IS FORCED DISPLACEMENT A BARRIER TO ACCEPTABLE TREATMENT OUTCOMES AMONG REFUGEES ON ANTIRETROVIRAL THERAPY?

A FIELD STUDY IN MALAYSIA AND KENYA

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DECLARATION

I, Joshua Mendelsohn, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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2 August 2012

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ABSTRACT

In response to a major gap in evidence regarding treatment outcomes among asylum-based refugees, the primary objective of the thesis was to investigate adherence to highly active antiretroviral therapy (HAART) and virological outcomes among refugees and to compare these outcomes with local host communities in one urban, Southeast Asia setting (Sungai Buloh, Kuala Lumpur, Malaysia) and one remote sub-Saharan refugee camp (Kakuma, Kenya) setting. Given limited resources for expanding treatment, questions have been raised as to whether refugees can achieve sufficient levels of adherence and viral suppression to justify sustaining and expanding access. Data sources included a structured questionnaire with self-reported adherence measures, a pharmacy-based prescription refill measure, HIV viral loads, and in-depth interviews. Analyses made use of quantitative and qualitative approaches. The thesis begins by presenting the rationale, aims, research questions, and a description of preparatory work. Paper One presents the results of a systematic review of the literature on adherence to HAART and treatment outcomes among conflict-affected and forcibly displaced populations, finding only 17 reports, five of which included less than <100 clients, adherence estimates in the range of 87-99.5%, and good treatment outcomes. Papers Two and Three present the quantitative findings from both settings, finding no differences in outcomes between refugees and the host community in either setting, but a large difference between the settings. In Malaysia, 83% of clients on HAART for ≥25 weeks were suppressed while only 11% were suppressed in Kenya. Female sex, longer time from HIV diagnosis to HAART start, and optimal adherence pharmacy refill schedule were protective in the Malaysian setting while temporary migration for ≥1 month (in the previous year) and ≥1 hour average transit time to clinic were independent risk factors. Larger household sizes were protective in the Kenyan setting. Paper Four offers an account of patient experiences based on the qualitative findings from both settings, and suggests that systemic barriers and resilient strategies were prevalent in both settings; however, intensive systemic barriers appeared to overwhelm personal resilience in the camp setting. Paper Five positions the work in the context of previous and future research and makes recommendations for programs and policy. The thesis concludes by suggesting that, just as good treatment outcomes were shown to be achievable in a range of forcibly displaced groups, asylum-based refugees were also capable of treatment success and maintain outcomes similar to those of the host communities. There is a clear public health and humanitarian interest in guaranteeing access to ART, promoting optimal adherence, and sustaining viral suppression in all who are in need of treatment. When problems in achieving and sustaining viral suppression occurred, they were not typically due to previous forced displacement, or refugee status itself. Overall, refugees ought to have equal access to HIV treatment based on the

principles of fairness, human rights, and individual and population-based public health benefits. Since HIV-positive individuals on HAART with good adherence will rarely transmit HIV to their sexual partners, it is in the enlightened self-interest of host country governments to support HIV programs that serve HIV-positive refugees and host clients equally.

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LIST OF ABBREVIATIONS

ACTG	AIDS Clinical Trials Group
AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral Therapy
AZT	Zidovudine
BID	Twice-daily dosing
CCCK	Comprehensive Care Clinic, Kakuma
CD4	T-helper (lymphocyte) surface protein
CI	Confidence Interval
DBS	Dried Blood Spot
DSA	Daily Subsistence Allowance
EMR	Electronic Medical Record
EFV	Efavirenz
HAART	Highly Active Antiretroviral Therapy
HCT	HIV Counselling and Testing
HIV	Human Immune Deficiency Virus
HR	Hazard Ratio
IDP	Internally Displaced Person
IRC	International Rescue Committee
KEMRI	Kenya Medical Research Institute
LSHTM	London School of Hygiene and Tropical Medicine
MEMS	Medication Event Monitoring System
MOU	Memorandum of Understanding
MREC	Medical Research and Ethics Committee (Malaysia)
MSF	Médecins Sans Frontières
NASCOP	National AIDS and STI Control Program (Kenya)
NGO	Non-Governmental Organisation
NNRTI	Non Nucleoside Reverse Transcriptase Inhibitor
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NSP	National Strategic Plan
NVP	Nevirapine
OR	Odds Ratio
OR_{adj}	Adjusted Odds Ratio
PEV	Post ElectionViolence
PI	Protease Inhibitor
RSD	Refugee Status Determination
SAT	Social Action Theory
SBH	Sungai Buloh Hospital
SMART	Strategies for Management of Antiretroviral Therapy
START	Strategic Timing of Antiretroviral Treatment
SMS	Short Message Service
SOP	Standard Operating Procedure
UNHCR	United Nations High Commissioner for Refugees
VAS	Visual Analogue Scale
VL	Viral Load
WHO	World Health Organisation
3TC	Lamivudine

GENERAL INTRODUCTION

Highly active antiretroviral therapy (HAART) has transformed HIV/AIDS in the developed world into a treatable chronic condition, yet it is not without its challenges. Adherence to therapy is a crucial determinant of overall treatment success: sustained optimal adherence is essential for the prevention of onward transmission of virus [1], drug resistance [2,3], treatment failure [4,5], disease progression [6], and mortality [7,8]. Refugees are unique insofar as they have been forcibly displaced across an international border and have been granted a legal status that entitles them to access the local standard of medical care. Yet, they are often accused of importing and transmitting disease despite [9,10], and are similarly prone to the claim that they may be unable to sustain adherence to treatment, and therefore experience inferior treatment outcomes in relation to other groups. These accusations may be linked to assumptions about pre- or post- migration stresses [11], treatment interruptions [12] during previous episodes of forced displacement, and the inherent hardships [13] of life in asylum. These arguments are disputed by advocates who invoke human rights principles such as access to essential medicines [14], humanitarian law that instructs States to provide refugees with a standard of public relief equivalent to what is received by host nationals [15,16], and the demonstrated feasibility of delivering HAART to similar groups [17,18]. A very small number of studies conducted among other conflict-affected groups showed that good adherence and treatment outcomes were feasible in these groups [19,20,21]. However, data on adherence and treatment outcomes among refugees residing in asylum settings was notably lacking. Moreover, only one study [22] sought to compare refugees with local host communities in resource-limited settings to verify that outcomes were acceptable and equitable.

In response to these challenges, this thesis investigated adherence to HAART and treatment outcomes in refugees and local host communities attending the same HIV treatment clinic in one urban setting (Kuala Lumpur, Malaysia) and one camp setting (Kakuma, Kenya), and to explore the reasons for any differences in treatment outcomes among these groups. These field sites provided variation with respect to the major types of protracted refugee situations and were logistically feasible. In addition to generating this evidence, this work was intended to inform strategy related to the United Nations High Commissioner for Refugees' (UNHCR) Antiretroviral Therapy Policy for Refugees [23] by evaluating the continuity and sustainability of HAART for refugees. By investigating adherence in surrounding host communities, the findings were also intended to bolster the evidence-base informing equitable and high quality treatment and care in refugee and local host community groups. Lastly, it was hoped that the findings would assist Ministries of Health, implementing partners, and providers in host countries, to formulate or revise policy and programmes for these groups.

DEFINITIONS

This work draws on two essential definitions. The term " refugee" explicitly refers to individuals who meet an internationally recognised, legal definition regarding persons who, "owing to well-founded fear of being persecuted for reasons of race, religion, nationality, membership of a particular social group or political opinion, is outside the country of his nationality and is unable, or owing to such fear, is unwilling to avail himself of the protection of that country; or who, not having a nationality and being outside the country of his former habitual residence as a result of such events, is unable or, owing to such fear, is unwilling to return to it" . By the end of 2010, there were 10.6 million refugees globally, who were displaced largely into camps and urban settings. Two-thirds were residing in "protracted situations", defined as 25,000 or more refugees of the same nationality living in exile for five years or more in an asylum country [24]. The average stay of a refugee in an asylum country is 17 years [25]. Refugees are distinguished from other displaced groups including internally-displaced persons (IDPs) who have not crossed international borders, and economic migrants who are not displaced as a result of conventional forms of persecution and violence. "Asylum-seekers" refer to persons who are seeking refugee status, but are awaiting a formal interview, called a "Refugee Status Determination" to determine their eligibility.

The term "adherence" was defined by WHO as "the extent to which a person's behaviour – taking medications, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider" [26, p.3]. In the present work, "adherence" is used to refer to medication adherence, and specifically to adherence to HAART, unless indicated otherwise. "Optimal adherence" will refer to adherence that is measured at a level 95% or more, in line with a body of research that has consistently shown superior outcomes at these very high levels [5,27,28].

AIMS

The primary aim of this study was to assess and compare HAART adherence and treatment outcomes among refugees and host communities. Secondary objectives sought to explore the factors associated with viral failure in each study setting. The study also aimed to bolster these findings with qualitative work detailing the experiences of refugees and host communities in attempting to sustain adherence over time, and to make recommendations for policy.

RESEARCH QUESTIONS AND HYPOTHESES

The primary research questions for this work were:

1. Do refugees adhere to treatment and achieve viral suppression while in asylum at levels that are comparable to local host communities?
2. If differences in treatment outcomes between refugees and local host communities exist, why do the outcomes vary? What are the risk factors for lack of viral suppression in the study settings?
3. How do refugees and host nationals experience their treatment while in asylum and what do they perceive to be the major threats and barriers to good adherence?
4. What policies can improve adherence to HAART in clinics shared by refugee and host community groups?

Table 1 lists the key questions and hypotheses. Hypotheses were generated based on an overview of relevant literature and initial preparatory fieldwork.

Table 1: Research questions, hypotheses, and methods

	Research question	Research hypothesis (H_1)	Method(s)
1	Do refugees adhere to treatment and achieve viral suppression while in asylum at levels that are comparable to local host communities?	Refugees will adhere to prescribed regimens less well and exhibit worse treatment outcomes when compared with host community populations.	Structured questionnaire on adherence Pharmacy refill adherence Viral load
2	If differences in treatment outcomes between refugees and local host communities exist, why do the outcomes vary? What are the risk factors for lack of viral suppression in the study settings?	Sub-optimal adherence will be a strong independent risk factor for virological failure in both refugee and host community clients. Other important risk factors in both sites may include serostatus disclosure and recent travel.	Structured questionnaire on adherence Pharmacy refill adherence Viral load
3	How do refugees and host nationals experience their treatment and what do they perceive to be the major threats, barriers, and facilitators of adherence?	Shared adherence challenges in both settings will include stigma and discrimination. Refugees will experience challenges pertaining to forced displacement and sequelae.	Client semi-structured interviews
4	What policies can improve adherence to HAART in clinics shared by refugee and host community groups?	The evidence will support recommendations for earlier initiation of therapy, adherence monitoring programs, and access to appropriate counselling services, to optimise adherence and treatment outcomes.	All data collected

PARTNERS, ROLES, AND FUNDING

The proposed study is the result of collaboration between the doctoral candidate and his supervisor based at the London School of Hygiene and Tropical Medicine (LSHTM) and colleagues at the Public Health and HIV Unit of the United Nations High Commissioner for Refugees (UNHCR). LSHTM provided research supervision and doctoral support, sponsored the study, and provided professional indemnity. UNHCR covered research costs, provided a "daily subsistence allowance" (DSA) to cover living costs during time spent in the field and provided logistical support. The DSA was valued at approximately 250 USD/day in Malaysia

and 100 USD/day in Kenya (65,000 USD for all field time). Research costs supported by UNHCR included all air travel, staff salaries, translations, lab fees, and miscellaneous research materials. This amounted to approximately 100,000 USD inclusive of both field sites; the most expensive single budget item was viral load testing (approximately 100USD/test and almost half of the total project cost). The study was also supported by a Canadian Institutes of Health Research Doctoral Research Award (84,000 Canadian dollars over three years), the Parkes Foundation (3000 GBP), the Department of Infectious Disease Epidemiology (LSHTM) research funds (3000 GBP), the University of London Central Research Fund (900 GBP), and the University College London Graduate Research Fund (500 GBP). The candidate was responsible for designing the study protocol, securing all research clearances and ethical approvals, implementing the data collection strategy, statistical and qualitative analyses and syntheses, interpreting findings, drafting manuscripts, updating manuscripts in light of comments and feedback from the thesis advisor, co-authors, and Advisory Committee members. Technical support was received by the Advisory Committee on aspects of the thesis germane to their particular areas of expertise. Alison Grant and Egbert Sondorp provided support on technical aspects of protocol design, analyses, and interpretation for Papers Two and Three. Natasha Larke provided all statistical support for Papers Two and Three. On Paper Four, Tim Rhodes provided support for qualitative study design, analyses and interpretation of results. Colleagues at UNHCR including Paul Spiegel and Marian Schilperoord sat as external members of the Advisory Committee and supported protocol and survey design and interpretation of results on Papers One, Two and Three. Protocol and questionnaire feedback was also received from the Upgrading Committee including Bayard Roberts, Judith Glynn, and Richard White and National Ethics Committees. David Ross (thesis advisor), supported every aspect of the project from design through implementation and reporting. Other co-authors on the manuscripts were key local collaborators and assisted with research tasks related to data collection and interpretation of findings on Papers Two, Three and Four. These collaborators included Susheela Balasundaram (UNHCR Malaysia), Chunting Wong (UNHCR Malaysia), Christopher Lee (Hospital Sungai Buloh, Malaysia), Anuradha Radhakrishnan (Hospital Sungai Buloh, Malaysia), Bosco Muhindo (UNHCR Kenya), Irene Mukui (NASCOP), Ibrahim Mohammed (NASCOP), John Burton (UNHCR) and Njogu Patterson (UNHCR). Chunting Wong also assisted with analyses of qualitative data for Paper Four.

THESIS STRUCTURE

The thesis is structured according to manuscripts drafted for submission to specific peer-reviewed journals. The first section, *General Introduction* outlines the basic rationale for the work, aims, research questions, hypotheses, partners, roles, and funding. It goes on to offer a

synopsis of preparatory work conducted before the start of the main study including preparatory field missions, survey design, training, pre-testing, and pilot-testing of instruments. *Paper One* presents the results of a systematic review of the literature on adherence to HAART and treatment outcomes among conflict-affected and forcibly displaced populations and has been provisionally accepted by *BMC Conflict and Health* pending minor discretionary revisions. *Paper Two* and *Paper Three* present the quantitative findings from the Malaysian and Kenyan settings, respectively. *PLoS Medicine* agreed to review *Paper Two* after a pre-submission inquiry. At the time of writing, this paper had been reviewed and approved by all but one co-author. *Paper Three* is currently designated for submission to *The Lancet* in anticipation of a possible special issue on conflict and health. *Paper Four* offers an account based on the qualitative findings from both settings and has been designated for *AIDS Care*. Finally, *Paper Five* is a summative manuscript that aims to position the work in the context of previous and future research and to make recommendations for programs and policy. Paper Five has been written with submission to *PLoS Medicine's "Policy Forum"* section in mind. At the time of writing, *Papers Three*, *Four*, and *Five* were with co-authors for review prior to submission for publication. Appendix A contains the final instruments from the Malaysian setting in English (including the structured questionnaire, in-depth interview topic guides, medical records and pharmacy data collection forms). Appendix B presents the same material used in the Kenyan setting. Appendix C contains all ethical approvals, information sheets and consent forms used in both settings.

PREPARATORY WORK

Collaborations and field site selection

The project concept originated at a UNHCR Satellite Conference to the International AIDS Conference (2006) in Toronto, Canada. I heard presentations at that Satellite Event that helped to clarify the key research questions and where they fit into the literature on HIV, conflict and displacement. At the main conference, I approached Paul Spiegel of UNHCR who invited a proposal. Initially, I proposed four ideas, one of which was a comparative study of adherence and treatment outcomes. This idea was a priority for UNHCR and was eventually supported by their Regional HIV Coordinators. UNHCR Headquarters ultimately decided to support the project financially and logistically. The next step was to design the project, apply for external funding, agree on the main research questions, develop a general outline of the methods and choose the location of the field sites. Initially, Kenya, Uganda, Rwanda, South Africa, Zambia, Ivory Coast and Malaysia were all proposed as possible field options. In order to be considered feasible as a field setting for this project, sufficient numbers of identifiable refugees had to be

accessing HAART from a single facility and facility managers had to have expressed interest in supporting the project and UNHCR Representatives (Heads of Mission) had to commit to supporting the effort. Early efforts were made to develop collaborations in Ivory Coast and South Africa on the basis of the number of forcibly displaced persons in the sampling frame. After initial contacts were developed in Ivory Coast, the project partners decided that distinguishing refugees from IDPs would be difficult and most of the persons of concern in Ivory Coast were, in fact, IDPs. We had agreed that the focus of the work would be refugees. Collaboration was also organised with Nazareth House (Johannesburg, South Africa), an urban clinic that had been treating a large number of Zimbabwean refugees and migrants. However, the political situation in South Africa was tense given the large migration influx from Zimbabwe, the status of many of these migrants was contested, and some tensions existed between civil society and UNHCR on these issues. Therefore, the project partners decided that this location was not politically feasible. Ultimately, Kenya and Malaysia were selected as the field settings as they fulfilled all key feasibility criteria. They also offered some geographic variation, and the opportunity to study both an urban and a refugee camp setting. Next, in consultation with collaborators and the contracts teams of both organisations, I developed a Memorandum of Understanding (MOU) to be agreed and signed by LSHTM and UNHCR. This MOU used an LSHTM contract template and is available upon request. The process took a full six months to negotiate, approve at both institutions, finalise and sign. From there, field missions were organised individually, with Terms of Reference issued by UNHCR and PT8s (an internal UNHCR contract type) issued and signed for the field missions indicating the dates, flights, and amount of DSA to be paid. Research expenditures were also usually claimed back from these contracts. Expenditures were either covered initially by the Candidate and reimbursed later by UNHCR or paid directly by the UNHCR (e.g. viral load testing).

Preparatory field work

The study was conducted in two phases. The first phase included an analysis of relevant reports and publications, an *in situ* preliminary assessment of both field sites (8-20 September 2008, Kenya; 8-12 December 2008, Malaysia), and a one-day coordination workshop held in Geneva (31 October 2008). These trips were undertaken to facilitate study planning, familiarisation with logistical and technical issues in each field setting including recruitment, data protection, research governance, budgets, timeline, and development of the research instruments. Informal meetings with providers, officials, and clients were undertaken in each setting and formal reports were generated for the funder. The second phase of work consisted of the two main sub-studies conducted in Malaysia 12 January - 4 September 2010 and in Kenya from 29 November 2011 – 21 March 2011.

