Antiretroviral Therapy and Program Retention in Urban Slums

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INTRODUCTION

Globally, nearly one billion people live in slums, and this number is projected to double to two billion in the next 30 years. The United Nations Human Settlement Program (UNHABITAT) defines a slum as an urban area characterized by lack of basic services, substandard housing, overcrowding, built on hazardous locations, insecure tenure, and social exclusion.¹ Currently, 43 % of the urban population of all developing regions lives in slums, and some 6 % of the urban population in developed regions lives in slum-like conditions.¹ The proportion of sub-Saharan African urban dwellers living in slums is 71.8 %, the highest of any region.²

While the evidence suggests that HIV rates are higher in most urban areas, there has been little research into the relative prevalence of HIV in urban slums or the dynamics of HIV in slum settings.³ UNHABITAT states that slum dwellers have worse health outcomes and are at an increased risk of HIV compared to the general population.¹ HIV care is more readily accessible in many urban areas; however, populations living in highly stressed urban environments may have more barriers to care as well as to remaining adherent to therapy. Well-described barriers to HIV care, such as cost, side effects, wait times, malnutrition, alcohol abuse, low health literacy, and use of traditional medicines, may be exacerbated in slum settings. Health services planning rarely takes the unique challenges of informal settlements into consideration.⁴

Adherence in resource-poor settings has been studied, with most authors finding comparable adherence rates between developed and developing country settings. For example, Mills and colleagues concluded that among 12 African antiretroviral therapy (ART) programs, 77 % of patients reached adequate adherence rates (>95 %) which compared favorably with adequate adherence rates of only 55 % in North American studies.⁵ By contrast, Rosen and colleagues analyzed 33 patient cohorts from 13 African countries and found that on average only 60 % of patients were retained in ART programs after 2 years from treatment initiation.⁶ This loss to follow-up was associated with both patient dropout and early mortality. A subsequent meta-analysis of antiretroviral therapy programs in sub-Saharan Africa showed a retention rate of 76 % at 24 months.⁷ The need for high adherence to ART to avoid the development of drug resistance is a major concern in sub-Saharan Africa because second-line or third-line HIV regimens are often prohibitively expensive for national healthcare systems.⁴ This paper focuses on the HIV treatment

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data and adherence strategies from studies conducted in challenging living conditions in an effort to support program planning and resource allocation.

METHODS

The objective of this evidence review is to assess the treatment outcomes and barriers to antiretroviral treatment programs in urban slum settings in developing countries. We searched MEDLINE and Embase from the period January 1990 to September 2010. We selected only cohort studies conducted in developing country urban slums with children and adult populations with at least 12 months of follow-up. We used the UNHABITAT definition of slum, which is an urban area with a lack of basic services, substandard housing, overcrowding, built on hazardous locations, insecure tenure, and social exclusion.¹ Where the study setting was unclear or the study was multicentered, we wrote to authors to clarify the setting. Multicenter studies that included non-slum urban settings were excluded. The study end points had to include at least one of CD4 count, viral load (VL), mortality, and adherence to therapy.

We scanned reference lists from pertinent articles to identify further studies for possible inclusion. We used Google Scholar to identify additional studies for inclusion. The following data items were extracted from each study: study setting (city and country), number of participants, ART regimen used initially, baseline CD4, change in CD4 at 12 months, baseline viral load, proportion of study subjects with VL <400 at 12 months, number of subjects lost to follow-up, survival at 12 months, probability of remaining in care, strategies for promoting adherence, and adherence rates. We descriptively synthesized the data. A meta-analysis was not attempted because of the heterogeneity of end points used across studies.

