td>
<td>Pre-tested self reported adherence survey and semi structured interview</td>
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<td>2005-2006</td>
<td>China/ hospital</td>
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<td>310/ (sampling procedure unclear)</td>
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<tr>
<td>Shah et al. 2007</td>
<td>2004-2005</td>
<td>India/ private outpatients clinics</td>
<td>Quantitative</td>
<td>279/ convenience sampling</td>
<td>Structured interview with pre-tested questionnaire</td>
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<tr>
<td>Sharma et al. 2007</td>
<td>November 2004-2005</td>
<td>India/ hospital</td>
<td>Mixed/ sampling (snowball sampling)</td>
<td>226/ purposive sampling</td>
<td>Semi-strucutured survey/ interview</td>
</tr>
<tr>
<td>Sogarwal &amp; Bachani 2009</td>
<td>2007</td>
<td>India/ 27 ARV centres</td>
<td>Quantitative</td>
<td>1366/ (sampling procedure unclear)</td>
<td>Face to face interview</td>
</tr>
<tr>
<td>Spire et al. 2008</td>
<td>2004-2005</td>
<td>Cambodia/ hospital</td>
<td>Quantitative</td>
<td>346 (sampling procedure unclear)</td>
<td>Individual face to face pretested standardizes questionnaire interview</td>
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<td>Not stated</td>
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<td>Qualitative/ interview</td>
<td>29/ (sampling procedure unclear)</td>
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<td>Location</td>
<td>Study Design</td>
<td>Sample Size</td>
<td>Data Collection Method</td>
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<tr>
<td>Wanchu et al. 2007</td>
<td>2004-2005</td>
<td>India/clinic</td>
<td>Quantitative</td>
<td>200 (sampling procedure unclear)</td>
<td>Self-reported questionnaire survey</td>
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<tr>
<td>Wang et al. 2008</td>
<td>2006</td>
<td>China/7 ART centres</td>
<td>Quantitative</td>
<td>308 (sampling procedure unclear)</td>
<td>Structured face to face survey</td>
</tr>
<tr>
<td>Wang &amp; Wu 2007</td>
<td>2005</td>
<td>China/rural areas</td>
<td>Quantitative</td>
<td>181 (sampling procedure unclear)</td>
<td>Interviewer administered pre-tested questionnaire</td>
</tr>
<tr>
<td>Venkatesh et al. 2010</td>
<td>Not stated</td>
<td>India/clinic</td>
<td>Quantitative</td>
<td>198 (sampling procedure unclear)</td>
<td>Structured interviewer administered questionnaire</td>
</tr>
</tbody>
</table>
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. 

\[\text{Starks et al., 2008, Sarna et al., 2008, Li et al., 2010, Wang and Wu, 2007, Sogarwal and Bachani, 2009, Sharma et al., 2007, Wanchu et al., 2007, Cauldbeck et al., 2009}\] and two studies found that inadequate counselling services (limited instruction provided) prevented adherence. 

\[\text{Starks et al., 2008, Wang and Wu, 2007}\]

**Drug-related factors:** Ten studies reported that drug side-effects were an important reason for non-adherence. 

\[\text{Sarna et al., 2008, Wang and Wu, 2007, Sharma et al., 2007, Li et al., 2010, Kumarasamy et al., 2005, Ruanjahn et al., 2010, Spire et al., 2008b, Safren et al., 2005, Shah et al., 2007, Wanchu et al., 2007}\]. Whilst two studies reported that the complexities of the medication regimens 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, predominantly partners, children and friends, played a significant role in increasing adherence. Similarly, three studies reported that self-efficacy, getting financial assistance, getting in higher income groups and being in higher income groups and being in higher income groups resulted in better adherence. Moreover, the use of electronic reminders, obligation to live for family, good relationship with care providers, status disclosure and worries regarding a fear of drug resistance 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. \[\text{Wang et al., 2008b, Wang et al., 2009, Starks et al., 2008, Sabin et al., 2008, Sogarwal and Bachani, 2009, Sarna et al., 2008, Sharma et al., 2007, Shah et al., 2007, Li et al., 2010, Wanchu et al., 2007, Venkatesh et al., 2010, Cauldbeck et al., 2009, Kumarasamy et al., 2005}\]. 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 patient’s 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.
### Appendix I: Factors negatively impacting on adherence

<table>
<thead>
<tr>
<th>Reference/year</th>
<th>Individual personal factors</th>
<th>Stigma &amp; discrimination</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Simply forgot</td>
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<td></td>
<td>Being too busy other things</td>
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<td></td>
<td>Away from home</td>
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<td></td>
<td>Don’t understand treatment</td>
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<tr>
<td>Family support</td>
<td>Self-efficacy</td>
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<td></td>
<td>Willingness to live longer</td>
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<td></td>
<td>Improved overall health</td>
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<td></td>
<td>Getting financial assistance</td>
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<td>Higher income</td>
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<td></td>
<td>Fear of drug resistance</td>
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<td></td>
<td>Use electronic reminder</td>
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<tr>
<td>Obligation to live for family</td>
<td>Good relationship with providers</td>
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<tr>
<td>Status disclosure</td>
<td>Akhila et al. 2010</td>
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<td>Kumarasamy et al. 2005</td>
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<tr>
<td>Li et al. 2010</td>
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<td>Ruanjahn et al. 2010</td>
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<td>Spire et al. 2008</td>
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<td>Starks et al. 2008</td>
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<td>Total studies</td>
<td>4</td>
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References


CRD (2009). *Undertaking systematic reviews of research on effectiveness: CRD’s guidance for those carrying out or commissioning reviews*. York, Centre for Reviews and Dissemination, University of York.


Harden, A & Thomas, J (2005). Methodological issues in combining diverse study types in systematic


Venkatesh, K, Srikrishnan, A, Mayer, K, Kumarasamy, N, Raminani, S, Thamburaj, E, Prasad, L, Triche, E,


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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

<table>
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Citation search paper = 6

Total = 18