Survey development

The survey was developed in advance of the main study, using a variety of sources, previously validated instruments and feedback from stakeholders. Table 2 credits the sources from where survey questions were drawn or adapted by question category (see Appendices A and B for full questionnaires).

Table 2: Study outcomes and covariates, and instrument sources

Variable	Category	Source instrument (where applicable)
Primary outcome	Virological outcomes	COBAS Ampliprep/Taqman (using full plasma samples in Malaysia; dried blood spots on Whatman 903 filter paper in Kenya)
Secondary outcomes	Pharmacy refill adherence	Nachega et al. [28]
	Self-reported adherence	One-month recall, Visual Analogue Scale: Lu et al. [29]; Oyugi et al. [30] Four-day dose-by-dose recall - ACTG questionnaire: Chesney et al. [31]
Covariates	Sociodemographic and displacement	UNHCR [32]
	Beliefs about HIV and medications	Chesney et al. [31]
	Clinical factors	ACTG questionnaire [31] Kiboneka et al. [33]
	Medications and side-effects	Chesney et al. [31]
	Adherence barriers	Chesney et al. [31] Mollica et al. [34] Antelman et al. [35]
	Alcohol/ Substance use	Chesney et al. [31]
	Food insecurity	Kendall et al. [36]
	Self-efficacy and social support	Chesney et al. [31]
	Social trust	Kawachi et al. [37]
	Patient-provider relationship	Nilsson Schonnesson et al. [38]
	Clinic factors	Ramsey et al. [39]
	Serostatus disclosure and stigma	Nyblade et al. [40]

Translation

Translation of questionnaires and topic guides followed a five-stage process for each language. First, the original English questionnaire was translated into target languages. Second, each translated instrument was independently back-translated to English. Third, a meeting was convened with both independent translators for each language where the back-translated and original English version of each instrument was compared, any points of disagreement were discussed, and a reconciled translation was produced. In the fourth stage, the research team were solicited for detailed feedback on the cultural and semantic validity of reconciled instruments, and translations were updated accordingly. Fifth, questionnaires were pre-tested in each language with pre-HAART clients, with adjustments made as appropriate.

Study power

Power calculations were initially completed based on the expected numbers of patients on HAART and the expected proportions with HIV viral suppression in each setting (Table 3). They were re-calculated post-hoc using the actual numbers recruited in each setting. Using viral suppression as the outcome, the absolute prevalence difference detectable in each setting was

15% in Malaysia, and 21% in the Kenyan setting. In other words, in Malaysia, if the proportion of hosts with viral suppression had been 80%, the study would have had an 80% chance of detecting a true proportion of refugees with viral suppression of 65% as statistically significant at the 5% level. Sub-group analyses were not conducted using multivariable analyses due to the relatively small numbers of study participants and resulting lack of power.

Table 3: Power calculations for detecting differences in viral suppression between refugee and host populations with 95% confidence, 80% power

Setting	N_1 (hosts)	N_2 (refugees)	Proportion viral suppression in hosts	Absolute prevalence difference
Malaysia - initial	81	81	0.80	0.21
Malaysia - final	148	153	0.80	0.15
Kenya - initial	59	59	0.80	0.26
Kenya - final	86	73	0.80	0.21

Survey pre-testing

Given the limited numbers of refugees on HAART in each setting, pre-HAART clients were chosen for pre-testing to avoid giving eligible participants a "preview" of the questionnaire. The aims of pre-testing were threefold: to check that the translations were accurate and easily understood by clients in the interview context; to check that interviewers administered all questions in a consistent manner; and to give interviewers further practice in administering the informed consent procedure and the questionnaire. Pre-tests were conducted in pairs. Clients were recruited and interviewed in the same language, independently, by two members of the research team. Pairs of questionnaires were then assessed for differences to assess whether interviewers had asked questions in a uniform manner such that the same responses were elicited from a single client. The second interviewer of the pair administered the questionnaire in either full-length form or in an abridged form that focused on questions relating to key factors of interest, outcomes, or questions that had proven difficult to understand or were potentially "lost in translation." Where clients consistently gave varied answers to the same question asked by independent interviewers, the translation was reviewed and updated if a better formulation could be agreed by two members of the research team. As pre-test clients were not on HAART, they instead were directed to answer adherence questions while thinking about their cotrimoxazole, multivitamins, or other chronic medications. At the end of each pre-testing session, a debriefing was held with the research team to discuss problems that arose in the administration or understanding of the questionnaire. Topic guides for in-depth interviews were not pre-tested directly with clients. Rather, they were tested by research staff in mock interview scenarios.

In Malaysia, 54 pre-tests (15 in English, six in Mandarin; nine in Malay; 22 in Burmese, and two in Falam, a dialect of Chin State, Burma) were conducted with 27 clients. Each interviewer completed at least two pre-tests (range 2, 9) and the average number completed by each

interviewer was 4.4. The Tamil questionnaire was late in development and pre-tested twice by each Tamil speaking interviewer prior to the start of the study. It was also thoroughly tested by the Tamil-speaking interviewers during the pilot-testing period. The main outcome of the Malaysian pre-test was to highlight and remedy any remaining semantic defects in the questionnaire. For example, in the Mandarin version pre-testing, it became clear that different vernaculars and levels of Mandarin were spoken by Chinese Malaysians whose mother tongues were Hakka or Cantonese. As a result, some of the written questions were updated to reflect colloquial pronunciations. In the Burmese version, a question stem that began "How confident are you that..." was altered after feedback suggested that "confidence" was misunderstood in the context of humility in Burmese culture. Burmese clients were simply more likely to answer "no" to any question that asked them to assess their own confidence. This question was updated to read "...how likely..." The options associated with a question about UN registration were also revised in light of the distinction between registration and refugee status determination, the former naturally occurring before the latter.

In Kenya, 58 pre-tests (13 in Nga'turkana, 23 in Kiswahili, four in English; two in French; eight in Somali, three in Amharic, and five in Juba Arabic) were conducted with 28 clients (two were unpaired). Each interviewer who participated in the main study completed at least two pre-tests (range 2, 7). The average number completed by each interviewer was 4.7. The pre-testing suggested that some Somalis in the refugee camp only ever attended language/religious school and had never attended regular schooling such as "primary school." As it was difficult to ascertain the comparability of language and routine schooling, a separate option was added to the questionnaire. An option was also added to distinguish *prima facie* refugees from those had completed a refugee status determination interview. *Prima facie* refugees, such as Somalis, are automatically accorded refugee status upon entry into a host country on account of a deteriorating political situation in their home countries.

Development of standard operating procedures (SOPs)

Following the pre-testing phase and prior to pilot-testing, all standard operating procedures (SOP) were re-assessed in light of what had been learned and finalised. The SOPs emphasised the following:

1. Pre-screening and recruitment in the clinic and scripts for telephone recruitment
2. Registration of participants
3. Procedures for guiding clients to routine clinic appointments if these were called in the middle of a research interview. and retaining them after routine appointments
4. Confidentiality, and checking to ensure that interview spaces were confidential

5. Judging whether a client was sufficiently fluent in a language for which translated instruments were available, usually by having a regular conversation in advance of administering the information sheet
6. Correct and consistent administration of the information sheet and informed consent procedure
7. Administration of the questionnaire, accurate data collection, and effective interview probing skills.
8. Confirming the client's HAART prescription from medical records and comparing this information to self-reports in real-time
9. Guiding the client to the phlebotomy centre in order to draw blood samples. In Malaysia, this procedure called for using clinic phlebotomists and routine procedures; in Kenya, the procedure involved skin-prick and dried-blood spot techniques
10. Reviewing questionnaires for quality assurance
11. Collecting supplementary data from the medical and pharmacy records
12. Double-entering data and reconciling mistakes
13. Selecting clients for in-depth interviews
14. Contact, scheduling, and administering in-depth interviews including all consent procedures
15. Research team codes of conduct

These standard operating procedures were drafted into a Training Manual and distributed to all members of the research team in advance of training.

Staff recruitment and training

Staff recruitment, interviewing, and hiring were the first tasks undertaken in each setting during the main study phase. Research team candidates were located through open advertisements and recommendations by study partners. The Training Manual was used to guide training sessions. In Malaysia, the basic research training consisted of 6 days, plus an additional refresher day for interviewers chosen to conduct qualitative research. Training consisted of basic principles of research, in-depth review and feedback on the survey questionnaires and topic guides and their translations, and considerable practice in administering the survey and improving accuracy and quality. In Malaysia, potential team members were required to pass an assessed, knowledge-based examination in advance of signing a contract. In Kenya, training was 7 days long and candidates were assessed by observation of their interviewing skills and the quality of practice surveys.

Survey and protocol pilot-testing

Once these SOPs were finalised, pilot-testing was initiated. The goal of pilot-testing was to ensure the proper functioning of all study procedures. Pilot-testing in Malaysia was completed with 10 Malaysians from the host community including 6 conducted in English, one in Mandarin; and three in Malay; and 15 refugees including 11 conducted in Burmese, and four in Falam. In Kenya, pilot-testing was completed with 9 Kenyans from the host community including 7 surveys conducted in Nga'turkana, one in Kiswahili, and one in English; and 7 refugees including three surveys conducted in Kiswahili, one in Somali, one in Amharic, and two in Juba Arabic. As no major problems were detected during the pilot test in either setting, all data from the pilot tests were advanced into the main dataset. Most staff involved in the pre-testing and pilot testing were also involved in the main survey. In Malaysia two new members of staff were hired during the study period, In Kenya, one additional staff member was added. Each new member read all SOPs, and practiced administering questionnaires with the Principal Investigator and at least two volunteer clients. If this process was completed satisfactorily, they were admitted to the rota.

REFERENCES

1. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, et al. (2011) Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med 365: 493-505.
2. Harrigan PR, Hogg RS, Dong WW, Yip B, Wynhoven B, et al. (2005) Predictors of HIV drug-resistance mutations in a large antiretroviral-naive cohort initiating triple antiretroviral therapy. J Infect Dis 191: 339-347.
3. Bangsberg DR, Acosta EP, Gupta R, Guzman D, Riley ED, et al. (2006) Adherence-resistance relationships for protease and non-nucleoside reverse transcriptase inhibitors explained by virologicalal fitness. AIDS 20: 223-231.
4. Low-Beer S, Yip B, O'Shaughnessy MV, Hogg RS, Montaner JS (2000) Adherence to triple therapy and viral load response. J Acquir Immune Defic Syndr 23: 360-361.
5. Lima VD, Harrigan R, Murray M, Moore DM, Wood E, et al. (2008) Differential impact of adherence on long-term treatment response among naive HIV-infected individuals. AIDS 22: 2371-2380.
6. Bangsberg DR, Perry S, Charlebois ED, Clark RA, Roberston M, et al. (2001) Non-adherence to highly active antiretroviral therapy predicts progression to AIDS. AIDS 15: 1181-1183.
7. Wood E, Hogg RS, Yip B, Moore D, Harrigan PR, et al. (2006) Impact of baseline viral load and adherence on survival of HIV-infected adults with baseline CD4 cell counts > or = 200 cells/microl. AIDS 20: 1117-1123.
8. Lima VD, Harrigan R, Bangsberg DR, Hogg RS, Gross R, et al. (2009) The combined effect of modern highly active antiretroviral therapy regimens and adherence on mortality over time. J Acquir Immune Defic Syndr 50: 529-536.
9. Farmer P (2004) An anthropology of structural violence. Curr Anthropol 45: 305-325.
10. Spiegel PB (2004) HIV/AIDS among conflict-affected and displaced populations: dispelling myths and taking action. Disasters 28: 322-339.
11. Porter M, Haslam N (2005) Predisplacement and postdisplacement factors associated with mental health of refugees and internally displaced persons - a meta-analysis. JAMA 294: 602-612.
12. Genberg BL, Wilson IB, Bangsberg D, Arnsten J, Goggin K, et al. (2012) Patterns of ART adherence and impact on HIV RNA among patients from the MACH14 study. AIDS 26 (epub).
13. Leserman J, Ironson G, O'Cleirigh C, Fordiani JM, Balbin E (2008) Stressful life events and adherence in HIV. AIDS Patient Care STDS 22: 403-411.
14. UN (1966) International Covenant on Economic, Social, and Cultural Rights (ICESCR). New York.
15. UN General Assembly (28 July 1951) Convention relating to the Status of Refugees. In: United Nations, editor. Treaty Series (vol 189, p 137).
16. UN General Assembly (31 January 1967) Protocol Relating to the Status of Refugees. In: United Nations, editor. Treaty Series (vol 606, p 267).
17. Jacob ST, Abongomera G (2009) Adherence to combination antiretroviral therapy in complex emergency settings. BMJ 338: a2662.
18. Ellman T, Culbert H, Torres-Feced V (2005) Treatment of AIDS in conflict-affected settings: a failure of imagination. Lancet 365: 278-280.

19. Culbert H, Tu D, O'Brien DP, Ellman T, Mills C, et al. (2007) HIV treatment in a conflict setting: outcomes and experiences from Bukavu, Democratic Republic of the Congo. PLoS Med 4: e129.

20. Kiboneka A, Nyatia RJ, Nabiryo C, Olupot-Olupot P, Anema A, et al. (2008) Pediatric HIV therapy in armed conflict. AIDS 22: 1097-1098.

21. Nisbet SM, Reeve AM, Ellis-Pegler RB, Woodhouse AF, Ingram RJ, et al. (2007) Good outcome in HIV-infected refugees after resettlement in New Zealand: population study. Intern Med J 37: 290-294.

22. Garang PG, Odoi RA, Kalyango JN (2009) Adherence to antiretroviral therapy in conflict areas: a study among patients receiving treatment from Lacor Hospital, Uganda. AIDS Patient Care STDS 23: 743-747.

23. UNHCR (2007) Antiretroviral Medication Policy for Refugees. Geneva: UNHCR.

24. UNHCR (2011) Statistical Yearbook 2010. Geneva: UNHCR.

25. UNHCR (2004) Protracted refugee situations - Standing committee 30th Meeting. Geneva: UNHCR.

26. WHO, editor (2003) Adherence to long-term therapies - evidence for action. Geneva: World Health Organization.

27. Paterson DL, Swindells S, Mohr J, Brester M, Vergis EN, et al. (2000) Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. Ann Intern Med 133: 21-30.

28. Nachega JB, Hislop M, Dowdy DW, Chaisson RE, Regensberg L, et al. (2007) Adherence to nonnucleoside reverse transcriptase inhibitor-based HIV therapy and virological outcomes. Ann Intern Med 146: 564-573.

29. Lu M, Safren SA, Skolnik PR, Rogers WH, Coady W, et al. (2008) Optimal recall period and response task for self-reported HIV medication adherence. AIDS Behav 12: 86-94.

30. Oyugi JH, Byakika-Tusiime J, Charlebois ED, Kityo C, Mugerwa R, et al. (2004) Multiple validated measures of adherence indicate high levels of adherence to generic HIV antiretroviral therapy in a resource-limited setting. J Acquir Immune Defic Syndr 36: 1100-1102.

31. Chesney MA, Ickovics JR, Chambers DB, Gifford AL, Neidig J, et al. (2000) Self-reported adherence to antiretroviral medications among participants in HIV clinical trials: the AACTG Adherence Instruments. AIDS Care 12: 255-266.

32. UNHCR, GLIA, World Bank (2008) Manual for Conducting HIV Behavioral Surveillance Surveys Among Displaced Populations and Their Surrounding Communities. Geneva: UNHCR.

33. Kiboneka A, Nyatia RJ, Nabiryo C, Anema A, Cooper CL, et al. (2009) Combination antiretroviral therapy in population affected by conflict: outcomes from large cohort in northern Uganda. BMJ 338: b201.

34. Mollica R, McDonald LS, Massagli MP, Silove DM (2004) Measuring Trauma, Measuring Torture: Instructions and Guidance on the utilization of the Harvard Program in Refugee Trauma's versions of The Hopkins Symptom Checklist-25 (HSCL-25) & The Harvard Trauma Questionnaire (HTQ) (Unpublished Manual). Cambridge: Harvard University.

35. Antelman G, Kaaya S, Wei RL, Mbwambo J, Msamanga GI, et al. (2007) Depressive symptoms increase risk of HIV disease progression and mortality among women, in Tanzania. Jaids-Journal of Acquired Immune Deficiency Syndromes 44: 470-477.

36. Kendall A, Olson CM, Frongillo EA, Jr. (1995) Validation of the Radimer/Cornell measures of hunger and food insecurity. J Nutr 125: 2793-2801.

37. Kawachi I, Kennedy BP, Lochner K, Prothrow-Stith D (1997) Social capital, income inequality, and mortality. Am J Public Health 87: 1491-1498.

38. Nilsson Schonnesson L, Williams ML, Ross MW, Bratt G, Keel B (2006) Factors associated with suboptimal antiretroviral therapy adherence to dose, schedule, and dietary instructions. AIDS Behav 11: 175-183.

39. Ramsey SD, Cheadle AD, Neighbor WE, Gore E, Temple P, et al. (2001) Relative impact of patient and clinic factors on adherence to primary care preventive service guidelines: an exploratory study. Med Care 39: 979-989.

40. Nyblade L, MacQuarrie K (2006) Can We Measure HIV/AIDS-Related Stigma and Discrimination? Washington, D.C.: USAID.

Cover sheet for each 'research paper' included in a research thesis

PAPER ONE: ADHERENCE TO ANTIRETROVIRAL THERAPY AND TREATMENT OUTCOMES IN CONFLICT-AFFECTED AND FORCIBLY DISPLACED POPULATIONS: A SYSTEMATIC REVIEW

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   JBM designed and implemented the search strategy, wrote the first draft of the manuscript, and edited the manuscript according to comments from co-authors. DAR reviewed the search strategy, supported interpretation of findings, and commented on the manuscript. MS and PS supported the interpretation findings and commented on the manuscript. All authors edited the final draft for intellectual content, and approved the final manuscript.

Candidate's signature

14/8/2012

Supervisor or senior author's signature to confirm role as stated in (2)

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PAPER ONE

ADHERENCE TO ANTIRETROVIRAL THERAPY AND TREATMENT OUTCOMES IN CONFLICT-AFFECTED AND FORCIBLY DISPLACED POPULATIONS: A SYSTEMATIC REVIEW

Brief title

A systematic review of ART treatment outcomes and displacement

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Dear Editor:

We are pleased to submit our manuscript entitled: "Adherence to antiretroviral therapy and treatment outcomes in conflict-affected and forcibly displaced populations: a systematic review."