RESULTS

Our search yielded seven cohort studies conducted in slum settings with a minimum of 100 participants and at least 12 months of follow-up. The cohort studies identified in our systematic review are summarized in Table 1. There were a total of 12,152 participants across the seven studies. The majority of the studies are prospective cohorts. All but one cohort involve adult populations, which had both an adult and child cohort.⁸ In most cases the initial regimen used two nucleoside reverse transcriptase inhibitors (NRTI) and one non-nucleoside reverse transcriptase inhibitor (NNRTI). The NRTIs used were zidovudine or stavudine or, lamivudine. The initial NNRTIs used were either nevirapine or efavirenz. Baseline CD4 averaged from 43–203. The proportion of subjects with suppressed viral load reported after the treatment period ranged from 69.7 to 98 %.

Three of the studies were undertaken in Nairobi, Kenya. It is estimated that 60 % of the population of Nairobi live in slums.⁹ Kibera, one of Nairobi's slum neighborhoods, is sub-Saharan Africa's largest urban informal settlement, with a population of over 700,000 people.¹⁰ The slum is characterized by temporary residences and a lack of basic sanitation services such as piped water and sewage disposal.¹⁰ The estimated HIV prevalence in Kibera is 12 % compared with the national prevalence in Kenya of 5.1 %.⁴

TABLE 1 Summary of key slum-based ART studies¹³

Author	Year	Setting	Number of participants	Initial regimen used	Baseline CD4 count	Change in CD4	Baseline VL	VL <400	Loss to follow-up (%)	Survival (%) at X months	Probability of remaining in care (%)
Coetzee et al.	2004a	Khayelishsha, South Africa	287	ZDV + LMV + NVP/EFZ	43	288 (24 months)	5.18 log ₁₀	84.2 % (12 month-s), 69.7 (24 months)	0 (24 months)	86.3 (12 and 24 months)	
Boulle et al.	2010	Khayelishsha, South Africa	7,323	ZDV + LMV + NVP/EFZ	–	297 (12 months); 512 (5 years)	–	87.6 (12 months), 83.8 (5 years)	23.4 (5 years)	84.5 (5 years)	
Bekker et al.	2006	Guguletu, South Africa	161 (2002 Cohort)	Stavudine + LMV + NVP/EFZ	84	–	4.98 log ₁₀	100 %	5	–	82
–	–	Guguletu, South Africa	280 (2003 Cohort)	Stavudine + LMV + NVP/EFZ	89	–	4.87 log ₁₀	92 %	6	–	86
–	–	Guguletu, South Africa	698 (2004 Cohort)	Stavudine + LMV + NVP/EFZ	110	–	4.72 log ₁₀	98 %	1	–	91
Hawkins et al.	2007	Nairobi, Kenya	1286	Stavudine + LMV + NVP	121	208 (12 months)	–	–	34	–	57.3 (12 months)
Marston et al.	2007	Kibera, Kenya	283	Stavudine + LMV + NVP/EFZ	157	124.5 (12 months)	5.16 log ₁₀	96 % (12 months)	8 (12 months)	93 (12 months)	0.87 (12 months)
Unge et al.	2009	Kibera, Kenya	830	–	203	–	5 log ₁₀	–	–	–	0.74 (12 months) 0.65 (24 months)

TABLE 1 (Continued)

Author	Year	Setting	Number of participants	Initial regimen used	Baseline CD4 count	Change in CD4	Baseline VL	VL <400	Loss to follow-up (%)	Survival (%) at X months	Probability of remaining in care (%)
Severe et al.	2005	Port-au-Prince, Haiti	910 (adults)	ZDV + LMV + EFZ/NVP	131	163 (12 months)	–	76 % (12 months)	8	87 (12 months) 79 (60 months)	–
–	–	Port-au-Prince, Haiti	94 (children)	ZDV + LMV + NVP/EFZ	13 %	13 % (12 months)	–	–	4	98 (12 months)	–

ZDV zidovudine, LMV lamivudine, NVP nevirapine, EFZ efavirenz

Three studies were undertaken in Khayelitsha, which is an informal township in Western Cape, South Africa with an estimated population of 400,000^{11, 12, 13, 14}. The township is recognized as one of the most marginalized urban communities in South Africa. The HIV-1 seroprevalence in antenatal clinics in Khayelitsha is 24.9 %.¹¹ The Guguletu Clinic is situated in the urban Nyanga district of Cape Town, which has an estimated 57 % unemployment rate and with 81 % of households living in informal dwellings.¹²

