Barriers and facilitators to antiretroviral medication adherence among HIV-infected paediatric patients in Ethiopia: A qualitative study

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Abstract
Medication adherence is a complex behaviour with multiple determinants. Understanding the barriers and facilitators of adherence is invaluable for programme improvement, which assists the foundation of adherence intervention strategies. A qualitative study was conducted in six selected hospitals of Addis Ababa in 2008, to explore barriers and facilitators to antiretroviral medication adherence among HIV-infected paediatric patients. Twelve caregivers of adherent and non-adherent children and 14 key informants in five hospitals were included in the study. The findings revealed that over-dosage (heavy pill burden), fear of stigma and discrimination, cost and access to transportation, lack of understanding of the benefit of taking the medication, economic problems in the household, and lack of nutritional support were the barriers to adherence to HAART. The presence of mobile/wall alarm, the presence of follow-up counselling, improved health of the child, ART clinic setups, and disclosure of HIV serostatus were among the facilitators. This study indicated that paediatric adherence to antiretroviral therapy faces a huge challenge. It suggests the provision of income-generating schemes to caregivers for assisting HIV-infected children. Health care providers should address proper usage of medication reminders.

Keywords: HIV/AIDS, adherence, antiretroviral therapy, children, Ethiopia.

Résumé
L'adhésion à un traitement médical est un comportement complexe aux déterminants multiples. La compréhension des obstacles à l'adhésion et ses facilitateurs sont inestimables pour l'amélioration des programmes contribuant à la fondation des stratégies d'intervention en matière d'adhésion. Une étude qualitative a été réalisée dans huit hôpitaux sélectionnés d'Addis-Abeba en 2008 afin d'explorer les obstacles à l'adhésion au traitement antirétroviral et ses facilitateurs chez les patients en pédiatrie infectés par le VIH. Douze soignants d'enfants adhérant et n'adhérant pas au traitement et 14 informateurs clés dans cinq hôpitaux ont participé à l'entretien. Les conclusions ont révélé que le surdosage (charge en pilule lourde), la peur de la stigmatisation et de la discrimination, le coût des transports et leur accès, l'absence d'une compréhension des bénéfices à prendre des médicaments, les problèmes économiques que rencontrent les ménages et l'absence de soutien nutritionnel constituaient des barrières à l'adhésion au traitement HAART. La présence d'une alarme mobile/murale, la fourniture d'une assistance psychosociale de suivi, la meilleure santé de l'enfant, les configurations cliniques de l'ART et la divulgation du statut sérologique faisaient partie des facilitateurs. Cette étude a indiqué que l'adhésion pédiatrique à la thérapie antirétrovirale se trouvait confrontée à un défi considérable. Cela nécessite la création d'un schéma de génération de revenus aux soignants pour aider les enfants infectés par le VIH. Les fournisseurs de soins de santé devraient traiter l'utilisation correcte des médicaments en surplus.

Mots clés: VIH/SIDA, adhésion, thérapie antirétrovirale, enfants, Ethiopie.
Introduction

Worldwide, about 2.3 million children are infected with HIV, of whom nearly 90% are in sub-Saharan Africa (UNAIDS/WHO, 2006). In 2006 alone, new infections in children under 15 years were estimated to be 530,000 (410,000 - 660,000) and there were 380,000 deaths (UNAIDS/WHO, 2006). It is currently estimated that 1.6 million children are infected every day (UNAIDS, 2004). During the last few years, the introduction of highly active antiretroviral therapy (HAART) has dramatically changed the natural course of HIV infection (Hogg et al., 1998; Palella et al., 1998).

Research indicates that consistently high levels of adherence are necessary for reliable viral suppression (Bangsberg et al., 2000; Paterson et al., 2000), prevention of resistance (Bangsberg et al., 2003), and disease progression (Bangsberg et al., 2001). Along with this, many factors can affect the ability of HAART to suppress viral replication, including low potency of one of the drugs in the combination, viral resistance, inadequate drug exposure and inadequate adherence to therapy. The major factor determining the success of HAART is sustained and optimum adherence to therapy (Starace, Massa, Amico, & Fisher, 2006), as poor adherence increases the risk of virological failure and viral resistance (Nischal, Khopkar, & Saple, 2005).