We believe that this work is appropriate for your Reviews section for the following reasons:

- We report on a systematic review of adherence to antiretroviral therapy and treatment outcomes for a key vulnerable group (forcibly displaced persons). Discussion of this group is currently under-represented in the health science literature. We are not aware of another recent systematic review on this topic.
- The topic will be useful and interesting to your readership and will benefit from the open-access format so that the humanitarian community might profit from the findings.
- We issue some basic suggestions for future research in the field.

Co-authors include colleagues from the United Nations High Commissioner for Refugees, who have responsibility for many of the groups referenced in the manuscript. We are grateful for your consideration and hopeful that this piece can find a place in your journal.

Sincerely,

Joshua Mendelsohn (on behalf of co-authors)

ABSTRACT

Background. Optimal adherence to highly active antiretroviral therapy (HAART) is required to promote viral suppression and to prevent disease progression and mortality. Forcibly displaced and conflict-affected populations may face challenges succeeding on HAART. We performed a systematic review of the literature on adherence to HAART and treatment outcomes in these groups, including refugees and internally-displaced persons (IDPs), assessed the quality of the evidence and suggest a future research program.

Methods. Medline, Embase, and Global Health databases for 1995-2011 were searched using the Ovid platform. A backward citation review of subsequent work that had cited the Ovid results was performed using the Web of Science database. ReliefWeb and Médecins Sans Frontières (MSF) websites were searched for additional grey literature.

Results and conclusion. We screened 297 records and identified 17 reports covering 15 quantitative and two qualitative studies from 13 countries. Three-quarters (11/15) of the quantitative studies were retrospective studies based on chart review; five studies included <100 clients. Adherence or treatment outcomes were reported in resettled refugees, conflict-affected persons, internally-displaced persons (IDPs), and combinations of refugees, IDPs and other foreign-born persons. The reviewed reports showed promise for conflict-affected and forcibly-displaced populations; the range of optimal adherence prevalence reported was 87-99.5%. Treatment outcomes, measured using virological, immunological and mortality estimates, were good in relation to non-affected groups. Given the diversity of settings where forcibly-displaced and conflict-affected persons access ART, further studies on adherence and treatment outcomes are needed to support scale-up and provide evidence-based justifications for inclusion of these vulnerable groups in national treatment plans. Future studies and program evaluations should focus on systematic monitoring of adherence and treatment interruptions by using facility-based pharmacy records, understanding threats to optimal adherence and timely linkage to care throughout the displacement cycle, and testing interventions designed to support adherence and treatment outcomes in these settings.

KEYWORDS

Antiretroviral therapy, treatment outcomes, forced migration, refugees, conflict, adherence, systematic review

LIST OF ABBREVIATIONS

ART: antiretroviral therapy; cART: combination antiretroviral therapy; CI: confidence interval; DRC: Democratic Republic of the Congo; HAART: highly active antiretroviral therapy; HR: hazard ratio; HIV: human immunodeficiency virus; IDP: internally displaced person; MSF: Médecins Sans Frontières; PEV: post-election violence; PMTCT: prevention of mother-to-child transmission; OR: odds ratio; TI: treatment interruption; UNHCR: United Nations High Commissioner for Refugees

COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHOR CONTRIBUTIONS

JBM designed and implemented the search strategy and wrote the first draft of the manuscript. DAR reviewed the search strategy, supported interpretation of findings, and commented on the manuscript. MS and PS supported the interpretation findings and commented on the manuscript. All authors edited the final draft for intellectual content, and approved the final manuscript.

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INTRODUCTION

It is widely accepted that for HIV-positive persons on highly active antiretroviral therapy (HAART), high levels of adherence to treatment regimens are essential for promoting viral suppression and preventing drug resistance. However, conflict-affected and forcibly displaced populations such as refugees and internally-displaced persons (IDPs) may face unique challenges in sustaining good adherence to HAART and treatment outcomes [1-2] while the potential for onward displacement presents a risk of pharmacy defaulting and treatment interruptions. An expectation of difficulty has clouded efforts to provide HAART in these settings [3]. Forcibly displaced populations consist mainly of refugees and IDPs, however, definitions are often confused. According to the Convention relating to the Status of Refugees, a refugee is a person who:

> ...owing to well-founded fear of being persecuted for reasons of race, religion, nationality, membership of a particular social group or political opinion, is outside the country of his nationality and is unable, or owing to such fear, is unwilling to avail himself of the protection of that country; or who, not having a nationality and being outside the country of his former habitual residence as a result of such events, is unable or, owing to such fear, is unwilling to return to it [4].

The Inter-agency Standing Committee defines IDPs as:

> ...persons or groups of persons who have been forced or obliged to flee or to leave their homes or places of habitual residence, in particular as a result of or in order to avoid the effects of armed conflict, situations of generalized violence, violations of human rights or natural or human-made disasters, and who have not crossed an internationally recognized State border [5].

"Conflict-affected persons" are defined as persons residing in active or recent conflict zones or in a post-conflict setting [6-8]. Around the world, some 1.5 billion people live in countries affected by violent conflict, 14.7 million people are internally displaced and 10.6 million are refugees. Of refugees, 68% had been living in exile for ≥5 years in "protracted situations" [9-10]. The primary aim of this review was to aggregate the available evidence on adherence to HAART and treatment outcomes in refugees, IDPs and conflict-affected persons, to assess the quality of work undertaken so far and to suggest future research needs.

METHODS

A systematic review of the published literature was conducted between 20 December 2011 and 20 January 2012 using a four step procedure. First, a search of the Cochrane Database of

Systematic Reviews yielded no previous reviews. Second, we applied our search strategy to the Medline, Embase, and Global Health databases (including conference abstracts) using the Ovid platform. The search strategy incorporated five themes: "HIV", "antiretroviral therapy", "adherence", "outcomes", and "forced migration." Key words were combined with medical subject headings (MeSH) to assess synonyms applicable to each theme. The terms "refugee", "internally-displaced", "conflict-affected", and "forced migration" were used to search the forced migration theme. Table 1 presents a complete list of key words and MeSH terms used. As adherence results are often reported in papers where the primary aim is to report on clinical or treatment outcomes, "disease" and "treatment" themes were combined using the "OR" operator to create a broad pool which could be cross-referenced using the "AND" operator with the "forced migration" theme (see Supp.Table i). Searches were limited to studies in English reported from 1995 onwards. Third, a backwards citation search was performed using the Web of Science "times cited" feature that identified all work cited by any previously identified report in the health science databases. Lastly, a check for sources that may have been posted online but omitted from health science databases was made by searching ReliefWeb and Médecins Sans Frontières (MSF) websites and three experts were consulted for additional sources. On the ReliefWeb and MSF-UK websites, we used the expressions "antiretroviral and refugee" and "antiretroviral and IDP." On ReliefWeb, we searched under the "Analysis", "Assessment", "Evaluation", "Situation Report", "UN document" and "Other" content categories. Abstracts of papers retrieved from all the above steps that were not editorials, commentaries, case reports or had irrelevant titles were subjected to a full-text review. Both qualitative and quantitative studies of adult populations were included in the final dataset if they presented relevant primary data, secondary analyses on adherence to HAART or treatment outcomes, and included adult conflict-affected or forcibly displaced populations. We extracted and presented basic study information and data related to adherence and treatment outcomes. PRISMA guidelines were followed in the reporting of this review [11].

RESULTS

Figure 1 presents the outcome of the search: out of 297 reports retrieved using the search strategy, 17 reports conducted in 13 countries with 8,930 clients were retained for this review. Table 1 summarises the data extracted from selected reports. Three studies reported results for IDPs only. Kiboneka and colleagues [12] conducted a prospective cohort study to measure clinical and immunological outcomes of HAART clients in Gulu District, northern Uganda, the site of civil strife and conflict between the Ugandan government and the Lord's Resistance Army guerrilla group. Adherence was measured by combining pharmacy monitoring, pharmacy refill records and patient self-reports, and dichotomised at the ≥95% level. Over a median

follow-up time of 13.7 months for clients with complete adherence data (n=1,521), 92.2% had ≥95% adherence. Among patients with <95% adherence, 9.3% died compared with 1.2% of patients with ≥95% adherence. In an adjusted analysis, mortality was less likely among women (Hazard ratio, HR=0.7, 95% confidence interval, 95%CI 0.55, 0.91; p=0.02) and clients with >200 CD4 at treatment start (HR=0.14, 95%CI 0.06, 0.34; p<0.001). A second cross-sectional study of IDPs in Gulu District reported a high (99.5%) mean self-reported four-day adherence to HAART [13]. In this study, clients who were on first-line therapy (Odds ratio, OR=22.22, 95%CI 1.53, 333.33; p=0.02) or who reported that clinic staff were "condemning" (OR=22.22, 95%CI 1.53, 333.33; p=0.02) were more likely to report non-adherence. A study of mortality among Kenyan IDPs in the post-election violence period of 2007-2008 found increased mortality in HIV-positive IDPs when compared with mortality during the same period among HIV-positive residents captured in the same Demographic Surveillance Survey catchment area prior to the violence [14].

We identified six studies that reported on conflict-affected, mixed refugee and IDP populations, or unspecified foreigners, including both refugees and asylum-seekers. O'Brien and colleagues [2], reporting on a pooled analysis of 12 MSF conflict and post-conflict HAART programs (n=2,572), found a median probability of survival at 12 months of 0.89 (95%CI 0.88, 0.91). Two further MSF studies of individual programs found good survival outcomes. In a post-conflict program in the Republic of Congo [15], the survival probability at 12 months was 0.89 (95%CI 0.82, 0.93). In a study from Bukavu, Democratic Republic of the Congo (DRC) during an active conflict involving the central government, insurgents and proxy armies from neighbouring states [16], optimal HAART adherence (defined as missing less than 5% of pills between clinic visits) measured by pill counts was attained by 99% of participants, although the limitations of this method in this setting were not specified. The conflict setting had higher 12-month mortality (7.9%, 95%CI 3.6, 12.1) than comparison settings, but the six-month median CD4 cell gain of 163 cells/mm^3 compared favourably with cohorts from a resource-limited setting (106 cells/mm^3) and a resource-rich setting (103 cells/mm^3). In the Equatorial province of Sudan, Salami and colleagues [17] found that 88% of refugees and IDPs on HAART for ≥6 months self-reported ≥95% adherence. A South African study comparing self-identified foreigners with local citizens reported that foreigners were less than half as likely (OR=0.45, 95%CI 0.23, 0.87; p= 0.017) to have suffered viral failure, defined as ART cessation, any decrease in CD4 from pre-ART levels, a viral load of >1000 copies/mL, or death [18]. In a Kenyan study that used a pre-post design to investigate treatment interruptions (TI) (defined as the proportion visiting pharmacy ≥48 hours after ARTs completed), 16.1% experienced a TI during post-election violence compared with 10.2% in the comparison period [19]. For clients who overlapped between the two periods, the odds of TI were elevated by 71% during post-

election violence (95%CI 34, 118, p<0.001]. Men (OR=1.37, 95%CI 1.07, 1.76; p=0.01) and clients travelling more than three hours to the clinic (OR=1.86, 95%CI 1.28, 2.71; p=0.001) also were more likely to experience a TI.

Four studies were conducted among HIV-positive refugees in high income settings. An HIV-positive refugee cohort in Rhode Island, USA, had lower odds of initiating HAART when compared with non-refugees (OR=0.37, 95%CI 0.13, 0.92; p=0.03) and had a lower attendance at scheduled appointments relative to non-refugees (75% v. 86%, p=0.17) [20]. In a New Zealand-based refugee cohort on HAART, 61% had an undetectable HIV viral load after one year of treatment [21]; a US study reported undetectable viral load in 87% of refugees receiving HAART [22]. In a Canadian study, 80% of a cohort consisting of native-born clients, refugees and other immigrants from Sub-Saharan African and elsewhere were virologically suppressed [23]. In this study, the rate of progression to new opportunistic infections or AIDS-defining events was higher among the former group (0.1 v. 0.06 events/1000 patient-days) while the mortality rate restricted to HIV-related deaths was higher among the latter group (0.8 v. 1.2 deaths/1000 patient-months).

Two studies dealt exclusively with pregnant mothers taking ART for prevention of mother-to-child transmission (PMTCT). The first study, conducted among a resettled group of refugees on HAART during pregnancy in Rhode Island, USA, reported a reduction in median viral load at the time of delivery [24]. A study conducted in a Tanzanian refugee camp reported a 98% (185/189) uptake of nevirapine at the time of delivery, but women who initially refused the medication or who were repatriated to their native countries prior to delivery were not included [25].

Two additional qualitative studies were also eligible for review. One study conducted in Teso, northern Uganda [26], identified security while attending clinics, food security, distance to health centres and access to health providers as the main concerns of clients and health workers in relation to HAART adherence. Respondents noted that food insecurity and single daily meals made multiple daily dosing a challenge during famines and floods. A second study from northern Uganda [27] reported on the impact of social networks on long-term provision of antiretrovirals. This study reported that community-based volunteers and health workers were effective in supporting adherence and the formation of social support groups, while social networks assisted in overcoming challenges that were independently related to displacement and stigma. Notably, but perhaps unsurprisingly, the study identified inadequate planning in the return phase of the forced displacement cycle as presenting significant challenges in patient monitoring, missed appointments, and loss to follow-up. Finally, in a qualitative sub-study (counted as a quantitative study for the purposes of Figure 1), Pyne-Mercier and colleagues [19]

reported that 6/ 13 interviewed clients had been attacked by mobs or had their homes or businesses vandalised during post-election violence in Kenya. Lack of transport and inflated transport costs were identified as barriers to accessing treatment, while personal commitment and support from family and clinic social workers facilitated access to treatment.

[*** Figure 1, p.42, and Table 1, p.43-46, near here ***]

DISCUSSION AND CONCLUSIONS

This review revealed a limited number of studies on adherence to HAART and treatment outcomes, however the outcomes observed in the reviewed studies showed promise for conflict-affected and forcibly displaced populations. The range of optimal adherence prevalence of 87-99.5% compared favourably with other settings. A meta-analysis of 84 observational studies reported a 62% average reporting rate of ≥90% adherence [28]. A second meta-analysis comparing resource-limited and resource-rich settings [29] reported that 55% of North American populations and 77% of sub-Saharan African populations achieved adequate adherence. In this study, factors negatively affecting adherence in sub-Saharan Africa included non-disclosure of HIV status to a loved one for fear of stigma, alcohol abuse, and difficulty following complex drug regimens. In a separate review of barriers to adherence, pooled results from ten quantitative studies in developing countries identified financial constraints (52%, 95%CI 16, 88) and forgetfulness (36%, 95%CI 19, 55) as major barriers [30]. A review of African studies [31] reported that 68-99% of patients were ≥95% adherent but found no studies documenting the use of formal adherence intervention programs. The present review identified one study [13] that compared conflict-affected or forcibly displaced groups to a local host community or that assessed potential barriers to, and facilitators of adherence and/or treatment outcomes. Garang and colleagues found no significant differences in adherence between IDPs and non-IDPs (99.6% v. 99.5%) and reported that being on first-line treatment and clients' perceived condemnation by medical staff reduced the odds of optimal adherence. Barriers to adherence in this study included depression after losing a child, forgetfulness, travelling, and not refilling medications on schedule.

We located one study that specifically studied treatment interruptions [19]. Understanding the prevalence and consequences of treatment interruptions is highly relevant for conflict-affected and forcibly displaced groups given their previous displacement history and the potential for onwards travel including resettlement or repatriation after initiation of therapy. Studies in other population groups that investigated interruptions as therapeutic alternatives to continuous therapy such as intentional treatment holidays and unintentional interruptions have found harmful results. Initial concerns about long-term safety and reports of a lack of improved

virological response in trials of structured interruptions [32-33] were confirmed by the Strategies for Management of Antiretroviral Therapy (SMART) study, which found that CD4-guided episodic therapy increases the risk of opportunistic disease or death in relation to continuous treatment [34]. A review of unstructured TIs found an increased risk of opportunistic infections, virological failure, drug resistance, poor immunological recovery and death [35]. Future studies on forcibly displaced and conflict-affected groups should facilitate the monitoring of TIs by combining data from facility-based pharmacy records and mobile phone follow-up contact with clients that confirm TIs when clients fail to report for routine pharmacy refill appointments.

The studies included in this review were conducted in a variety of contexts including camps, rural, and urban areas in low-income settings and urban areas in high-income settings. Although the studies did not describe the specific features of the clinics where HAART was delivered, these were likely variable in relation to the type of institutional provider, which ranged from publicly-run hospitals to non-governmental organisations, and their respective resource levels. Given the importance of context for outcomes, the variation in settings may have affected the reported findings and merit further study. The majority (14/15) of the reviewed quantitative studies were facility-based. When clients present at new treatment facilities, HIV testing and counselling is routinely administered where indicated and HAART is initiated according to national guidelines, regardless of treatment history. With the exception of the MSF study settings where no previous HIV testing had taken place, there was no way to verifty whether treatment start at the study facility was equivalent to treatment initiation, or if treatment had been started elsewhere prior to onwards displacement and arrival at the study facility. Establishing the date and location of HAART initiation is challenging in any setting where medical records are not routinely shared and client recall of their complete treatment history may be compromised. Where possible, investigations that attempt to address these shortcomings will be useful for estimating the effect of forced displacement on adherence and treatment outcomes and for correctly interpreting findings. Moreover, the categorisation of displaced persons presents additional challenges; definitions may affect the network of providers, the availability of particular services, and the extent of co-payments (if any). For example, in non-refugee camp settings a lack of documentation or xenophobic attitudes may present obstacles to accessing key services including HIV counselling, testing, and ART. To facilitate generalisability to similar settings and population groups, future studies should be mindful of these categorizations and their impact on outcomes.

There were some limitations to this review. Although we searched health databases and grey literature, it is possible that relevant studies were omitted; moreover, we limited our search to reports published in English. To minimise this risk of exclusion, we used a backwards citation

search and expert consultation. Most identified studies used a single adherence indicator, which suggested a possibility of measurement bias. Self-report and pharmacy refills are the most commonly used instruments in resource-limited settings; however there is no widely accepted standard for measuring adherence [36-37]. Triangulation is one way to enhance confidence in measurement validity, especially in challenging multi-linguistic or complex emergency settings. Guidelines developed by an International Association of Physicians in AIDS Care Panel recommended routine use of both self-reports and pharmacy refill measures [38]. Where possible, multiple adherence measurements should be used, especially when more objective measures such as medication event monitoring systems (MEMS) are not feasible and biomarkers are not available from medical records or are too difficult or expensive to collect.