The Haitian study, which is the only one undertaken outside of sub-Saharan Africa, was conducted at the GHESKIO hospital which provides care to a slum population in Port-au-Prince.⁸ Port-au-Prince is the poorest city in the western hemisphere, with an adult HIV prevalence of 2.2 %.³ More than 80 % of Haiti's urban population lives in slums, and only 23 % of households in Port-au-Prince have access to an improved water supply.²

Adherence Strategies

Table 2 specifically looks at adherence strategies and the probability of remaining in care in the studies for which these data were reported. A range of strategies for promoting adherence was employed. The probability of remaining in care ranged from a low of 57.3 % at 12 months to a high of 91 % at 12 months.

All the study programs but one provided medication and services free of charge. A combination of home visits, peer support groups, pillboxes, education sessions, and intensive sessions with health care providers was used to improve adherence. Buddy systems, in which a friend or family member was assigned to assist the patient to remember and adhere to dosage schedules, were used in one study.¹⁰

One study, conducted in Kibera, provided HIV services and medications at a "small fee" which may have contributed to that cohort's high rate of loss to follow-up, including a number of patients known to have transferred to another HIV program which provided free care and medications.¹⁵

DISCUSSION

The proportion of sub-Saharan African urban dwellers living in slums is 71.8 %, the highest in the world.² It is believed that slum dwellers have worse health outcomes compared to the general population.¹ For example, in Nairobi, where 60 % of the city's population live in informal settlements, child mortality in the slums is 2.5 times greater than that in other areas of the city.⁹ Slum populations lack fixed, easily identifiable addresses; they have lower levels of education and literacy than surrounding urban areas, and they have less access to healthcare. Slums are predisposed to infectious disease outbreaks due to their high population density.¹⁶ Slums dwellers are also more likely to be malnourished than other urban dwellers, which is a risk factor for HIV-associated mortality.²

Study Outcomes

Despite the challenges faced in slum settings, our analysis shows that for the most part, ART programs can be successful in such contexts, at least in the short term. The majority of the 12,152 patients analyzed achieved virological suppression; however, the rates in Table 1 only refer to those patients remaining in care and may thus overestimate treatment success. These results are not unexpected given the success of ART programs in other resource-limited settings. Furthermore, many of the studies used exceptional programs to promote adherence such as counselors,

TABLE 2 Adherence strategies and probability of remaining in care in slum-based ART programs¹⁷

Author	Year	Strategies for promoting adherence	Probability of remaining in care (%)
Coetzee et al.	2004a, 2004b	1. Use of treatment assistants 2. Home visits 3. Peer support groups 4. Material supports: pillboxes, drug identification charts, daily schedules, diaries, educational materials	–
Boulle et al.	2010	1. Nurse-based care 2. Routine home visits and signed patient contracts have been discontinued.	–
Bekker et al.	2006	1. Community-based counselors provided adherence support. 2. Group-based sessions 3. Home visits	82 (2002) 86 (2003) 91 (2004)
Hawkins	2007	1. Medication adherence counseling	57.3 (12 months)
Marston et al.	2007	1. Visual and written info provided 2. Pillboxes 3. Group sessions 4. Visits by community health workers 5. Buddy system	87 (12 months)
Unge et al.	2009	1. Counselors 2. Post test clubs 3. Treatment literacy training for children and adults 4. Social assessments	74 (12 months); 65 (24 months)
Severe et al.	2005	1. Patients seen q 2 weeks×3 months by MD then each month by nurse 2. Meds dispensed q month 3. Provided daily multivitamin + food	–

Meds and services were free in all studies except Hawkins et al.

home visits, and treatment clubs.¹⁴ The significant public health challenge lies in operationalizing a scale-up of such treatment provision in slum settings across Africa and the developing world. It is here that the challenges identified in the seven studies are of note.