Sustaining adherence represents a significant challenge for children receiving treatment and for their caregivers. In order to facilitate adherence and improve outcome of HAART in HIV-infected children it is necessary to identify potential relevant issues in paediatric patients that influence adherence, and to determine the possible interventions to improve adherence in children (Shah, 2007). There is a paucity of reports on HAART in children from resource-poor settings. Therefore, understanding of barriers and facilitators helps in planning interventions to address adherence concerns. The objective of this study was to explore the barriers and facilitators to HAART adherence among HIV-infected children.

Methods

Study setting

The study was conducted in selected hospitals in Addis Ababa, the capital city of the Federal Democratic Republic of Ethiopia. In 2008 the total number of children on ART in Ethiopia was 5,245 (Federal Ministry of Health / HIV/AIDS Prevention and Control Office, 2008). The study was carried out in selected antiretroviral therapy units in Addis Ababa hospitals including Black Lion, St Peter, Yekatit 12, Zewditu, and ALERT Hospitals. Among these, Black Lion Hospital is a teaching hospital under the Federal Ministry of Education; St Paul Hospital is a general specialised hospital under the Federal Ministry of Health; St Peter Hospital is a generalised hospital for TB treatment and recently opened an ART clinic for adults and children; ALERT Hospital is also under the Federal Ministry of Health; and Yekatit 12 and Zewditu hospitals are under the Addis Ababa Regional Health Bureau, known to serve most of the patients on ART follow-up. The study was conducted from 18 February to 28 April 2008.

Design and participants

For this study, two population groups were chosen to be interviewed. The first group was patients who had received continuous antiretroviral therapy for the previous 12 weeks before the study in the selected hospitals, with caregivers who were parents or guardians who were counselled on the importance of drug adherence. In addition, this group needed to present for follow-up during the data collection period. In-depth interviews were undertaken with the caregivers in six selected adherent and six selected non-adherent cases of children with diverse socioeconomic and demographic characteristics (Table 1). Participants were eligible for the study if they expressed a willingness to share their views on adherence to ART. The second group was individuals involved in or supporting the provision of treatment and care for patients on ART. These individuals consisted of 14 key informants, eight counsellors and four physicians, including two paediatricians (Table 2).

Table 1. Characteristics of health care providers (N=14)

| Characteristics     | Number |
|---------------------|--------|
| Age in years        |        |
| 20 - 29             | 8      |
| 30 - 39             | 6      |
| Sex                 |        |
| Male                | 4      |
| Female              | 10     |
| Professionals       |        |
| Counsellor          | 8      |
| Physician           | 4      |
| Paediatrician       | 2      |

The number of interviews was determined by saturation of data (successive interviews become repetitive and redundant so that no new information can be gathered by further data collection). A purposive sampling technique was carried out to select the participants. The key informants were selected based on exposure to children in all circumstances, their ability to appreciate the problems of adherence, and their perceptions of what helps and/or hinders patients from taking ART regularly, as well as capability to suggest intervention mechanisms for improving adherence to ART.
In-depth interviews were conducted by the principal investigator with caregivers of HIV-positive children and health workers, including counsellors and paediatrician. An interview guide was used, which consisted of open-ended questions related to broad subject areas regarding: knowledge of the disease and its treatment, factors that influence adherence, personal perspectives of the medication, and barriers and facilitators of patient adherence to treatment. The interviews were conducted in a hospital setting that was convenient for key informants as well as caregivers. The level of adherence was assessed by self-report (of the primary caregiver). Field notes were written at the conclusion of each interview and all tapes were transcribed. Ethical clearance was obtained from Jimma University and Addis Ababa Health Bureau. Caregivers were informed that refusing to participate in the study would not affect their access to treatment. All participants who were interviewed individually gave consent.

Data analysis
The interview data were analysed manually, using thematic content analysis. This approach is a comparative process by which the various accounts gathered are compared with each other to classify those ‘themes’ that recur or are common in the data set (Green, & Thorogood, 2004). All transcripts were read several times by the investigators separately to bring out the main ideas, barriers and facilitators of adherence. Later the data were reviewed and combined into broader categories in terms of key variables; the information was then ordered, reduced and classified or coded, displayed, summarised and finally interpreted. Identification of barriers and facilitators of ART adherence were evaluated according to the principles of phenomenological analysis, in that inquiry aimed to fully describe the lived experience of those children who took antiretroviral therapy, as well as the perceptions of the caregivers on the barriers and facilitators in day-to-day life (Polit & Beck, 2004).

Results
In this study several barriers and facilitators of paediatric adherence were identified. These factors are presented below.