The geographic breadth of quantitative studies was limited: 53% (8/15) of the studies were conducted with asylum-based refugees and IDPs in African settings. Notably, only one study dealt with documented refugees in low-income settings [17]. The limited number of studies, small sample sizes (five included <100 clients), lack of comparison groups and varied outcomes and indicators suggest that estimates may have suffered from selection and response biases. We did not undertake a meta-analysis due to substantial differences between client groups, methods and outcomes across studies. Despite these difficulties, the reviewed studies were designed around local circumstances: samples were either limited by the absolute number of clients with available records to review, the study was facility-based and only had access to a limited pool of clients, or an evaluation of adherence and treatment outcomes was not the primary aim. Response bias was likely to have been less of a concern in the study by Kiboneka and colleagues [12], where a comprehensive adherence assessment of all HIV-positive clients attending one hospital was undertaken. However, the risk that the small number of studies available for review were conducted in settings more suitable for research, for example where data existed in a form particularly conducive to chart reviews, may have biased the findings towards better outcomes.

If HAART is to be scaled-up in conflict-affected and forcibly displaced clients, studies designed to assess adherence and treatment outcomes will be critical for optimising treatment outcomes and preventing drug resistance, the latter associated with widespread distribution of medications, the use of less tolerated regimens, restricted virological monitoring, and the potential for inconsistent drug supply [39]. The World Health Organisation's public health strategy to mitigating drug resistance recommends providing highly effective first-line regimens, prescribing previously unused drug classes when switching after first-line treatment failure, reserving the drugs that are least likely to provoke resistance for patients whose first-line treatments are no longer effective, and administering regimens that encourage adherence [40]. For forcibly-displaced and conflict-affected clients, these principles raise important questions.

What is the most effective first-line regimen for these settings [41]? When clients are displaced and have a poor knowledge of their treatment history, which HAART regimen should be used? Are HIV-positive individuals who were started on HAART prior to displacement identified quickly in the host setting, linked to care in a timely manner, and succeeding on treatment? Are best practices correctly implemented prior to voluntary repatriation or resettlement to a third country? Which factors, regimen-related or otherwise, encourage good adherence? Recent intervention studies in resource-limited settings have shown that counselling services and mobile phone-based reminders helped to maintain adherence and viral suppression [42-43]. Although trials have not been conducted among conflict-affected and forcibly-displaced populations, a useful basis for intervention consisted of 7-step support package delivered by MSF in Musina, South Africa, tailored to the needs of migrants, refugees, and asylum-seekers. This report, published after our review period, found that 92% (95%CI 75.2, 97) of clients were virologically suppressed (<400 copies/mL) at 12 months after receiving this intervention, which included a patient-held record ("health passport"), an alternative treatment site road map, anticipation of travel at regular clinic visits, a safe travel pack (including buffer stock of ARVs, a washout regimen, and a transfer letter), migrant-adapted treatment counselling, a questionnaire for returning patients and migrant-adapted monitoring of retention in care [44].

The limited evidence from the small series of studies available for this review suggests that HAART adherence and treatment outcomes among conflict-affected and forcibly displaced adults may be as good as outcomes attained in unaffected population groups. Future research should consider stronger study designs that address TIs throughout the displacement cycle, more geographic variation, the use of a systematic, replicable, and triangulated approach to adherence measurement and monitoring and the design and testing of interventions to improve adherence and treatment outcomes. Given that refugees in asylum countries tend to remain for an average of 17 years [45], there is a strong national interest and humanitarian rationale for ensuring universal access to HIV treatment and care, promoting optimal outcomes among all vulnerable groups and developing a consensus approach to achieving these goals [46]. For effective HAART scale-up in conflict-affected and forcibly displaced clients, assessing adherence and treatment outcomes will be critical for promoting viral suppression, preventing drug resistance and reducing transmission.

REFERENCES

1. International Federation of Red Cross and Red Crescent Societies: **World Disaster Report 2008: Focus on HIV and AIDS.** In. Geneva; 2008: 118-141
2. O'Brien DP, Venis S, Greig J, Shanks L, Ellman T, Sabapathy K, Frigati L, Mills C: **Provision of antiretroviral treatment in conflict settings: the experience of Médecins Sans Frontières.** *Confl Health* 2010, **4**:12.
3. Mills EJ, Ford N, Singh S, Eyawo O: **Providing antiretroviral care in conflict settings.** *Curr HIV/AIDS Rep* 2009, **6**:201-209.
4. **Convention relating to the Status of Refugees** [http://www.unhcr.org/refworld/docid/3be01b964.html]
5. **Handbook for the Protection of Internally Displaced Persons** [http://www.unhcr.org/refworld/docid/4790cbc02.html]
6. **Uppsala Conflict Data Program Conflict Encyclopedia** [http://www.pcr.uu.se/research/ucdp/definitions/#Active]
7. **Definitions of Fragility and Conflict** [http://web.worldbank.org/WBSITE/EXTERNAL/PROJECTS/STRATEGIES/EXTLICUS/0,,contentMDK:22230573~pagePK:64171531~menuPK:4448982~piPK:64171507~theSitePK:511778,00.html]
8. Strand H, Dahl M: **Paper commissioned for the EFA Global Monitoring Report 2011, The hidden crisis: armed conflict and education.** UNESCO; 2010.
9. **Statistical Yearbook 2010** [http://www.unhcr.org/statistics]
10. **Select Fact and Figures on Fragility and Conflict** [http://web.worldbank.org/WBSITE/EXTERNAL/PROJECTS/STRATEGIES/EXTLICUS/0,,contentMDK:22934897~pagePK:64171531~piPK:64171507~theSitePK:511778,00.html]
11. Moher D, Liberati A, Tetzlaff J, Altman DG: **Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement.** *PLoS Med* 2009, **6**:e1000097.
12. Kiboneka A, Nyatia RJ, Nabiryo C, Anema A, Cooper CL, Fernandes KA, Montaner JS, Mills EJ: **Combination antiretroviral therapy in population affected by conflict: outcomes from large cohort in northern Uganda.** *BMJ* 2009, **338**:b201.
13. Garang PG, Odoi RA, Kalyango JN: **Adherence to antiretroviral therapy in conflict areas: a study among patients receiving treatment from Lacor Hospital, Uganda.** *AIDS Patient Care STDS* 2009, **23**:743-747.
14. Feikin DR, Adazu K, Obor D, Ogwang S, Vulule J, Hamel MJ, Laserson K: **Mortality and health among internally displaced persons in western Kenya following post-election violence, 2008: novel use of demographic surveillance.** *Bull World Health Organ* 2010, **88**:601-608.
15. O'Brien DP, Mills C, Hamel C, Ford N, Pottie K: **Universal access: the benefits and challenges in bringing integrated HIV care to isolated and conflict affected populations in the Republic of Congo.** *Confl Health* 2009, **3**:1.
16. Culbert H, Tu D, O'Brien DP, Ellman T, Mills C, Ford N, Amisi T, Chan K, Venis S: **HIV treatment in a conflict setting: outcomes and experiences from Bukavu, Democratic Republic of the Congo.** *PLoS Med* 2007, **4**:e129.

17. Salami O, Buzu A, Nzeme C: **High level of adherence to HAART among refugees and internally displaced persons on HAART in western equatorial region of Southern Sudan.** *J Int AIDS Soc* 2010, **13:**123.

18. McCarthy K, Chersich MF, Vearey J, Meyer-Rath G, Jaffer A, Simpwalo S, Venter WDF: **Good treatment outcomes among foreigners receiving antiretroviral therapy in Johannesburg, South Africa.** *Int J STD AIDS* 2009, **20:**858-862.

19. Pyne-Mercier LD, John-Stewart GC, Richardson BA, Kagondu NL, Thiga J, Noshy H, Kist N, Chung MH: **The consequences of post-election violence on antiretroviral HIV therapy in Kenya.** *AIDS Care* 2011, **23:**562-568.

20. Beckwith CG, DeLong AK, Desjardins SF, Gillani F, Bazerman L, Mitty JA, Ross H, Cu-Uvin S: **HIV infection in refugees: a case-control analysis of refugees in Rhode Island.** *Int J Infect Dis* 2009, **13:**186-192.

21. Nisbet SM, Reeve AM, Ellis-Pegler RB, Woodhouse AF, Ingram RJ, Roberts SA, McAllister SM, Thomas MG: **Good outcome in HIV-infected refugees after resettlement in New Zealand: population study.** *Intern Med J* 2007, **37:**290-294.

22. Moreno A, Crosby S, Labelle C, Sullivan M, Samet JH: **Health assessment of HIV-infected refugees.** *J Acquir Immune Defic Syndr* 2003, **34:**251-254.

23. Krentz H, Gill MJ: **The five-year impact of an evolving global epidemic, changing migration patterns, and policy changes in a regional Canadian HIV population.** *Health Policy* 2009, **90:**296-302.

24. Blood E, Beckwith C, Bazerman L, Cu-Uvin S, Mitty J: **Pregnancy among HIV-infected refugees in Rhode Island.** *AIDS Care* 2009, **21:**207-211.

25. Rutta E, Gongo R, Mwansasu A, Mutasingwa D, Rwegasira V, Kishumbu S, Tabayi J, Masini T, Ramadhani H: **Prevention of mother-to-child transmission of HIV in a refugee camp setting in Tanzania.** *Glob Public Health* 2008, **3:**62-76.

26. Olupot-Olupot P, Katawera A, Cooper C, Small W, Anema A, Mills E: **Adherence to antiretroviral therapy among a conflict-affected population in Northeastern Uganda: A qualitative study.** *AIDS* 2008, **22:**1882-1884.

27. Wilhelm-Solomon M: **Social networks and sustainable antiretroviral provision to displaced communities in northern Uganda.** *Trop Med Int Health* 2009, **14:**35-36.

28. Ortego C, Huedo-Medina TB, Llorca J, Sevilla L, Santos P, Rodriguez E, Warren MR, Vejo J: **Adherence to highly active antiretroviral therapy (HAART): a meta-analysis.** *AIDS Behav* 2011, **15:**1381-1396.

29. Mills EJ, Nachega JB, Buchan I, Orbinski J, Attaran A, Singh S, Rachlis B, Wu P, Cooper C, Thabane L, et al: **Adherence to antiretroviral therapy in sub-Saharan Africa and North America: a meta-analysis.** *JAMA* 2006, **296:**679-690.

30. Mills EJ, Nachega JB, Bangsberg DR, Singh S, Rachlis B, Wu P, Wilson K, Buchan I, Gill CJ, Cooper C: **Adherence to HAART: a systematic review of developed and developing nation patient-reported barriers and facilitators.** *PLoS Med* 2006, **3:**e438.

31. Akileswaran C, Lurie MN, Flanigan TP, Mayer KH: **Lessons learned from use of highly active antiretroviral therapy in Africa.** *Clin Infect Dis* 2005, **41:**376-385.

32. Pai NP, Lawrence J, Reingold AL, Tulsky JP: **Structured treatment interruptions (STI) in chronic unsuppressed HIV infection in adults.** *Cochrane Database Syst Rev* 2006, **3:**CD006148.

33. Pai NP, Tulsky JP, Lawrence J, Colford JM, Jr., Reingold AL: **Structured treatment interruptions (STI) in chronic suppressed HIV infection in adults.** *Cochrane Database Syst Rev* 2005:CD005482.

34. El-Sadr WM, Lundgren JD, Neaton JD, Gordin F, Abrams D, Arduino RC, Babiker A, Burman W, Clumeck N, Cohen CJ, et al: **CD4+ count-guided interruption of antiretroviral treatment.** *N Engl J Med* 2006, **355**:2283-2296.

35. Kranzer K, Ford N: **Unstructured treatment interruption of antiretroviral therapy in clinical practice: a systematic review.** *Trop Med Int Health* 2011.

36. Chesney MA: **The elusive gold standard - future perspectives for HIV adherence assessment and intervention.** *J Acquir Immune Defic Syndr* 2006, **43**:S149-S155.

37. Nachega JB, Mills EJ, Schechter M: **Antiretroviral therapy adherence and retention in care in middle-income and low-income countries: current status of knowledge and research priorities.** *Curr Opin HIV AIDS* 2010, **5**:70-77.

38. Thompson MA, Mugavero MJ, Amico KR, Cargill VA, Chang LW, Gross R, Orrell C, Altice FL, Bangsberg DR, Bartlett JG, et al: **Guidelines for improving entry into and retention in care and antiretroviral adherence for persons With HIV: evidence-based recommendations from an International Association of Physicians in AIDS Care panel.** *Ann Intern Med* 2012, **156**:817-33.

39. Hamers RL, Wallis CL, Kityo C, Siwale M, Mandaliya K, Conradie F, Botes ME, Wellington M, Osibogun A, Sigaloff CE, et al: **HIV-1 drug resistance in antiretroviral-naive individuals in sub-Saharan Africa after rollout of antiretroviral therapy: a multitcentre observational study.** *Lancet Infect Dis* 2011, **11**:750-759.

40. Gilks CF, Crowley S, Ekpini R, Gove S, Perriens J, Souteyrand Y, Sutherland D, Vitoria M, Guerma T, De Cock K: **The WHO public-health approach to antiretroviral treatment against HIV in resource-limited settings.** *Lancet* 2006, **368**:505-510.

41. Adlington R, Richens J, Shahmanesh M: **First-line antiretroviral therapy in resource-limited settings: time to reconsider?** *J Infect Dis* 2009, **199**:1407; author reply 1407-1408.

42. Chung MH, Richardson BA, Tapia K, Benki-Nugent S, Kiarie JN, Simoni JM, Overbaugh J, Attwa M, John-Stewart GC: **A randomized controlled trial comparing the effects of counseling and alarm device on HAART adherence and virologic outcomes.** *PLoS Med* 2011, **8**:e1000422.

43. Lester RT, Ritvo P, Mills EJ, et al: **Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya1): a randomised trial.** *Lancet* 2010, **376**:1838-1845.

44. Médecins Sans Frontières: **Providing antiretroviral therapy for mobile populations: lessons learned from a cross border ARV program in Musina, South Africa.** Cape Town: Médecins Sans Frontières; 2012.

45. UNHCR: **Protracted refugee situations - Standing Committee 30th Meeting.** Geneva: UNHCR; 2004.

46. Ford N: **Treating AIDS in complex emergencies: the need for clear policy consensus.** *Progress in Development Studies* 2009, **9**:55-61.

TABLES AND FIGURES

Figure 1: Study selection flowchart

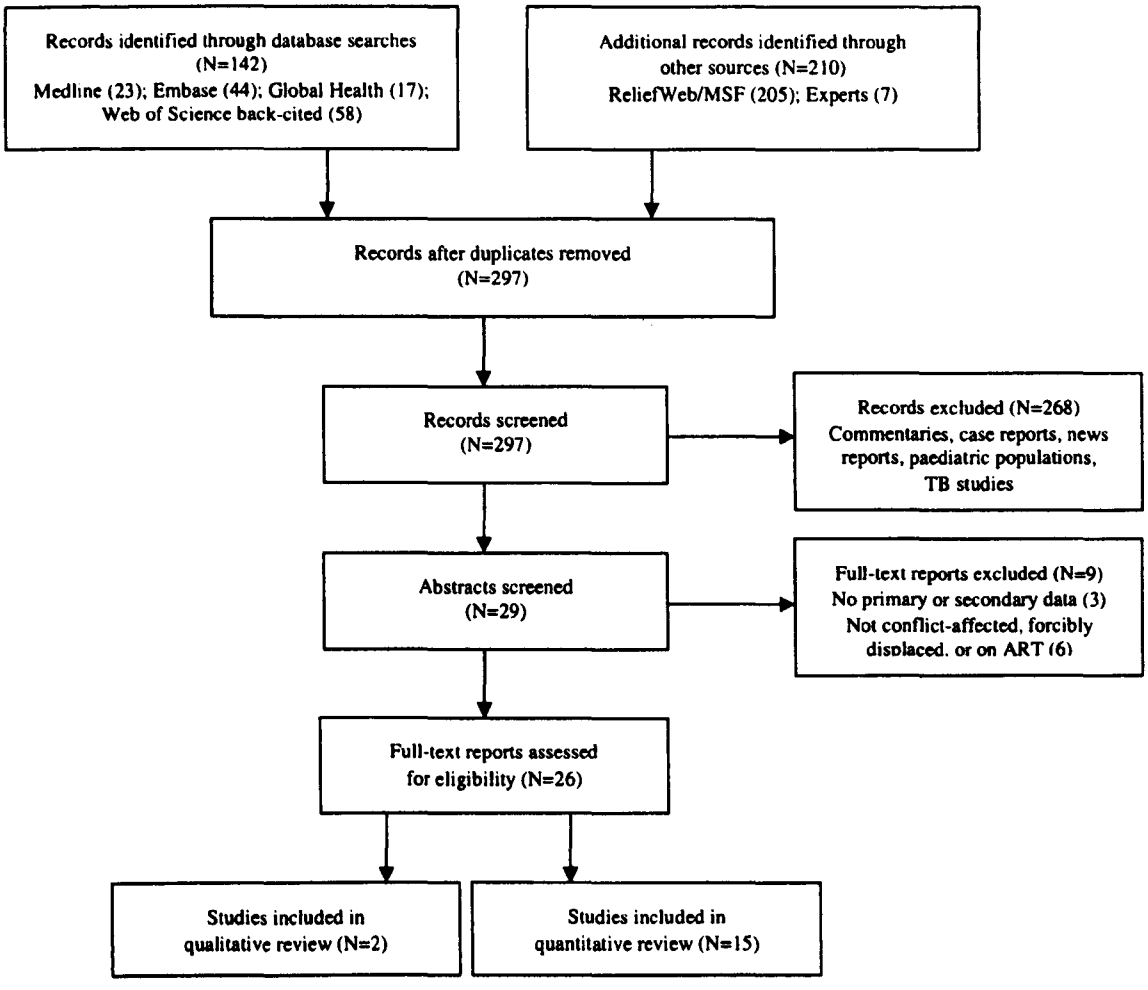

Table 1: Descriptions of quantitative studies included in the systematic review

Location; study period [Ref]	Study type	Population [comparison group]	Time on HAART	Relevant reported HAART adherence outcome	Relevant reported treatment outcome	Adjusted analysis (outcome; factors associated with outcome with p<0.05)
Lacor Hospital, Gulu District, Uganda; June 2005-Jan 2008 [12]	Prospective cohort study by structured questionnaire	IDPs, n=1625; 14% residing in IDP camps, 86% residing in outlying areas; >14 years-old [No comparison group]	Cumulative patient-years follow-up=1981	Composite of pharmacy monitored drug possession ratio, pharmacy refill records, and 3-day self-reported recall by patients or caregivers: ≥95% doses taken as prescribed=92.2%	Mortality incidence=3.48 (95% CI 2.66-4.31) per 100 person-years, log rank p-value<0.01. Median CD4 change (IQR)= 0 (0-0)	Lower all-cause mortality: -Sex, female vs. male (HR=0.7 95% CI 0.55-0.91, p=0.02) -Baseline CD4 count, per 100 cell increase (HR=0.14, 95% CI 0.06-0.34, p<0.001)
Lacor Hospital, Gulu District, Uganda. Jan-Feb 2008 [13]	Cross-sectional survey by semi-structured questionnaire	IDPs, n=200, 29% residing in IDP camps, 71% residing in outlying areas, ≥18 years-old [No comparison group]	≤12 months=33.0% 13-24 months= 29.5% >24 months=37.5%	Mean 4-day self-reported adherence recall, ≥95% doses taken as prescribed= 99.5%	NA	<95% adherence: -First line vs. second line treatment [OR=22.22, 95% CI 1.48-333.33, p=0.03] -Staff were condemning, yes vs. no (OR=22.22, 95% CI 1.5-333.33, p=0.02)
Nyanza province, Kenya, Dec 2007-July 2008 [14]	Retrospective cohort study by review of demographic surveillance data	IDPs, n=28 (proportion on HAART unknown); rural; ≥5 years-old [IDP HIV mortality compared with prior DSS residents]	Not known	NA	53% (28/53) HIV mortality in IDPs vs. 25% (235/936) HIV mortality in 2008 DSS residents, p<0.001	NA
Kinkala/Mindouli, Republic of Congo. May 2006-Dec 2007 [15]	Retrospective cohort study by chart review	Conflict-affected, n=222; rural; adults ≥15 years-old [No comparison group]	Mean follow-up time on HAART=9 months	NA	Probabilities of survival -(n=129) at 6 months=0.94 95% CI 0.89-0.96 -(n=70) at 12 months=0.89 95% CI 0.82-0.93	NA