The poorest outcomes came from two of the three studies undertaken in the slum of Kibera in Nairobi. The two studies with a combined patient number of 2,116 showed a probability of remaining in care of between 52.3 % after 12 months and 65 % after 24 months.^{4,15} These numbers may not correlate with failure to continue with therapy, as some patients are known to have switched to other ART programs, a problem in some slum settings where numerous national and international agencies provide HIV care with little coordination.¹⁷ Nonetheless, the findings have raised concerns about the feasibility of providing long-term ART in the unstable environment of a slum. One paper also found that a large number of patients receiving ART are at immediate risk of developing drug resistance due to poor adherence even while remaining in treatment programs.¹⁷ In one Kibera study, 27 % of patients had an overall adherence below 95 % and 8 % of the total had a mean adherence below 80 %.⁴ A more recent study in Kibera not included in our analysis found that 38 % of the patients were nonadherent using an adherence index, while 23 % of the patients had dropped out of the study within 2.5 years.¹⁷ What reasons can be identified for the poor adherence in the Kibera studies? Of note, is the fact

that the Saint Mary's Mission study charged a fee for clinical care, and only had minimal adherence promotion measures in place. Costs associated with ART have been associated with poor adherence, interruption or discontinuation of ART, loss to follow-up, and poorer outcomes in several other studies.¹⁵ The AMREF study found that residency in the Kibera slum was strongly correlated with program dropout.⁴ Kibera residents had 11 times higher risk than non-Kibera residents of dropping out. A logistic regression on a cohort in Kibera found that low education, living on less than US\$2/day, not disclosing HIV status, and not having a treatment buddy were significant predictors of nonadherence.¹⁷

The Kibera studies represent less than 20 % of the patients included in our review. The survival rates and probability of remaining in care were much higher in the South African studies as well as the Port-au-Prince study, even with much longer follow-up. The Port-au-Prince study reported in a subsequent paper that only 8 % of the original cohort were lost to follow-up and 79 % were alive at 5 years.¹⁸ Furthermore, the largest cohort (7,323 participants) which was followed in Khayelitsha, South Africa had a survival rate of 84.5 % at 5 years. Nonetheless, we can postulate from this review that some more vulnerable slum populations may be at increased risk of dropout and low adherence and thus intensified patient support may be required for such population groups to minimize the risk of dropout and nonadherence.⁴

Potential Weaknesses

Our review had a number of potential weaknesses. First, it was very difficult to determine the residency of the patients included in each study. While the studies were performed in slum settings serving a majority of patients from the urban area, patients from surrounding urban areas may have been included in the analyses particularly as all but one of the studies offered free care and medications. A related critique of our analyses is that the studies examined used large amounts of material and human resources to improve adherence and outcomes among the patient population. Many of these interventions may not be cost effective or feasible in the non-study setting. Furthermore, our results may be biased towards improved outcomes due to a publication bias whereby programs with poor outcomes may have less motivation to publish their results. Finally, the outcome data in Table 1 is biased insofar as it includes only patients who have remained in care and excludes patients who have been lost to follow-up.

CONCLUSION

Globally, nearly one billion people live in slums, and this number is projected to double to two billion in the next 30 years. This is likely to be a very heterogeneous population. Slum populations face unique challenges when accessing HIV treatment such as income poverty, a paucity of sanitation services, and a high burden of comorbid conditions. Our review assessed seven studies of ART programs in slum settings. Five studies conducted in Haiti, South Africa, and Kenya involving over 10,000 patients report excellent rates of adherence, follow-up, and laboratory improvement in study participants with up to 5 years of follow-up. Two studies undertaken in Kibera, Kenya showed low levels of adherence and follow-up, in line with an earlier meta-analysis of ART programs. The evidence is in favor of successful ART programs in slum settings; however, certain slum populations may be more vulnerable to poor adherence and program dropout. Given the progressive

urbanization of developing countries, more research is needed into the barriers slum populations face in accessing HIV care, as well as the strategies and resources needed to support these vulnerable population groups in accessing and remaining in HIV care.

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