Key barriers

Caregiver factors/characteristics

From all the in-depth interviews with caregivers and health care providers, reasons for missing health facility appointments include caregivers visiting holy water places or another area outside of their place of residence. A 34-year-old female caregiver reported a reason for not giving the medication as leaving home to visit relatives:

I was visiting my relatives in rural area as a result of my mother's death. I left the child with his grandfather. He is very old to follow-up.

Potential barriers to adherence include non-disclosure of HIV status, poverty and nutritional problems, lack of social support, and absence of a private place to take the medicine when relatives/neighbours came to their home, for fear of stigma and discrimination. Both the caregivers and health care providers reported non-disclosure as a significant barrier in handling HIV-infected children:

I have worked in this hospital for several years. Most of the time the children do not know their serostatus, and this results in difficulties of treating HIV infected children.

(28-year-old female nurse, in hospital setting)

The majority of caregivers reported a common barrier as moving from house to house, as most of them did not have their own house. Many caregivers experienced problems like access to transportation, and economic problems in the household:

My family didn't have adequate money to spend toward the child's transportation. I came from a long distance. We usually come on foot.

(43-year-old grandfather of non-adherent children)
As explained by the caregivers, nutritional problems were a common barrier to patient adherence to medication regimens. The issue of food security is a prerequisite for the initiation, as well as the continuation of the treatment. One 32-year-old male caregiver expressed this idea in few words: no food, no drug to take.

A 28-year-old female nurse counsellor from one of the hospitals stated the situation as follows:

There is no food /nutrition in the households, so the children are not taking the medication. As most of the caregivers are HIV positive, they don’t have any food to eat for themselves let alone their children.

The health care providers described the issue of barriers to adherence from the caregivers’ perspective. They described the caregivers of non-adherent children as grandparents, less educated, or having a lack of understanding of the benefits of taking the medication. Children did not have the capacity and ability to take the medication; hence, this is a critical component of the administration of the drugs. However, caregivers were reportedly unconvinced that these matters could affect the medication adherence of the children.

Providers found a significant challenge in adherence counselling due to the fears of stigma and discrimination that caregivers possess. A 27-year-old male health care provider stated:

At the time the child should take the drugs he/she is not given them since relatives are at home. The child immediately goes to the bedroom without taking his/her medication.

Medication-related factors

Most of the caregivers and health care workers reported the high dosages (heavy pill burden), patient dislike of taking the medication, and the children spitting out the medication as causes of poor adherence to the medication regimens. Caregivers also reported that the time of administration of the prescribed drugs was conflicting with normal working hours.

Caregivers’ and health care providers’ relationship

Counsellors stressed the importance of the physician’s communication of the importance of ART adherence. In the initial phase, before the start of treatment, there might be problems in communication between patients and providers. However, repeated counselling could lead to better understanding among caregivers. One problem in patient-provider relationships in treating HIV-infected children was the rotation of residents in the hospital setting, particularly in two of the teaching hospitals:

As they shift, the child may be seen by different physicians throughout his/her treatment course... that poses a challenge. (30-year-old female nurse counsellor)

I already gave the whole history of my child to the physician one year ago but still the new physician asks the child’s status now and then... it is boring (37-year-old government employed male caregiver)

Key facilitators

Both the caregivers and health care providers reported facilitators of adherence to prescribed medication as: equipment for children to play with in hospitals; the presence of both parents alive at home with the child; the receipt of ongoing counselling to the caregivers on adherence; disclosure of the diagnosis of HIV to the child; a well-educated caregiver; and seeing the improvement in quality of life in the children. The majority of the children came to the hospital without missing their follow-up appointments because they felt content in the hospital setting and they were able to play with children of the same age group:

Children have an opportunity to draw a picture, paint on paper, and have a good relationship with us in this manner (28-year-old female nurse counsellor in hospital setting)

The other facilitator identified by respondents was the presence of medication reminders. A 29-year-old male caregiver noted:

I use a calendar for memorising/reminding me of the time the drugs should be given.

The most common denominator for facilitating adherence was the approach of the health worker toward the caregiver at all times, in order to enhance the dialogue process:

... Approach and deep understanding of the caregiver during discussion is vital for the smoothness of the communication process. (32-year-old female hospital paediatrician)

Successful strategies for improving adherence

During interviews participants not only identified barriers and facilitators to adherence, but also developed specific strategies to overcome barriers that they had. Several patients believed that improving their communication with their providers was a feasible and important goal in improving adherence. Health care professionals pointed out strategies to be recommended
for improving adherence to antiretroviral therapy, including educating the community about adherence as well, disclosure of HIV status to children as early as possible based on the developmental stage of the child. Others explained the importance of providing income-generating schemes and harmonisation of the work rendered by non-governmental organisations. Moreover, patient-provider interaction should be encouraged before the commencement of the medication, in order to improve adherence. Enhancing the psychological make-up of the caregivers is of importance, as continued education for illiterate attendants and counselling might help improve adherence. The majority of adherent caregivers indicated that early clinical visits to the hospital helped them to monitor and control their medication in a better way.