Table 1: Descriptions of quantitative studies included in the systematic review

Location; study period [Ref]	Study type	Population (comparison group)	Time on HAART	Relevant reported HAART adherence outcome	Relevant reported treatment outcome	Adjusted analysis (outcome; factors associated with outcome with p<0.05)
12 MSF programs. Oct 2003- [2]	Retrospective cohort study by chart review	Conflict-affected, n=2572; rural; adults ≥15 years-old (No comparison group)	Median follow-up time on HAART=11.8 months (IQR 3.9-22.7)	NA	-Median probability of survival at 12 months 0.89, 95% CI 0.88-0.91 -Proportion lost to follow-up 0.11, 95% CI 0.09-0.12 -Median 6-month CD4 gain=129 cells/mm^3	NA
MSF Project, Bukavu, Democratic Republic of the Congo. May 2002-Jan 2006 [16]	Retrospective cohort study by chart review	Conflict-affected, n=494; urban and outlying areas (Compared with 18 low-income setting cohorts in Africa, Asia, and South America and 12 high-income setting cohorts in Europe and North America)	Person-years follow-up=235	>95% pills taken as prescribed as of last clinic visit, measured by pill counts=99%	6-month median CD4 gain (IQR): 163 (82-232) 12-month mortality (95% CI)=7.9% (3.6-12.1)	NA
Equatorial region of southern Sudan. July 2009-March 2010 [17]	Retrospective cohort study by chart review	Refugees and IDPs, n=159 (69% living in refugee camps, 12% internally-displaced at time of HAART start), rural, adults age-cut-off not reported (No comparison group)	64% on HAART for ≥6 months	>95% adherence by self-report over past month=88% (of those on HAART for ≥6 months)	NA	NA

Table 1: Descriptions of quantitative studies included in the systematic review

Location; study period [Ref]	Study type	Population [comparison group]	Time on HAART	Relevant reported HAART adherence outcome	Relevant reported treatment outcome	Adjusted analysis (outcome; factors associated with outcome with p<0.05)
Nazareth House, Johannesburg, South Africa, April 2004-March 2007 [18]	Retrospective cohort study by chart review	Foreigners, n=568 (% refugees or IDPs unknown); urban; age≥16 [Compared with local citizens (n=431) and persons of unknown citizenship (n=298)]	Median (IQR) person-years on HAART: -Foreigners=0.5 (0.1-0.9) -Local citizens=0.6 (0.2-1.1) -Unknown citizenship=0.5 (0.2-1.1)	NA	Viral failure (ART cessation, patient death, viral load >1000 copies/mL, any decrease in CD4 from pre-ART levels): -Foreigners=24% -Local citizens=42% -Unknown=53% p-value (foreigners vs. local citizens) = 0.001	Viral failure (ART cessation, patient death, viral load >1000 copies/mL, any decrease in CD4 from pre-ART levels) -Citizenship status, foreigner vs. local citizen (OR=0.45, 95% CI 0.23-0.87,p= 0.017) -Opportunistic infections, TB before ART vs. none (OR=2.5, 95% CI 1.4-4.5, p=0.002)
Coptic Hope Centre for Infectious Diseases, Nairobi, Kenya, December 2006-February 2007 [19]	Retrospective cohort by chart review	Local population, n=2,534; Kenyan residents; age ≥18 [Compared with n=2,167 one year earlier, before post-election violence]	Median duration on treatment (IQR) 19.5 months (9.8-28.5) Comparison group was "similar"	Proportion interrupting treatment (visiting pharmacy ≥48 hours after ARTs completed) -16.1% in PEV group -10.2% in comparison group	NA	-Odds of TI during PEV increased by 71% 95%CI 34 to 118] -During post-election violence, odds of TI increased for men (OR=1.37, 95%CI 1.07 to 1.76, p=0.01) and clients travelling ≥3 hours to clinic (OR=1.86, 95%CI 1.28 to 2.71, p=0.001)
Miriam Hospital, Providence, Rhode Island, USA, 2000-2006 [20]	Matched case-control study by retrospective chart review	Refugees, n=52 (29 started ART); non-refugees, n=52 (41 started ART); urban [Controls were non-refugees matched on gender]	NR	Adherence to scheduled appointments: -Refugees=75% -Non-refugees=86%, p=0.17 -Initiation of HAART: Refugees=56% -Non-refugees=79% (OR=0.37, 95% CI 0.13-0.92, p=0.03)	Not reported	NA

Table 1: Descriptions of quantitative studies included in the systematic review

Location; study period (Ref)	Study type	Population (comparison group)	Time on HAART	Relevant reported HAART adherence outcome	Relevant reported treatment outcome	Adjusted analysis (outcome; factors associated with outcome with p<0.05)
Mangere Refugee Resettlement Centre, Auckland, New Zealand, June 1993-June 2004 [21]	Retrospective cohort study by chart review	Refugees from Africa and Asia, n=98 (n=60 started HAART); urban [No comparison group]	NR	NA	Undetectable viral load 1 year after HAART start= 61% (36/59)	NA
Boston Medical Centre, USA, June 2000-June 2001 [22]	Retrospective cohort study by chart review	Refugees, n=34, n=15 on HAART; urban [No comparison group]	NR	"Reported adherence with medications"= 87%	Undetectable viral load (not defined)=87%	NA
Southern Alberta, Canada, Jan 2001-Jan 2007 [23]	Retrospective cohort study by chart review	Sub-Saharan African, n=126 (68% refugees); Other foreign-born, n=72 (14% refugees) [Canadian-born, n=455]	NR	"Good adherence within foreign-born patients to HAART" (data not shown)	80% viral suppression (no comparison between groups reported)	NA
Miriam Hospital, Providence, Rhode Island, USA, 2000-2006 [24]	Retrospective cohort study by chart review	Pregnant, resettled refugee women, n=14; rural [No comparison group]	NR	Lost to follow-up=1/14 (7%)	Median viral load at time of pregnancy=3.36 $\log_{10}$ copies/mL Median viral load at time of delivery=1.88 $\log_{10}$ copies/mL	NA
Great Lukole camp, Tanzania, Oct 2002-Sept 2004[25]	Retrospective cohort study by chart review	Women delivering in camp, n=189 [No comparison group]	NA	Single dose nevirapine uptake at labour=98% (185/189) excluding repatriated women and 62% (185/301) including refusals and repatriations	NA	NA

NA (not applicable)=outcome not applicable/analysis not done; NR (not reported)=data not reported
IDP=internally-displaced person, OR=odds ratio, HR=hazard ratio; CI=confidence interval; IQR=inter-quartile range; HAART=highly active antiretroviral therapy; ART=antiretroviral therapy; TB=tuberculosis; TI=treatment interruption

SUPPLEMENTARY MATERIALS

Submitted as an Additional file.

Supp. Table I: Systematic review search strategy used in MEDLINE*

Step	Search theme	Key word(s) and MeSH term(s)
1	**Forced migration**	[refugee*] or [forced migra*] or [internally-displaced] or [conflict-affected] or [exp Refugees/]
2	**HIV disease**	[HIV] or [AIDS] or [exp HIV/] or [exp HIV-2/] or [exp HIV-1/]
3	**Adherence**	[adherence] or [compliance] or [exp Medication Adherence/] or [exp Patient Compliance/] or [treatment interruption*]
4	**Antiretroviral therapy**	[antiretroviral therapy] or [HAART] or [ART] or[cART] or [exp Anti-HIV Agents/] or [exp Antiretroviral Therapy, Highly Active/]
5	**Treatment outcomes**	[treatment outcome*] or [exp Treatment Outcome/] or [exp RNA, Viral/] or [exp Viral Load/] or [cd4] or [exp Antigens, CD4/] or [viral load]
6	**Adherence AND Treatment outcomes**	[adherence] or [compliance] or [exp Medication Adherence/] or [exp Patient Compliance/] or [treatment interruption*] AND [antiretroviral therapy] or [HAART] or [ART] or[cART] or [exp Anti-HIV Agents/] or [exp Antiretroviral Therapy, Highly Active/]
7	**Adherence AND HIV disease**	[adherence] or [compliance] or [exp Medication Adherence/] or [exp Patient Compliance/] or [treatment interruption*] AND [HIV] or [AIDS] or [exp HIV/] or [exp HIV-2/] or [exp HIV-1/]
8	**Antiretroviral therapy AND Treatment outcomes**	[antiretroviral therapy or HAART or ART or cART] OR [exp Anti-HIV Agents/ OR exp Antiretroviral Therapy, Highly Active/] AND [treatment outcome*] or [exp Treatment Outcome/] or [exp RNA, Viral/] or [exp Viral Load/] or [cd4] or [exp Antigens, CD4/] or [viral load]
9	**HIV disease AND Treatment outcomes**	[HIV] or [AIDS] or [exp HIV/] or [exp HIV-2/] or [exp HIV-1/] AND [treatment outcome*] or [exp Treatment Outcome/] or [exp RNA, Viral/] or [exp Viral Load/] or [cd4] or [exp Antigens, CD4/] or [viral load]
10	**Forced migration AND all themes**	[Forced migration] AND [(Adherence AND Treatment outcomes) or (Adherence AND HIV disease) or (Antiretroviral therapy AND Treatment outcomes) or (HIV disease AND Treatment outcomes)]
11	**Limits**	Limited to English studies from 1995 onwards

"or" preceded "AND" in order of operations

exp=explode a MeSH term

" / "=included all MeSH subheadings

*similar strategies were used in Global Health and Embase databases, with the exception of differences in MeSH terms

Cover sheet for each 'research paper' included in a research thesis

PAPER TWO: GOOD ADHERENCE AND TREATMENT OUTCOMES IN REFUGEE AND HOST COMMUNITIES ON HIGHLY ACTIVE ANTIRETROVIRAL THERAPY IN URBAN KUALA LUMPUR, MALAYSIA

1. For a 'research paper' prepared for publication but not yet published

   1.1. Where is the work intended to be published?
   PLoS Medicine

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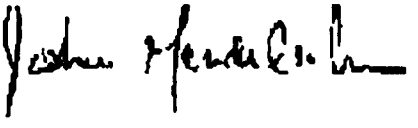
   JBM designed the research protocol, managed data collection, completed statistical analyses and interpretation of results, wrote the first draft of the manuscript, and edited the manuscript according to comments from co-authors. DAR reviewed the research protocol, supported statistical analyses and interpretation of results, and commented on the manuscript. MS and PS supported protocol design, interpretation of results, and commented on the manuscript. SB, AR, and CL provided support for data collection, assisted with interpretation of results, and commented on the manuscript. NL provided statistical support, supported interpretation of results, and commented on the manuscript. AG and ES supported protocol design, interpretation of results, and commented on the manuscript.

Candidate's signature



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PAPER TWO

GOOD ADHERENCE AND TREATMENT OUTCOMES IN REFUGEE AND HOST COMMUNITIES ON HIGHLY ACTIVE ANTIRETROVIRAL THERAPY IN URBAN KUALA LUMPUR, MALAYSIA

Brief title

HIV treatment outcomes among urban refugees

Prospective authors, addresses, and affiliations

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1 September 2012

Dear Editor:

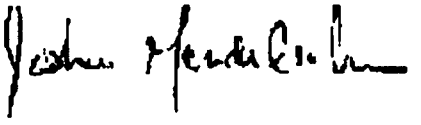
We are pleased to submit our manuscript entitled: "Good adherence and treatment outcomes in refugee and host communities on highly active antiretroviral therapy in urban Kuala Lumpur, Malaysia." We believe that this work is suitable for PLoS Medicine and will be of interest to its audience for the following reasons:

- Your general readership will find the subject matter of interest given current debates around the feasibility of HIV treatment as prevention in various community settings, the importance of adherence to treatment outcomes in a wide range of chronic conditions, and the general interest in refugee health in spite of the lack of coverage in non-specialist journals.
- Both researchers and practitioners in the field of conflict epidemiology, refugee health, and HIV treatment and care will find this paper of particular interest as it is the first study that we are aware of that has investigated adherence and viral outcomes in the large and increasing number of asylum-based refugees residing in an urban setting.
- Many urban clinics around the world treat refugees. The few previous studies on the subject have been undertaken with internally-displaced persons or resettled refugees. Therefore, the contribution is novel and PLoS Medicine's open access format and visibility will make it widely accessible to a range of end-users in the primary care and humanitarian communities.
- We report excellent clinical outcomes in the Burmese refugees accessing HAART from this urban clinic setting, and these were comparable to the outcomes found in the local host community. This evidence supports a policy of equal provision of treatment for

refugees and local host communities. This finding will be of interest to policymakers and researchers in migration-related fields.

We thank you for your consideration of our manuscript.

Sincerely,



Joshua Mendelsohn (on behalf of the co-authors)

ABSTRACT

Background. In response to a dearth of data among refugees and host communities accessing HAART in urban settings, our objective was to compare adherence and virological outcomes among clients attending a public clinic in Kuala Lumpur, Malaysia.

Methods and findings. A cross-sectional survey was conducted among adult clients (≥18y). Data sources included a structured questionnaire measuring self-reported adherence, a pharmacy-based measure of HAART prescription refills over 24 months (Rx), and HIV viral loads. The primary outcome was unsuppressed viral load (cut-off <40 copies/mL). We recruited 90% of all eligible refugees (n=153) and 81% (n=148) of host clients. Refugees were younger (median age 35y (IQR 31, 39) v.40y (IQR 35, 48); $p<0.001$), more likely to be female (36% v.21%;$p=0.004$), and to have been on HAART for less time (61weeks (IQR 35, 108) v. 153 weeks (IQR 63,298); $p<0.001$). Similar proportions of those on treatment for ≥25 weeks from both groups had achieved viral suppression (81% v.84%; $p=0.54$). Optimal adherence to Rx was 74% v.66%; $p=0.15$. Refugee status was not independently associated with the outcome ($OR_{adj}=1.28$, 95%CI 0.52, 3.14; $p=0.60$). Female sex ($OR_{adj}=0.39$, 95%CI 0.14, 1.05; $p=0.05$), optimal adherence to Rx ($OR_{adj}=0.47$, 95%CI 0.27, 0.81; $p=0.007$), and longer time from diagnosis to HAART start were protective ($OR_{adj}=0.64$, 95%CI 0.41, 0.99; $p=0.04$). Temporary migration for one consecutive month in the past year ($OR_{adj}=4.12$, 95%CI 1.70, 9.99; $p=0.002$) and clinic transit times ≥1hr ($OR_{adj}=3.05$, 95%CI 1.09, 8.49; $p=0.02$) increased the odds of unsuppressed viral load.

Conclusions. The proportions of refugee and host community clients with optimal adherence to HAART and viral suppression were similar and at reasonably good levels. The results support the hypothesis that refugees in protracted asylum situations are able to sustain adherence to HAART and good treatment outcomes, and should explicitly be included in the HIV strategic plans of host countries with a view to expanding access for all in accordance with national guidelines for HAART.

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FINANCIAL DISCLOSURE

Financial support was provided by Canadian Institutes of Health Research (Priority Announcement for HIV/AIDS), the Parkes Foundation, and the United Nations High Commissioner for Refugees. UNHCR, but not the other two funding agencies, assisted in study design, interpretation of results, and drafting of the manuscript.

COMPETING INTERESTS

These authors declare that they have no conflicts of interest.

AUTHOR CONTRIBUTIONS

JBM designed the research protocol, managed data collection, completed statistical analyses and interpretation of results, and wrote the first draft of the manuscript. DAR reviewed the research protocol, supported statistical analyses and interpretation of results, and commented on the manuscript. MS and PS supported protocol design, interpretation of results, and commented on the manuscript. SB, AR, and CL provided support for data collection, assisted with interpretation of results, and commented on the manuscript. NL provided statistical support, supported interpretation of results, and commented on the manuscript. AG and ES supported protocol design, interpretation of results, and commented on the manuscript. All authors edited the manuscript for intellectual content and approved the final manuscript (to be confirmed).