Discussion

Resource-limited settings present unique challenges to ART adherence. A multitude of structural barriers prevent access to health care and the regular supply of antiretroviral drugs. These include the cost of medical care, drugs, and the difficulty of making follow-up appointments due to long distances, family responsibilities, and the prohibitive cost of transportation (Mukherjee et al., 2006). This finding is consistent with our findings, in that cost of transportation becomes a huge burden to the family, so the family income becomes a major barrier for sustained treatment with ART in low-income countries. Again, this is supported by a body of literature (Bangsberg, Ware, & Simoni, 2006; Byakika-Tusime et al., 2005; Lanièce et al., 2003; Nachega et al., 2004; Weiser et al., 2003).

Nutritional support was found to be a significant contributor to medication adherence, as lack of nutritional support at the health facilities level emerged as an important factor for ART non-adherence in our study. In similar fashion, other qualitative studies found that food security was a barrier to successful utilisation of HAART (Howland et al., 2000; Martínez et al., 2000). This is a critical factor in implementation of an ART programme, so that it is imperative to take a look at nutritional support as a precursor to ART uptake leading to better adherence. In addition, in this study, housing instability was demonstrated as a barrier, which is consistent with Martínez et al. (2000) and Howland et al. (2000), who identified negative life events (e.g. housing instability, poverty) and economic instability as significant factors in predicting adherence. This has important implications, as participants who could secure stability concerning financial matters were more likely to take their medication regularly.

The present study’s findings suggest that HIV serostatus disclosure influences adherence to ART regimens for some HIV-positive children. This is supported by a study of HIV-infected adults, which found that the most frequent reasons for non-adherence reflected general concerns about treatment as a reminder of one’s HIV status, not wanting other people to know one’s HIV status, and difficulty remembering to ask health care providers questions about treatment (Catz, Kelly, Bogart, Benotsch, & McAuliffe, 2000). This is probably due to the fear of stigma and discrimination attached to taking medication at home, as relatives or neighbours might be present at the time. The majority of participants listed being away from home and getting holy water for themselves and their children as reasons for not providing medication. Various other studies support the finding that being away from home is a barrier to medication adherence (Laws, Wilson, Bowser, & Kerr, 2000; Ryan, & Wagner, 2003; Witteveen, & van Ameijden, 2002). The number of medications prescribed has also been found to affect adherence (Samet et al., 1992), which was consistent with our findings.

In our study, physician communication with patients was successful as reported by both nurse counsellors and caregivers, but problems arose in selected hospitals where physician rotation presented a potential gap between physician and caregiver. An expanded view that takes account of this fact is that poor provider-patient relationships have an impact on adherence (Okuno, Yanagi, & Tomura, 2001). Many of the study participants interviewed identified the presence of medication reminders as methods that successfully helped them to remember their prescribed medication. Similar findings have been documented in studies carried out by Adam, Maticka-Tyndale and Cohen (2003) and Lyon et al. (2003), which also found little support for using cue-based strategies to improve adherence among children and adolescents with HIV.

This study has several important strengths. The identification of both the barrier and facilitator questions was selected systematically from different bodies of literature, and the participants represented varied patient populations in order to strengthen the conclusions of this study. Qualitative studies are well suited to identifying patient-important barriers and facilitators: the use of an in-depth interview approach permitted us to discover a diversity of ideas and practices which most likely would not have been detected using a quantitative approach. Additionally, complementing patient information with provider information enables a more complete picture of adherence issues. The study encompassed the major reference paediatric ART hospitals in Ethiopia, enabling a broad sampling of geographical variability as well as socio-cultural phenomena that are associated with culturally relevant barriers to adherence. Finally, the findings of this study hold significance...
relevant to the developing world as there is a paucity of such studies in low-income countries (Mills, Nachega et al., 2006). Despite this, the study had some limitations. The findings from this study reflect the caregiver’s perceptions of reported barriers and facilitators of adherence to antiretroviral therapy. The cross-sectional nature of the interviews limited our ability to assess changes in adherence, while adherence is a dynamic process not to be predicted at a single point in time. A qualitative study may limit the generalisability of findings, yet be relevant for idea/hypothesis generation concerning further research.