ABBREVIATIONS

ART: antiretroviral therapy; CI: confidence interval; HAART: Highly Active Antiretroviral Therapy; HIV: human immunodeficiency virus; IDP: internally-displaced person; LSHTM: London School of Hygiene and Tropical Medicine; MSF: Médecins Sans Frontières; NGO: non-governmental organisation; OR: odds ratio; OR_{adj}: adjusted odds ratio; PMTCT: prevention of mother-to-child transmission; Rx: prescription; UNHCR: United Nations High Commissioner for Refugees; VAS: visual analogue scale

INTRODUCTION

For HIV-positive persons, optimal adherence (≥95% of tablets taken as prescribed) to highly active antiretroviral therapy (HAART) is essential for achieving and sustaining viral suppression. Estimates suggest that 6.6 million people in low- and middle income-countries, or 47% of 14.2 million eligible, are now receiving treatment [1]. Refugees have a recognised international legal status that should enable them to receive access to public relief on an equivalent basis to host nationals in countries of asylum, where 10.6 million refugees were situated as of 2010 [2,3]. However, there are concerns as to whether refugees who are on HAART in asylum are sufficiently stable and therefore capable of sustaining optimal adherence and good treatment outcomes in the face of potential obstacles such as language barriers, lack of employment, fractured support networks, and onwards displacement [4,5]. In some instances, States may be reluctant to provide treatment to refugees, citing the prerogatives of supplying their own citizens and concerns about stability among refugees. Previous studies of adherence and treatment outcomes in other conflict-affected groups have reported high levels of adherence and acceptable outcomes, suggesting that such obstacles may be overcome [6,7,8]. Yet there are few data available to verify the acceptability of treatment outcomes in relation to local host communities in asylum settings. In addition, most previous work on forced migration and HIV treatment outcomes has been conducted in sub-Saharan Africa, or with refugees based in high-income countries [9]. In response, our objective was to study adherence and treatment outcomes in a refugee and local host community accessing HAART from the same clinic in Kuala Lumpur, Malaysia.

METHOD

Study setting

Sungai Buloh Hospital, Kuala Lumpur, Malaysia was chosen as the study setting as it met our criteria of an urban, Southeast Asian setting, with sufficient numbers of refugees accessing HIV treatment and care services from a single point of care. At the start of the study (April 2010), over 91,985 individuals were registered by UNHCR as refugees and asylum seekers in Malaysia, most having fled the protracted conflict between the Burmese junta and rebel groups from the ethnic periphery. At the end of 2009, the average length of a stay for an HIV-positive refugee in Malaysia was 3.7 years. Of this group, 32% were resettled to high-income countries after an average of 2.9 years (UNHCR Malaysia, Pers. Comm.). The Malaysian government has not signed the 1951 Refugee Convention and its 1967 Protocol; however, the Ministry of Health issued a circular in 2006 that permitted refugees to access public health services, including antiretroviral therapy (ART) as part of the national HIV treatment and program. The National

HIV/AIDS Strategic Plan 2006-2010, referred to refugees as a "vulnerable group" but no specific strategies were formulated [10]. Refugees were formally included in the 2011-2015 Strategic Plan [11]. The Malaysian host community is composed primarily of Malay, Chinese, and Tamil ethnic groups. For Malaysians, the national treatment program fully subsidises first-line treatment and a range of services including virological monitoring; second-line treatment is partially subsidised. For refugees, the national program fully subsidises first-line fixed-dose treatments, however, more expensive first and second-line drugs (e.g. efavirenz; lopinavir/ritonavir) and virological monitoring are supported by UNHCR so that refugees may receive all treatment for free. In relation to treatment decisions, UNHCR defers to national guidelines and their implementation by local clinicians. At the start of the study, there were 315 HIV-positive refugees known to UNHCR, 171 on HAART, over 98% of whom were from Burma. Only refugees, meaning those who possessed documented approval of their refugee status, received subsidised treatment and support. HIV-positive asylum seekers in need of HAART are expedited through the Refugee Status Determination process in order to facilitate timely access to treatment. The usual pathway to treatment for refugees was diagnosis at a free clinic run by a non-governmental organisation (NGO) and subsequent referral to the reference hospital; the host community was either referred to the reference hospital from elsewhere, or diagnosed and treated on site. Sungai Buloh Hospital is the national reference hospital for HIV and was the first hospital to offer ARTs in Malaysia. HIV-positive refugees and host nationals received routine counselling from hospital nurses and more frequent individual and group-based support from NGO adherence support counsellors. Counsellors serving refugees were recruited from among their communities and assisted with routine counselling on disease and treatment, and refugee-specific challenges such as overcoming language barriers, arranging transport to the clinic, and preparing for eventualities such as arrest or detention. Malaysian counsellors fulfilled similar functions for the host community. For the most vulnerable refugees, financial assistance was provided for travel to the clinic and pharmacy. Immunological and virological tests were routinely administered to all clients upon enrolment. Up until and during the study period, if CD4 was <250 cells/μL, clients were counselled, prescribed multivitamins and cotrimoxazole, and started on first-line HAART.

Study design

We conducted a 15-week (March-July 2010) cross-sectional survey at Sungai Buloh Hospital that aimed to recruit all refugees identified by UNHCR as recipients of HAART and a similar number of serially-recruited host community clients attending the same outpatient clinic. Clients ≥18 years and on regular HAART for at least 30 days were systematically recruited at the time of their regular clinic appointment. Refugees who did not attend during the study period or who could not be seen by the research team on an appointment day were contacted through an active

recruitment protocol implemented by research staff. Efforts were made to contact all known, eligible refugee clients on HAART who met the inclusion criteria. Host community clients were recruited serially at the time of clinic appointment and were not actively sought if they failed to attend. To assess representativeness of the recruited host community sample, a sampling frame was constructed and basic demographic data were collected on a randomly selected comparison sample of 150 clients. We focused our recruitment efforts on refugees during the designated refugee clinic day (once per week) and matched this with one designated host community recruitment day per week.

Data sources

Data sources included a structured questionnaire with self-reported adherence measures, a pharmacy-based measure of HAART prescription (Rx) refills, and HIV viral loads. The primary outcome was unsuppressed viral load (cut-off <40 copies/mL). The questionnaire was translated into Bahasa Malaysia, Tamil, Mandarin, Burmese, and Falam (Chin dialect), and then backwards translated into English. The original and backwards-translated English versions were reconciled prior to pre-testing and pilot-testing. Key self-reported adherence measures included a retrospective four-day dose-by-dose recall [12] and a retrospective one-month general recall measured on a visual analogue scale (VAS) [13]. Adherence to pharmacy refill schedule was assessed using a pharmacy-based measure of HAART prescription refills and calculated as the proportion of prescribed refills collected divided by the total required refills up to 24 months prior to the interview date. A successful refill was determined by dividing the number of tablets claimed into the number of tablets required to avoid a personal stock-out, allowing a 14-day grace period for each collection. The pharmacy data were extracted from a confidential electronic pharmacy database by the hospital pharmacists. For all adherence measures, ≥95% of doses taken as prescribed was used to signify "optimal adherence". HIV viral loads were collected using routine hospital phlebotomy procedures and analysed at a private laboratory using the COBAS Ampliprep/Taqman platform (Roche Diagnostics Systems, Branchburg, New Jersey, USA).

Statistical methods

Socio-demographic characteristics were compared between host and refugee groups using Mann-Whitney tests for continuous variables, Chi-square or Fisher's exact test for categorical variables, and Chi-square test for trend for ordered categorical variables. Risk factors for unsuppressed viral load were evaluated using unconditional logistic regression; effect estimates were odds ratios (OR) and corresponding 95% confidence intervals (CI). The order of entry of factors into the model was determined using a three-level, forwards, step-wise modelling approach. Drawing on social action theory [14], factors were grouped into levels representing

treatment contexts such as socio-demographic, displacement-related, and treatment factors; self-change processes such as knowledge scores, self-efficacy, and reported serostatus disclosure; and action state factors incorporating adherence measures (Figure 1). First, associations between unsuppressed viral load and factors from all levels were evaluated in univariable analyses using log-likelihood ratio tests. A "treatment context model" was then fitted by adjusting for treatment context factors with $p<0.1$ in univariable analyses. A "self-change processes model" was fitted by adjusting each new factor by all retained treatment context factors, then adjusting again for any additional factors with $p<0.1$. A model evaluating the effect of "action state (adherence) factors" was fitted in a similar fashion. As these adherence measures were collinear, the "action state" model restricted adjustment to factors from previous levels only. The final multivariable logistic regression model was obtained by excluding the factor with the highest p-value one at a time, until all remaining factors had $p<0.05$. Covariates of interest retained throughout the modelling process included refugee status, age, and time on HAART. Adherence factors were not included in final model building to avoid over-adjustment bias [15,16,17] due to their putative role as mediators. Therefore, any adherence factor with an adjusted OR of $p<0.05$ in the "action state model" was presented in the final model and adjusted for other factors, however, other factors were not adjusted for adherence factors.

Ethical approval

Ethical approval was received by the Clinical Research Centre and the Medical Research Ethics Committee, Malaysia (Approval 3275) and the London School of Hygiene and Tropical Medicine Research Ethics Committee (Approval 5547).

[*** Figure 1, p.72, near here ***]

RESULTS

Study population

We recruited 153 refugees and 148 Malaysians adults reflecting 90% and 81% participation rates (eligible clients who were seen or contacted and agreed to participate), respectively. The serially-recruited Malaysian group comprised 6% of the target population of eligible clients (N=2,870) and was similar on key socio-demographic indicators to a randomly sampled host comparison group (Supp. Table i), with the exception of ethnicity ($p<0.001$). Almost all (95%) HIV-positive refugees accessing services from the study clinic were Burmese while the host community group was 61% Chinese, 25% Malay, and 15% Tamil or other ethnic groups. The recruited refugee and host community groups were statistically different on a variety of other indicators (Table 1). The refugee group was younger (median age 35y v. 40y, $p<0.001$) and had

a higher proportion of females (36% v. 22%, p=0.006). The refugee group had a considerably shorter median time on HAART (61 v. 153 weeks, p<0.001), median time since HIV diagnosis (113 v. 315 weeks, p<0.001), and a lower most recent routine CD4 count (278 v. 350 cells/μL, p=0.03). There was no difference between the two groups with respect to current pharmacy defaulters (7% v. 11%, p=0.19). Among refugees, the median time of residence in asylum was 3.6 years (IQR 2.0, 6.2) compared with a median time since having received formal refugee recognition of 1.8 years (IQR 1.0, 2.9).

[*** Table 1, p.73, near here ***]

Virological and adherence outcomes

Viral load results indicated that 76% (224/ 296) of clients had achieved viral suppression (<40 copies/mL). There were no statistical differences between the proportions of refugees and host community clients who achieved viral suppression overall (74% v. 78%, p=0.41), or when restricting analyses to clients on treatment for ≥25 weeks (81% v. 84%, p=0.54; Table 2). On key measures of self-reported adherence among all surveyed clients, refugee and host community clients performed similarly (Table 3). The four-day recall showed that a high proportion of both refugee and host clients self-reported optimal adherence (92% v. 96%, p=0.20), whereas the proportions who self-reported optimal adherence on the one-month VAS were lower but similar in both groups (72% v. 70%, p=0.79). The Rx results were also lower but similar in both groups (74% v. 66%, p=0.15). Within each group, there was evidence for ordered trends, among clients on treatment for ≥25 weeks, between the self-reported measures of adherence and the proportions who fully suppressed viral load (four-day recall: p=0.07 v. p=0.06; VAS: p=0.06 v. p=0.002). On the Rx measure, there was strong evidence for this trend among refugees (p=0.004), but this did not hold for the host community (p=0.10) (see Supp. Table ii).

[*** Table 2, p.73, and Table 3, p.74, near here ***]

Risk factors for unsuppressed virological outcomes

Unsuppressed viral load was defined as ≥40 copies/mL. In initial analyses of contextual factors (Table 4), among clients on HAART for ≥1y, 17% were not suppressed. The proportion not suppressed was 15% among those on HAART for <1y. There was no significant relationship between increasing time on treatment above one year and virological outcomes (OR_{adj}=1.17, 95%CI 0.69, 1.96; p=0.56).

[*** Table 4, p.75-6, near here ***]

There were no statistically significant associations between self-change process factors and the outcome (Table 5). Among exposures modelled in the action state level (Table 6), there was

strong evidence for a protective effect of adherence to pharmacy refill schedule modelled as a linear effect (OR_{adj}=0.47, 95%CI 0.27, 0.83; p=0.009), and a harmful effect of having reported any treatment interruption in the past month (OR_{adj}=2.77, 95%CI 0.91, 8.43; p=0.08). These associations were adjusted for age group, time on HAART, refugee status, sex, temporary travel in past year, time to clinic, time from diagnosis to HAART start, and previous regimen switch.

[*** Table 5, p.77, and Table 6, p78, near here ***]

The final multivariable model (Table 7) identified female sex (OR_{adj}=0.39, 95% CI 0.14, 1.05; p=0.05), increasing time between diagnosis and treatment start (OR_{adj}=0.64, 95%CI 0.41, 0.99; p=0.04), and adherence to pharmacy claim schedule (OR_{adj}=0.47, 95%CI 0.27, 0.81; p=0.007) as protective, while temporary migration of ≥1 month in the past year (OR_{adj}=4.12, 95%CI 1.70, 9.99; p=0.002) and average travel time to clinic of ≥1 hour (OR_{adj}=3.05, 95%CI 1.09, 8.49; p=0.02) were independent risk factors that increased the odds of unsuppressed viral load. There was no evidence for an association between refugee status and unsuppressed viral load (OR_{adj}=1.28, 95%CI 0.52, 3.14; p=0.60). The final multivariable model was adjusted for age group, refugee status, time on HAART, sex, temporary migration in the past year, average time to clinic, and time from HIV diagnosis to HAART start. Age, refugee status, and time on HAART were retained in the final model as *a priori* factors of interest, despite showing no evidence of associations at previous modelling levels.

[*** Table 7, p.79, near here ***]

Discussion

In this study, the first we are aware of to investigate both adherence and treatment outcomes among both refugee and a host community in an asylum setting, the majority of both refugee (74%) and host community clients (78%) achieved viral suppression. As expected, the proportion who had achieved suppression was higher in those who had been on HAART for at least 25 weeks, increasing to 81% of refugees and 84% of host community clients. Despite some differences on socio-demographic measures and time on treatment, there were only minor differences, none statistically significant, between the refugee and host community groups on virological and adherence measures. Adherence and treatment outcomes in the present study were acceptable insofar as they were similar to reported results from other Asian HIV clinics. Oyomopito and colleagues observed 83% suppression after 12 months on HAART in a multicentre prospective cohort of 17 Asian settings [18]. In a multicohort study of second-line treatment failure in 27 Asian and African settings, the observed rate of failure was 16 (9, 30) per 1000 person-years, while the rate of optimal adherence was 176 (124, 249) per 1000 person-years [19].

Although there are currently no other reports of virological outcomes among refugees or other conflict-affected persons residing in active- or post-conflict areas, the data that has been collected among these groups has shown acceptable adherence and treatment outcomes, consistent with the present study. For example, in conflict-affected northern Uganda, Kiboneka and colleagues [20] found optimal adherence (≥95%) in 92% of internally-displaced persons (IDP), as measured by a composite score including a pharmacy-monitored drug possession ratio, pharmacy refill records, and a three day recall by patients or caregivers. Among clients with sub-optimal adherence, 9.3% died compared with 1.2% of those sustaining optimal adherence. In a separate cross-sectional study of IDPs in Uganda, mean self-reported adherence was 99.5% [7]. In the western Equatorial province of Sudan, 88% of refugees and IDPs on HAART for ≥6 months self-reported ≥95% adherence [21]. Similarly, during active conflict in the Democratic Republic of the Congo, optimal adherence, measured by pill counts, was found in 99% of clients. In this study, CD4 gain at 6 months was similar to other stable cohorts, although the 12-month mortality of 7.9% was elevated in comparison to stable resource-limited settings [6]. These studies provided further evidence that refugees and other conflict-affected persons are able to sustain adherence to HAART and benefit from good treatment outcomes.

Multivariable analyses confirmed the lack of an association between refugee status and failure to suppress viral load after adjusting for age, sex, time on HAART, time from diagnosis to HAART start, temporary migration in the past year, and time to clinic. Given the potential vulnerabilities connected with cross-border displacement that may increase the vulnerability of refugees to inferior outcomes, it was reassuring that the study showed that a high proportion of refugees were achieving excellent viral suppression. This has important equity and policy implications. In addition to refugee status, we assessed other migration-related factors. Temporary migration outside of current residence for at least one month in the past year resulted in a fourfold increase in the odds of unsuppressed viral load, a result that may be explained by difficulties accessing medications when personal stocks were depleted in the absence of any back-up source or contingency plan for replenishment. This finding was consistent with evidence from a Canadian setting also showing an adverse impact of temporary migration [22]. A longer travel time to clinic (≥1 hour) was linked to a threefold increase in the odds of failing to suppress viral load, consistent with similar evidence concerning the harmful effects of longer travel times on outcomes in a variety of settings [23,24,25]. A longer time between diagnosis and HAART start was protective, a surprising result given that starting HAART at a higher CD4 counts is known to reduce mortality [26]. Clients with longer lead-in times to routine treatment may have been better prepared for the adherence requirements of HAART. The expected negative effect of delaying treatment may have been confounded by longer delays between seroconversion and diagnosis. Motivation may, therefore, have been an issue; if diagnoses were

delayed, clients may have started HAART during periods of acute illness when the will to recover may have encouraged excellent adherence. With respect to CD4 measurement, it was not possible to identify if clients were HAART naive at the time of the first routinely-reported CD4, so we did not include these data in analyses.

The strong evidence for a protective effect of female sex in the final adjusted analysis was a notable sex difference and may be related to differences in the proportions of men and women who reported disclosing their status to their partners (49% of males vs. 66% of females, p=0.05) and in the proportions with children (40% of males vs. 61% of females, p=0.004). These factors may operate on adherence and virological outcomes through non-disclosure of HIV status [27], and through encouraging earlier pathways to HIV services by way of antenatal screening, respectively [28]. This sex difference was also consistent with a protective effect observed in a Chinese study [29] and evidence from South Africa showing that men who present for ART are typically sicker than women [30]. However, most previous studies have either not found any evidence of sex differences in HAART clients or have been insufficiently powered to detect them, a gap that should be addressed in future research [31].

Consistent with other findings showing that pharmacy-based adherence is an effective indicator of immunological and virological status [32,33], there was strong evidence for a protective effect of pharmacy refill adherence on unsuppressed viral load. These findings support the usefulness of this measure for routine monitoring of adherence and treatment outcomes in this setting. Self-reported treatment interruptions of one day or more in the past month were weakly associated with the outcome (p=0.08) in the action state level and was not included in the final model. Similarly, the other self-reported adherence measures were strongly associated with virological outcomes in crude analyses, but failed to reach statistical significance in adjusted analyses. The slightly lower proportion of Malaysians adhering optimally to the pharmacy claim schedule may have been a consequence of a system that allowed the host community to collect their medications from external pharmacies on an occasional or supplementary basis. One-sixth of host community clients reported collecting drugs in this manner within the assessed pharmacy refill period lending support to the principle that multiple routine proxy measures are needed to identify patterns of adherence over time and to make up for deficits in any single measure [34].

The findings suggested that many of the "typical" obstacles thought to negatively affect treatment outcomes among refugees such as language barriers, unemployment, deficiency in support networks, and overall stability were either not linked to outcomes or were not unique to refugees. There was no evidence for any harmful effect of unemployment or mother tongue. We did not directly study deficiencies in support networks, however satisfaction with primary

providers was high among both refugee and host community clients (see Supp. Table v). Moreover, there was no association between disclosure of HIV status to partners or family and outcomes. Refugees often build strong networks among their families and ethnic communities while in asylum and for those who find themselves isolated, linkage to treatment and care may provide a natural network of peer- and counsellor-based support upon which they can rely. Language barriers in medical contexts are clearly important, but may be overcome by judicious clinicians who use interpreters effectively and by employing support counsellors from among refugee communities. We did not study onwards displacement directly; however the average length of stay for an HIV-positive refugee of 3.7 years was generally indicative of stability. The finding that temporary migration (for ≥1 continuous month in the past year) was a risk factor after adjusting for refugee status suggested that this was common to the full study group. The absence of a link between the number of reported barriers to adherence and failure to suppress viral load was suggestive that both groups of clients were resilient and may have identified adherence barriers in order to formulate practical solutions.

Although the proportion who did not suppress HIV viral load decreased with better self-reported or pharmacy claim adherence, suppression appeared to be relatively tolerant of deviations from ideal adherence using multiple indicators, in both population groups. A level of routine adherence of at least 95% is generally considered to be optimal for achieving and sustaining viral suppression [35,36] but this threshold may be pliable in relation to regimen-specific genetic barriers to resistance. For example, NNRTI-based (non-nucleoside reverse transcriptase inhibitor) therapy, received by 96% of clients in the present study, may facilitate viral suppression at adherence levels below 95% [37,38]. In this study there were insufficient numbers of HAART naive clients on protease-inhibitors to enable analyses on interaction effects between regimen type and adherence. In spite of the fact that viral outcomes were tolerant of sub-optimal adherence, these results suggested opportunities for further improvement in viral suppression by working to shift moderate adherers to optimal levels. To this end, interventions targeting poor adherers or defaulters ought to be mindful of the fact that the minimum levels of NNRTI adherence needed for optimal levels of viral suppression are unclear [39,40,41] and that, in comparison to negligible levels of drug pressure, moderate but sub-optimal ART plasma concentrations may increase the likelihood of secondary resistance [42]. To avoid scenarios where marginal improvements in adherence actually increase the likelihood of resistance, close monitoring of adherence interventions outside of trials is critical, especially among clients with past episodes of poor adherence and at high risk of future difficulties.

Caution must be used in generalising these findings to other refugee populations given that only one setting was studied and HAART delivery systems are often specific to country and clinic setting. However, contingent generalisations may be made to refugee groups elsewhere upon

careful comparison of settings. The refugee caseload overall, and the HIV-positive caseload among refugees, were both considerably higher in Malaysia when compared with other major programs in the region. Bangkok and New Delhi have only 10 identified cases each. Moreover, there are many differences between urban and camp or rural/dispersed refugee groups with respect to demographic and epidemiological profiles and service-provision challenges [43]. Socioeconomic differences between different refugee settings such as high unemployment may at least be partially mitigated by the fact that the direct financial assistance provided by UNHCR is assessed at the country-level and partly determined by local socioeconomic considerations. As with other studies that have compared different clinical settings within one national program [44], the clinic setting itself may be the crucial consideration when evaluating generalisability. In the present setting, refugees accessed HIV services from a leading reference hospital. These conditions may be found in other urban refugee populations where UNHCR and Ministries of Health have cultivated close links, but are unlikely to be replicated among rural/dispersed or camp-based refugee groups where top reference facilities are unavailable. In addition to the quality of the facility, the attitude of providers to refugees is critical for delivering equitable care. In the current setting, refugees also benefitted from routine laboratory monitoring, including viral load testing. As laboratory monitoring for refugees is implemented in line with national protocols, any differences between refugee groups attributable to levels of monitoring would be expected to track national differences.

Factors identified from these data will help to locate those who might benefit from targeted interventions. To this end, additional counselling for men on HAART, support for those HAART clients who spend lengthy periods in transit to access routine care, and those who do not consistently refill their HAART prescriptions as monitored by the pharmacy, might be beneficial. Risk assessments for clients who may travel for extended periods could be implemented to ensure that consistent medication supply is available and contingency plans are in place in the event that medication is exhausted; this applies to refugees and host communities. Use of mobile phones, either through training in using personal alarms, or more actively through a text-message intervention may help to mitigate some of these challenges [45,46].

Notably, this study only included refugees and host communities, yet HIV-positive asylum-seekers who have been receiving HAART in their country of origin may be particularly vulnerable to poor outcomes given the possibility that their HAART supplies were exhausted prior to obtaining formal refugee status. UNHCR actively attempts to expedite these cases, and programs should continue to facilitate pathways to treatment and care for vulnerable asylum seekers. Given the importance of the pharmacy-based adherence assessment, this measure should be formalised as a routine adherence indicator, be linked to medical records, and monitored. When the reported result is poor, this should alert providers and trigger more

advanced and expensive testing (e.g. viral loads). Host community clients who collect medications from elsewhere on an occasional or supplementary basis should be identified to ensure that they are not missed by monitoring programs. If a means of tracking external refills cannot be found, an alternative monitoring measure such as pill counts ought to be implemented for these clients.

This study had important limitations. As only a single study viral load sample was collected, outcomes may have been subject to sporadic viral escape, or "viral blips" leading to misclassification of the outcome. Such episodes may be classified as low-level viraemia, typically caused by random biological or statistical variation around mean HIV-levels (e.g. release of virus from latent reservoirs) and high-level viraemia, usually of longer duration and possibly indicative of treatment failure and/or inadequate adherence [47,48,49]. Given that ≥500 copies/mL is an indicator of viral rebound [50], the area of concern for misclassification bias due to viral blips is in the range of 40-499 copies/mL. Moreover, viral blips are only relevant for patients who were recently virologically suppressed. Among clients for whom the most recent routine viral load prior to the study fell in the suppression range of <40 copies/mL, 5% (7/147) tested in the range of 40-499 copies/mL for the study, suggesting that viral blips contributed a minimal amount of bias by misclassifying suppressed clients as unsuppressed.

Selection bias in the host community group may also have affected our findings. Although the response rates of the interviewed samples were high in both groups, the lower rate in the host community could have introduced some differential bias. The serially-recruited host community study sample represented 6% of the target population and those not included may have been sicker or possessed other characteristics leading to bias. To examine this limitation, we extracted and compared routine socio-demographic data from a simple random sample of 150 host community clients to interviewed host community clients. The random sample was statistically similar to the study sample on all key socio-demographic indicators with the exception that ethnic Chinese clients were over-represented in the study sample. This difference may have introduced bias linked to socioeconomic status: the ethnic Chinese community in Malaysia typically has a lower incidence of poverty and the highest mean monthly gross household income when compared with other ethnic groups [51]. Also, the study groups were ethnically and linguistically diverse. To minimise the effects of this, the questionnaire was translated and independently back-translated and the study used local research staff in order to increase confidence in the technical and semantic equivalence of our questionnaires [52]. Finally, the cross-sectional design of the study limited our ability to draw any firm causal conclusions, and to accurately measure and classify longer-term viral suppression and adherence [53]. In multivariable analysis, the n for each strata was often small, which limited our ability to

conduct sub-group analyses and the power available for detecting the true effects of independent risk factors.

Strengths of the study included detailed adherence assessment using self-report and pharmacy claim measures in accordance with recent best-practice guidelines [34], collection of blood samples by using the routine phlebotomy service, analysis of samples conducted in a private laboratory with a good quantitative platform and effective quality control, translated and back-translated questionnaires, and the use of well-trained local research staff.

In summary, it was encouraging that a high proportion of both host and refugee clients attending this public sector clinic had achieved viral suppression at <40 copies/mL (83% at ≥25 weeks). Prevalence of ≥95% self-reported adherence was similar in host and refugee clients, and although adherence to pharmacy claim schedule was slightly higher in refugees compared with host clients, this may have been due to host clients having occasional, undocumented access to HAART medications at alternative pharmacies. Overall, our findings support the feasibility of providing HAART on an equitable basis to both refugees and host communities in this urban setting. The results also suggest that interventions among men, clients who travel or migrate for extended periods, clients who have excessive transit times to access HIV services, and those who have inconsistent pharmacy refill schedules, may improve outcomes. Formalised approaches to adherence monitoring may assist in this regard.

Some Governments are concerned that equitable provision of HAART will constitute a pull factor for refugees to come to their country and a possible impediment for their return if HAART is unavailable in their country of origin. This places ever more emphasis on demonstrating the public health benefits of HAART in a range of settings and underscores the need for research on the effects of potential "pull" factors, if any, on the provision of HAART to refugees in countries of asylum as well as the potential of delaying repatriation if HAART is unavailable in the areas from where they have come. Future studies should also consider prospective designs that may assess causal differences between refugee and host community groups over time.

Importantly, the future sustainability of HAART to refugees needs to be critically evaluated. Currently, the national program fully subsidises first-line fixed-dose treatments for refugees, however, efavirenz, second-line treatments, and virological monitoring are paid for by UNHCR. Given the current global reduction of funding for HIV, we are concerned that in the future, national programs that currently include refugees may begin excluding them as funding continues to decline. Our findings reinforce the imperatives of refugee protection over the full duration of asylum, as codified in international humanitarian law, by showing that effective provision of HAART treatment and support results in tangible public health benefits. If we are

to reach to the goal of universal access, then refugees, asylum seekers and other persons affected by conflict must be included in country and regional proposals and planning for HIV to the fullest extent possible.

REFERENCES

1. UNAIDS (2011) UNAIDS World AIDS Day Report 2011. Geneva.
2. UN General Assembly (28 July 1951) Convention relating to the Status of Refugees. In: United Nations, editor. Treaty Series (vol 189, p 137).
3. UNHCR (2011) Statistical Yearbook 2010. Geneva: UNHCR.
4. International Federation of Red Cross and Red Crescent Societies (2008) World Disaster Report 2008: Focus on HIV and AIDS. Geneva. pp. 118-141.
5. UNHCR, Southern African HIV Clinicians Society (2007) Clinical Guidelines for Antiretroviral Therapy Management for Displaced Populations - Southern Africa. Geneva: UNHCR.
6. Culbert H, Tu D, O'Brien DP, Ellman T, Mills C, et al. (2007) HIV treatment in a conflict setting: outcomes and experiences from Bukavu, Democratic Republic of the Congo. PLoS Med 4: e129.
7. Garang PG, Odoi RA, Kalyango JN (2009) Adherence to antiretroviral therapy in conflict areas: a study among patients receiving treatment from Lacor Hospital, Uganda. AIDS Patient Care STDS 23: 743-747.
8. Kiboneka A, Nyatia RJ, Nabiryo C, Anema A, Cooper CL, et al. (2009) Combination antiretroviral therapy in population affected by conflict: outcomes from large cohort in northern Uganda. BMJ 338: b201.
9. Mendelsohn JB, Schilperoord M, Spiegel P, Ross DA (Submitted) Adherence to antiretroviral therapy and treatment outcomes in conflict-affected and forcibly displaced populations: a systematic review. Confl Health.
10. Ministry of Health Malaysia (2006) National Strategic Plan on HIV/AIDS 2006-2010. Kuala Lumpur.
11. Ministry of Health Malaysia (2011) National Strategic Plan on HIV/AIDS 2011-2015. Kuala Lumpur.
12. Chesney MA, Ickovics JR, Chambers DB, Gifford AL, Neidig J, et al. (2000) Self-reported adherence to antiretroviral medications among participants in HIV clinical trials: the AACTG Adherence Instruments. AIDS Care 12: 255-266.
13. Walsh JC, Mandalia S, Gazzard BG (2002) Responses to a 1 month self-report on adherence to antiretroviral therapy are consistent with electronic data and virological treatment outcome. AIDS 16: 269-277.
14. Ewart C (1991) Social-action theory for a public health psychology. Am Psychol 46: 931-946.
15. Schisterman EF, Cole SR, Platt RW (2009) Overadjustment bias and unnecessary adjustment in epidemiologic studies. Epidemiology 20: 488-495.
16. Cole SR, Hernan MA (2002) Fallibility in estimating direct effects. Int J Epidemiol 31: 163-165.
17. Kaufman JS, Maclehose RF, Kaufman S (2004) A further critique of the analytic strategy of adjusting for covariates to identify biologic mediation. Epidemiol Perspect Innov 1: 4.
18. Oyomopito R, Lee MP, Phanuphak P, Lim PL, Ditangco R, et al. (2010) Measures of site resourcing predict virologic suppression, immunologic response and HIV disease progression following highly active antiretroviral therapy (HAART) in the TREAT Asia HIV Observational Database (TAHOD). HIV Med 11: 519-529.

19. Pujades-Rodriguez M, Balkan S, Arnould L, Brinkhof MA, Calmy A (2010) Treatment failure and mortality factors in patients receiving second-line HIV therapy in resource-limited countries. JAMA 304: 303-312.

20. Kiboneka A, Wangisi J, Nabiryo C, Tembe J, Kusemererwa S, et al. (2008) Clinical and immunological outcomes of a national paediatric cohort receiving combination antiretroviral therapy in Uganda. AIDS 22: 2493-2499.

21. Salami O, Buzu A, Nzeme C (2010) High level of adherence to HAART among refugees and internally displaced persons on HAART in western equatorial region of Southern Sudan. J Int AIDS Soc 13: 123.

22. Lima V, Fernandes K, Rachlis B, Druyts E, Montaner J, et al. (2009) Migration adversely affects antiretroviral adherence in a population-based cohort of HIV/AIDS patients. Soc Sci Med 68: 1044-1049.

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

24. Ochieng-Ooko V, Ochieng D, Sidle JE, Holdsworth M, Wools-Kaloustian K, et al. (2010) Influence of gender on loss to follow-up in a large HIV treatment programme in western Kenya. Bull World Health Organ 88: 681-688.

25. Wasti SP, Simkhada P, Randall J, Freeman JV, van Teijlingen E (2012) Factors influencing adherence to antiretroviral treatment in Nepal: a mixed-methods study. PLoS One 7: e35547.

26. Kitahata MM, Gange SJ, Abraham AG, Merriman B, Saag MS, et al. (2009) Effect of early versus deferred antiretroviral therapy for HIV on survival. N Engl J Med 360: 1815-1826.

27. Stirratt MJ, Remien RH, Smith A, Copeland OQ, Dolezal C, et al. (2006) The role of HIV serostatus disclosure in antiretroviral medication adherence. AIDS Behav 10: 483-493.

28. Cornell M, Myer L, Kaplan R, Bekker LG, Wood R (2009) The impact of gender and income on survival and retention in a South African antiretroviral therapy programme. Trop Med Int Health 14: 722-731.

29. Dou Z, Xu J, Jiao JH, Ma Y, Durako S, et al. (2011) Gender difference in 2-year mortality and immunological response to ART in an HIV-infected Chinese population, 2006-2008. PLoS One 6: e22707.

30. Bekker LG, Myer L, Orrell C, Lawn S, Wood R (2006) Rapid scale-up of a community-based HIV treatment service: programme performance over 3 consecutive years in Guguletu, South Africa. S Afr Med J 96: 315-320.

31. Nicastri E, Leone S, Angeletti C, Palmisano L, Sarmati L, et al. (2007) Sex issues in HIV-1-infected persons during highly active antiretroviral therapy: a systematic review. J Antimicrob Chemother 60: 724-732.

32. Bisson GP, Gross R, Bellamy S, Chittams J, Hislop M, et al. (2008) Pharmacy refill adherence compared with CD4 count changes for monitoring HIV-infected adults on antiretroviral therapy. PLoS Med 5: e109.

33. Grossberg R, Zhang YW, Gross R (2004) A time-to-prescription-refill measure of antiretroviral adherence predicted changes in viral load in HIV. J Clin Epidemiol 57: 1107-1110.

34. Thompson MA, Mugavero MJ, Amico KR, Cargill VA, Chang LW, et al. (2012) Guidelines for improving entry into and retention in care and antiretroviral adherence for persons

With HIV: evidence-based recommendations from an International Association of Physicians in AIDS Care panel. Ann Intern Med. 156(11):817-833.

35. Paterson DL, Swindells S, Mohr J, Brester M, Vergis EN, et al. (2000) Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. Ann Intern Med 133: 21-30.

36. Li JZ, Paredes R, Ribaudo HJ, Svarovskaia ES, Kozal MJ, et al. (2012) Relationship between minority nonnucleoside reverse transcriptase inhibitor resistance mutations, adherence, and the risk of virologic failure. AIDS 26: 185-192.

37. Bangsberg DR (2006) Less than 95% adherence to nonnucleoside reverse-transcriptase inhibitor therapy can lead to viral suppression. Clin Infect Dis 43: 939-941.

38. Bangsberg DR, Acosta EP, Gupta R, Guzman D, Riley ED, et al. (2006) Adherence-resistance relationships for protease and non-nucleoside reverse transcriptase inhibitors explained by virological fitness. AIDS 20: 223-231.

39. Bangsberg DR (2007) Adherence, viral suppression, and resistance to antiretroviral therapy. AIDS Read 17: S11-S15.

40. Maggiolo F, Airoldi M, Kleinloog HD, Callegaro A, Ravasio V, et al. (2007) Effect of adherence to HAART on virologic outcome and on the selection of resistance-conferring mutations in NNRTI- or PI-Treated patients. HIV Clin Trials 8: 282-292.

41. Maggiolo F, Ravasio L, Ripamonti D, Gregis G, Quinzan G, et al. (2005) Similar adherence rates favor different virologic outcomes for patients treated with nonnucleoside analogues or protease inhibitors. Clin Infect Dis 40: 158-163.

42. Lima VD, Harrigan R, Murray M, Moore DM, Wood E, et al. (2008) Differential impact of adherence on long-term treatment response among naive HIV-infected individuals. AIDS 22: 2371-2380.