In conclusion, paediatric adherence to antiretroviral therapy faces huge challenges in the future. Disclosure of HIV status, food insecurity, costs of transportation, housing instability, medication factors, and patient-provider communication were found to be of major concern among caregivers and providers. This highlights the importance of income-generating schemes for the caregiver in assisting HIV-infected children. Also, health care providers should address proper usage of alarms and mass media for medication reminders. The health worker should stress ART drug adherence, health education should be tailored in mass media to the community, and provision of nutritional support to the caregiver should be stressed as well. Though the challenges are large, they are by no means insurmountable, and the identification of facilitators and barriers to patient medication adherence is a start in finding solutions for our paediatric patients on ART therapy.

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References
Adam, B.D., Matica-Tyndale, E., & Cohen, J.J. (2003). Adherence practices among people living with HIV. AIDS Care, 15: 263-274.
Bangsberg, D.R., Hecht, F.M., Charlebois, E.D., Grant, R.M., Holodniy, M., Deeks, S.G., Perry, S., Conroy, R.N., Clark, R., Guzman, D., Zolopa, A., & Moss, A. (2003). High levels of adherence do not prevent accumulation of HIV drug resistance mutations. AIDS, 13: 1925-1932.
Bangsberg, D.R., Hecht, F.M., Charlebois, E.D., Zolopa, A.R., Holodniy, M., Sheiner, L., Bamberger, J.D., Chesney, M.A., & Moss, A. (2008). Adherence to protease inhibitors, HIV-1 viral load, and development of drug resistance in an indigent population. AIDS, 4: 357-366.

Bangsberg, D.R., Perry, S., Charlebois, E.D., Clark, R.A., Roberson, M., Zolopa, A.R., & Moss, A. (2003). Non-adherence to highly active antiretroviral therapy predicts progression to AIDS. AIDS, 9: 1181-1183.
Bangsberg, D.R., Ware, N., & Simon, J.M. (2006). Adherence without access to antiretroviral therapy in sub-Saharan Africa. AIDS, 19: 140-141.
Bägdilian, S., Deribew, A., Amberbir, A., & Kebede, D. (2008). Adherence to highly active antiretroviral therapy and its correlates among HIV infected paediatric patients in Ethiopia. BMC Paediatrics, 8: 53.
Byalka-Tusimte, J., Oggy, J.H., Temsikirize, W.A., Katabira, E.T., Mugyenyi, P.N., & Bangsberg, D. (2005). Adherence to HIV antiretroviral therapy in HIV+ Ugandan patients purchasing therapy. International Journal of STD & AIDS, 16: 38-41.
Chatz, S.L., Kelly, J.A., Bogart, L.M., Benotsch, E.G., & McAlifife, T.L. (2000). Patterns correlates and barriers to medication adherence among persons prescribed new treatments for HIV disease. Health Psychology, 19: 124-133.
Federal Ministry of Health /HIV/AIDS Prevention and Control Office (2008). Monthly HIV Care and ART Update. Federal Ministry of Health /HIV/AIDS Prevention and Control Office, Addis Ababa, Ethiopia.
Green, J., & Thorogood, N. (2004). Qualitative methods for health research. 1st edition. London: Sage.
Hogg, R.S., Heath, K.Y., Yip, B., Craib, K.J., O'Shaughnessy, M.V., Schechter, M.T., & Montaner, J.S. (1998). Improved survival among HIV-infected individuals following initiation of antiretroviral therapy. JAMA, 279: 450-454.
Howland, L.C., Gortmaker, S.L., Mofenson, L.M., Spino, C., Gardner, J.D., Gorski, H., Fowler, M.G., & Oleke, J. (2000). Effects of negative life events on immune suppression in children and youth infected with human immunodeficiency virus type 1. Paediatrics, 106: 540-546.
Lanèére, L., Cass, M., Desciaux, A., Diop, K., Mbodi, F., Ndiaye, B., Sylla, O., Delaporte, E., & Ndiaye, I. (2003). Adherence to HAART and its principal determinants in a cohort of Senegalese adults. AIDS, 17 Suppl 3: S103-S108.
Laws, M.R., Wilson, I.B., Bowser, D.M., & Kerr, S.E. (2000). Taking antiretroviral therapy for HIV infection: Learning from patients’ stories. Journal of General Internal Medicine, 15: 848-858.
Lyon, M.E., Trexler, C., Alkan-Townsend, C., Pao, M., Selden, K., Fletcher, J., Addelstone, J.C., & D'Angelo, L.J. (2003). A family group approach to increasing adherence to therapy in HIV infected youths: Results of a pilot project. AIDS Patient Care STDs, 17: 299-308.
Martinez, J., Bell, D., Camacho, R., Henry-Redi, L.M., Bell, M., Watson, C., & Rodríguez, F. (2000). Adherence to antiretroviral drugs in HIV-infected adolescent patients engaged in care in a comprehensive adolescent and young adult clinic. Journal of the National Medical Association, 92: 55-61.
Mills, E.J., Nachega, J.B., Bangsberg, D.R., Singh, S., Rachlis, B., Wu, P., Wilson, K., Buchan, I., Gill, C.C., & Cooper, C. (2006). Adherence to HAART: A systematic review of developed and developing nation patient reported barriers and facilitators. Plast Medicine, 3: e438.
Mukherjee, J.S., Ivers, L., Leandre, F., Farmer, P., & Behforouz, H. (2006). Antiretroviral therapy in resource-poor settings: Decreasing barriers to access and promoting adherence. Journal of Acquired Immune Deficiency Syndrome, 1, 4 Suppl 1: S123-S126.
Nachega, J.B., Stein, D.M., Lehman, D.A., Hlatshwayo, D., Mothopeng, R., Chaissin, R.E., & Karstaedt AS. (2004). Adherence to antiretroviral therapy in HIV-infected adults in Soweto, South Africa. AIDS Research and Human Retroviruses, 20: 1053-1056.
Nischal, K.C., Khopkar, U., & Saple, D.G. (2005). Improving adherence to antiretroviral therapy. Indian Journal of Dermatology, Venerology and Leprology, 71: 316-320.
Okuno, J., Yanagi, H., & Tomura, S. (2001). Is cognitive impairment a risk factor for poor compliance among Japanese elderly in the community? European Journal of Clinical Pharmacology, 57: 589-594.
Palella, F.J. Jr, Delaney, K.M., Moorman, A.C., Loveless, M.O., Fuhrer, J., Satten, G.A., Aschman, D.J., & Holmberg, S.D. (1998). Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIC Outpatients Study Investigators. New England Journal of Medicine, 338: 853-860.
Paterson, D.L., Swindells, S., Mohr, J., Brester, M., Vergis, E.N., Squier, C., Green, J., & Thorogood, N. (2004). Qualitative methods for health research. 1st edition. London: Sage.
Pratt, D.F., & Beck, T.C. (2004). Nursing research: Principles and methods (7th edition). Philadelphia: Lippincott Williams & Wilkins.
Ryan, G., & Wagner, G.J. (2003). Pill taking 'routinization'. A critical factor to understanding episodic medication adherence. AIDS Care, 6: 795-806.
Samet, J.H., Libman, H., Steger, K.A., Dhawan, R.K., Chen, J., Shevitz, A.H., Deweers-Dunk, R., Levenson, S., Kufe, D., & Craven, D.E. (1992). Compliance with zidovudine therapy in patients infected with human immunodeficiency virus type 1: a cross-sectional study in a municipal hospital clinic. *American Journal of Medicine*, 92: 495-502.

Shah, C.A. (2007). Adherence to high activity antiretroviral therapy (HAART) in paediatric patients infected with HIV. Issues and Interventions. *Indian Journal of Paediatrics*, 74: 55-60.

Starace, F., Massa, A., Amico, K.R., & Fisher, J.D. (2006). Adherence to antiretroviral therapy: An empirical test of the information motivation-behavioral skills model. *Health Psychology*, 25: 153-162.

UNAIDS (2004). *Report on the Global AIDS Epidemic*. Geneva: UNAIDS.

UNAIDS/WHO (2006). *AIDS Epidemic Update*. Geneva: UNAIDS.

Weser, S., Wolfe, W., Bangsberg, D., Thior, I., Gilbert, P., Makhema, J., Kebaabetswe, P., Dickenson, D., Mopati, K., Essex, M., & Marlink, R. (2003). Barriers to antiretroviral adherence for patients living with HIV infection and AIDS in Botswana. *Journal of Acquired Immune Deficiency Syndromes*, 34: 281-288.

Witteveen, E., & van Ameijden, E.J.C. (2002). Drug users and HIV-combination therapy (HAART): Factors with impede or facilitate adherence. *Substance Use & Misuse*, 14: 1905-1925.