43. Spiegel PB, Checchi F, Colombo S, Paik E (2010) Health-care needs of people affected by conflict: future trends and changing frameworks. Lancet 375: 341-345.

44. Dahab M, Charalambous S, Karstaedt AS, Fielding KL, Hamilton R, et al. (2010) Contrasting predictors of poor antiretroviral therapy outcomes in two South African HIV programmes: a cohort study. BMC Public Health 10: 430.

45. Horvath T, Azman H, Kennedy GE, Rutherford GW (2012) Mobile phone text messaging for promoting adherence to antiretroviral therapy in patients with HIV infection. Cochrane Database Syst Rev 3: CD009756.

46. Lester RT, Ritvo P, Mills EJ, et al (2010) Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya1): a randomised trial. Lancet 376: 1838-1845.

47. Zhang S, van Sighem A, Gras L, Reiss P, Smit C, et al. (2010) Clinical significance of transient HIV type-1 viraemia and treatment interruptions during suppressive antiretroviral treatment. Antivir Ther 15: 555-562.

48. Nettles RE, Kieffer TL, Kwon P, Monie D, Han Y, et al. (2005) Intermittent HIV-1 viremia (Blips) and drug resistance in patients receiving HAART. JAMA 293: 817-829.

49. Fung IC, Gambhir M, van Sighem A, de Wolf F, Garnett GP (2012) The clinical interpretation of viral blips in HIV patients receiving antiviral treatment: are we ready to infer poor adherence? J Acquir Immune Defic Syndr 60: 5-11.

50. Grennan JT, Loutfy MR, Su D, Harrigan PR, Cooper C, et al. (2012) Magnitude of virologic blips is associated with a higher risk for virologic rebound in HIV-infected individuals: A recurrent events analysis. J Infect Dis 205: 1230-1238.

51. Yusof ZA, Bhattasali D (2008) Economic growth and development in Malaysia: policy making and leadership (Working paper No.27). Washington DC: Commission on Growth and Development.

52. Mollica R, McDonald LS, Massagli MP, Silove DM (2004) Measuring Trauma, Measuring Torture: Instructions and Guidance on the utilization of the Harvard Program in Refugee Trauma's versions of The Hopkins Symptom Checklist-25 (HSCL-25) &The Harvard Trauma Questionnaire (HTQ) (Unpublished Manual). Cambridge: Harvard University.

53. Tesoriero J, French T, Weiss L, Waters M, Finkelstein R, et al. (2003) Stability of adherence to highly active antiretroviral therapy over time among clients enrolled in the treatment adherence demonstration project. J Acquir Immune Defic Syndr 33: 484-493.

TABLES AND FIGURES

Figure 1: Hierarchical conceptual framework

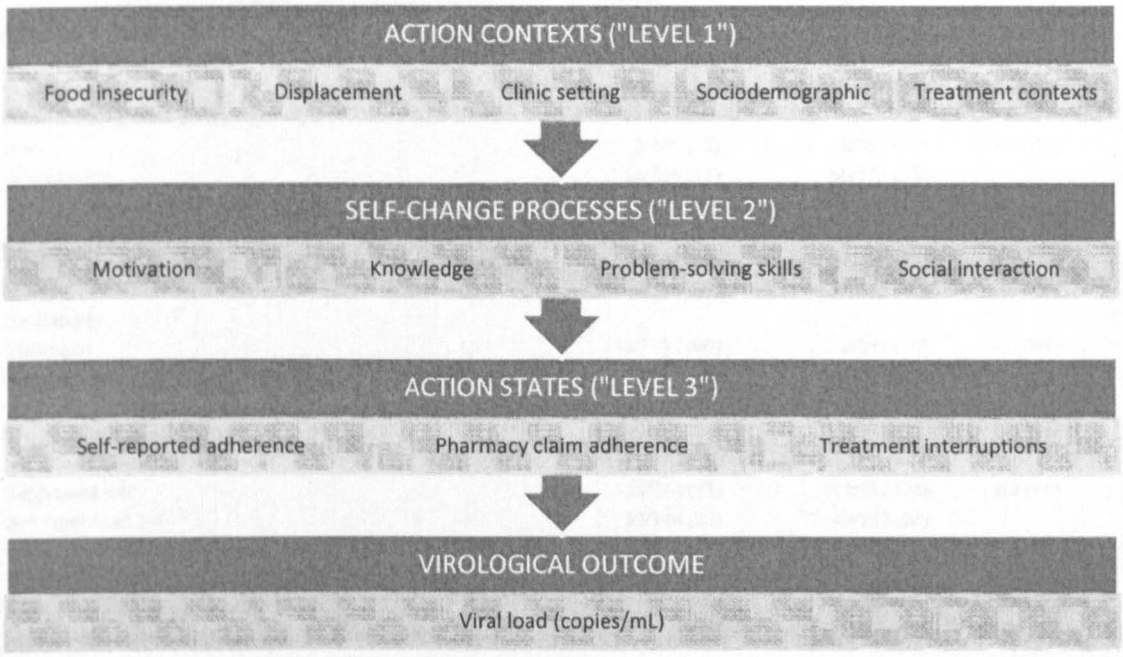


Table 1: Baseline socio-demographic and treatment factors among host community (n_1=148) and refugee (n_2=153) clients

Factor	Host	Refugee§	p-value
Female/transgender, n (%)	33/148 (22)	55/153 (36)	0.006†
Age, median years (IQR)	40 (35, 48)	35 (31, 39)	<0.001††
Unemployed, n (%)	50/148 (34)	91/152 (60)	<0.001†††
Educational status, n (%)			
None	3/148 (2)	8/153 (5)	<0.001†
Any primary	16/148 (11)	60/153 (39)	
Any secondary or above	129/148 (87)	85/153 (56)	
Marital status, n (%)			
Single	90/148 (61)	61/153 (40)	<0.001†
Married	58/148 (39)	92/153 (60)	
Nationality			
Malaysian	148/148 (100)	0/151 (0)	<0.001†
Burmese	0/148 (0)	146/151 (97)	
Other	0/148 (0)	5/151 (3)	
Current defaulters, n (%)*	16/148 (11)	10/153 (7)	0.19†††
Viral load, copies/mL (%)			
Suppressed <40	112/144 (78)	112/152 (74)	0.41†††
Not suppressed ≥40	32/144 (22)	40/152 (26)	
Most recent routine CD4, median cells/μL (IQR) ‡	350 (202, 486)	278 (182, 423)	0.03††
Time on HAART, median weeks (IQR) ‡‡	153 (63, 298)	61 (35, 108)	<0.001††
Time since HIV diagnosis, median weeks (IQR)‡‡‡	315 (152, 571)	113 (66, 170)	<0.001††
Time since entry to host country, median weeks (IQR)	NA	186 (105, 324)	NA
Time since refugee status approval, median weeks (IQR)‡‡‡‡	NA	91 (54, 149)	NA

†Chi-square test ††Mann-Whitney test †††Fisher's exact test

*1-5 consecutive months without pharmacy refill

§Three refugees were traced to the inpatient and TB wards and were retained in analyses (two had suppressed viral load)

‡n_1=140, n_2=141; ‡‡n_1=147, n_2=150; ‡‡‡n_1=146, n_2=153; ‡‡‡‡n_2=152

Table 2: Comparison of virological outcomes in host community and refugee clients

Time on HAART (weeks)	Group	<40 copies/mL, n (%)	Total, n (%)	p-value†
All	Host	112 (78)	144 (100)	0.41
	Refugee	112 (74)	152 (100)	
< 25	Host	6 (33)	18 (100)	1.00
	Refugee	12 (41)	29 (100)	
≥ 25	Host	105 (84)	125 (100)	0.54
	Refugee	98 (81)	121 (100)	

†Chi-square test

Table 3: Adherence in host community and refugee clients

Adherence measure	Host, n (%)	Refugee, n (%)	p-value†
Dose-by-dose self-report (4 days)	(n=148)	(n=153)	0.20
0+	6 (4)	11 (7)	
80+	0 (0)	1 (1)	
95+	142 (96)	141 (92)	
Visual analogue scale self-report (1 month)	(n=148)	(n=153)	0.79
0+	11 (7)	11 (7)	
80+	33 (22)	32 (21)	
95+	104 (70)	110 (72)	
Pharmacy claim adherence (24 months)§	(n=143)	(n=136)	0.15
0+	14 (10)	9 (7)	
80+	34 (24)	26 (19)	
95+	95 (66)	101 (74)	

† Chi-square test for trend (Cochran-Armitage test) §Since started on HAART to a maximum of 24 months.

Table 4: Association of contextual factors with unsuppressed viral load among refugees and local host community on HAART for ≥25 weeks in Kuala Lumpur, Malaysia (N=222*)

Factor	Prevalence ≥40 copies/mL, n/N (%)††	p-value, crude odds ratio (95% CI)	p-value, adjusted odds ratio (95% CI)†††
Age group (years)†		*p*=0.69	*p*=0.68
18-	5/25 (20)	1	1
30-	18/114 (16)	0.90 (0.52, 1.55)	1.15 (0.60, 2.20)
40+	13/83 (16)		
Refugee status		*p*=0.19	*p*=0.60
Host	15/114 (13)	1	1
Refugee	21/108 (19)	1.59 (0.77, 3.28)	1.28 (0.52, 3.14)
Time on HAART (years)†		*p*=0.79	*p*=0.56
0-	7/46 (15)	1	1
1-	9/57 (16)	1.06 (0.68, 1.67)	1.17 (0.69, 1.96)
2+	20/119 (17)		
Sex		*p*=0.04	*p*=0.05
Male	30/155 (19)	1	1
Female/Transgender	6/67 (9)	0.41 (0.16, 1.04)	0.39 (0.14, 1.05)
Time from diagnosis to start (weeks)†		*p*=0.07	*p*=0.04
0-	19/98 (19)	1	1
25-	8/30 (27)	0.69 (0.47, 1.03)	0.64 (0.41, 0.99)
50+	9/94 (10)		
HAART regimen, dosing		*p*=0.32	*p*=0.13
EFV-based, twice-daily	21/140 (15)	1	1
NVP-based, twice-daily	12/74 (16)	1.10 (0.51, 2.38)	1.03 (0.44, 2.43)
Other	3/8 (38)	3.40 (0.76, 15.31)	6.00 (1.14, 31.74)
Current employment		*p*=0.23	*p*=0.21
No	13/101 (13)	1	1
Yes	23/121 (19)	1.59 (0.76, 3.32)	1.70 (0.74, 3.95)
Mother tongue		*p*=0.19	*p*=0.26
Bahasa Malaysia (Malay)	5/39 (13)	1	1
Tamil	5/26 (19)	1.62 (0.42, 6.27)	1.56 (0.36, 6.73)
Chinese dialects	3/46 (7)	0.47 (0.11, 2.13)	0.47 (0.09, 2.32)
Chin dialects	13/54 (24)	2.16 (0.70, 6.66)	6.21 (0.57, 67.53)
Burmese	3/24 (13)	0.97 (0.21, 4.49)	2.52 (0.17, 38.58)
Other	7/33 (21)	1.83 (0.52, 6.43)	3.20 (0.30, 34.63)
Household size†		*p*=0.73	*p*=0.97
1-	9/56 (15)	1	1
3-	17/112 (15)	1.09 (0.66, 1.82)	1.01 (0.59, 1.73)
7+	10/54 (19)		
No. dependent minors in household		*p*=0.59	*p*=0.98
0	23/133 (17)	1	1
1+	13/89 (15)	0.82 (0.39, 1.72)	1.01 (0.44, 2.33)
Temporary migration (≥1 continuous month in past year)		*p*<0.001	*p*=0.002
No	23/187 (12)	1	1
Yes	13/35 (37)	4.21 (1.87, 9.50)	4.12 (1.70, 9.99)
Pathway to diagnosis		*p*=0.50	*p*=0.65
Voluntary test	7/43 (16)	1	1
Mandatory test	8/40 (20)	1.29 (0.42, 3.94)	2.01 (0.56, 7.18)
Illness/hospitalisation	16/88 (18)	1.14 (0.43, 3.03)	1.00 (0.34, 2.93)
Other	5/51 (10)	0.56 (0.16, 1.91)	1.07 (0.27, 4.25)
Average time to clinic (hours)		*p*=0.01	*p*=0.02
0-	6/74 (8)	1	1
1+	30/148 (20)	2.88 (1.14, 7.27)	3.05 (1.09, 8.49)
Regimen switch, ever		*p*=0.20	*p*=0.07
No	16/120 (13)	1	1
Yes	20/102 (20)	1.59 (0.77, 3.25)	2.14 (0.94, 4.85)

Table 4: Association of contextual factors with unsuppressed viral load among refugees and local host community on HAART for ≥25 weeks in Kuala Lumpur, Malaysia (N=222*)

Factor	Prevalence ≥40 copies/mL, n/N (%)††	p-value, crude odds ratio (95% CI)	p-value, adjusted odds ratio (95% CI)†††
Unable to refill prescription, past 3 months		*p*=0.41	*p*=0.44
No	35/210 (17)	1	1
Yes	1/12 (8)	0.45 (0.06, 3.64)	0.45 (0.05, 4.08)
Any symptom or side-effect, past 4 weeks		*p*=0.23	*p*=0.41
No	6/54 (11)	1	1
Yes	30/168 (18)	1.74 (0.68, 4.44)	1.51 (0.55, 4.19)
Food security‡		*p*=0.17	*p*=0.23
Secure	10/84 (12)	1	1
Insecure	26/138 (19)	1.72 (0.78, 3.77)	1.83 (0.67, 5.00)
Satisfaction with primary health care provider, mean score‡‡	Mean= 4.21; SD=0.70	*p*=0.85; 0.95 (0.57, 1.59)	*p*=0.64; 0.88 (0.51, 1.51)

*32 clients with incomplete data excluded (5 missing viral loads; 13 missing pharmacy claim records); respondents with missing data were not significantly different (p>0.05) from those retained for analyses on age, sex, refugee status, and time on HAART

†Factor modelled as a linear effect (common odds ratios presented)

††Unless otherwise noted

†††Adjusted for age group, sex, refugee status, travel in past year, time to clinic, time on HAART, and time from HIV diagnosis to HAART start

‡Item constructed from 3 questions, each measured on a 3-point Likert scale. An endorsement of "some of the time" or " all of the time" on any of the three questions was scored as "insecure"

‡‡Item constructed from 2 questions, each measured on a 5-point Likert scale; ascending score was consistent with greater satisfaction

Table 5: Association of self-change factors with unsuppressed viral load among refugees and local host community on HAART for ≥25 weeks in Kuala Lumpur, Malaysia (N=222*)

Factor	Prevalence ≥40 copies/mL, n/N (%)	p-value, crude odds ratio (95% CI)	p-value, adjusted odds ratio (95% CI)††
Adherence self-efficacy (self-rated ability to take medications as prescribed over previous month)†		*p*=0.37	*p*=0.95
Excellent	16/99 (16)	1	1
Good/very good	14/105 (13)	1.30 (0.74, 2.26)	1.02 (0.56, 1.86)
Very poor/poor/fair	6/18 (33)		
Serostatus disclosure to partner		*p*=0.67	*p*=0.77
No	4/22 (18)	1	1
Yes	17/120 (14)	0.74 (0.22, 2.46)	1.11 (0.29, 4.23)
No partner	15/80 (19)	1.04 (0.31, 3.52)	1.45 (0.38, 5.53)
Serostatus disclosure to family/friends		*p*=0.23	*p*=0.49
No	10/81 (12)	1	1
Yes	26/141 (18)	1.61 (0.73, 3.53)	1.37 (0.56, 3.34)
Alcohol use, past month		*p*=0.29	*p*=0.69
Never	24/164 (15)	1	1
One or more times	12/58 (21)	1.52 (0.71, 3.28)	0.83 (0.33, 2.06)
Use of illegal/harmful substances, past 6 months		*p*=0.23	*p*=0.83
No	32/208 (15)	1	1
Yes	4/14 (29)	2.20 (0.65, 7.45)	1.18 (0.27, 5.31)
Use of traditional medicines, past 6 months		*p*=0.46	*p*=0.75
No	29/188 (15)	1	1
Yes	7/34 (21)	1.48 (0.57, 3.57)	1.31 (0.47, 3.70)
No. of reported barriers to adherence†		*p*=0.46	*p*=0.89
0	13/82 (16)	1	1
1+	8/67 (12)	1.13 (0.82, 1.56)	1.03 (0.71, 1.49)
3+	8/36 (22)		
5+	7/37 (19)		
Knowledge of HIV and AIDS (% correct of 4 questions)		*p*=0.15	*p*=0.23
0+	1/18 (6)	1	1
50+	35/204 (17)	3.52 (0.45, 27.33)	3.21 (0.37, 28.05)

*32 clients with incomplete data excluded (5 missing viral loads; 13 missing pharmacy claim records); respondents with missing data were not significantly different (p>0.05) from those retained for analyses on age, sex, refugee status, and time on HAART

†Factor modelled as a linear effect (common odds ratios presented)

††Adjusted for age group, sex, refugee status, travel in past year, time to clinic, time on HAART, time from HIV diagnosis to HAART start, and previous regimen switch

Table 6: Association of action state (adherence) factors with unsuppressed viral load among refugees and local host community on HAART for ≥25 weeks in Kuala Lumpur, Malaysia (N=222*)

Factor	Prevalence ≥40 copies/mL, n/N (%)	p-value, crude odds ratio (95% CI)	p-value, adjusted odds ratio (95% CI)††
Adherence to medication schedule, self-reported		*p*=0.44	*p*=0.81
Never, sometimes, half of the time, most of the time	12/62 (19)	1	1
All of the time	24/160 (15)	0.74 (0.34, 1.58)	0.90 (0.39, 2.08)
Adherence, visual analogue scale self-report, past month (%)†		*p*=0.01	*p*=0.17
0-	5/13 (39)	1	1
80-	10/46 (22)	0.50 (0.29, 0.86)	0.65 (0.35, 1.19)
95+	21/163 (13)		
Adherence, dose-by-dose self-report, past 4 days (%)		*p*=0.04	*p*=0.30
0-	4/9 (44)	1	1
95+	32/213 (15)	0.22 (0.06, 0.87)	0.32 (0.06, 1.76)
Adherence, pharmacy refill schedule, HAART start or 24 months†		*p*=0.002	*p*=0.009
0-	8/22 (36)	1	1
80-	12/53 (23)	0.45 (0.28, 0.73)	0.47 (0.27, 0.83)
95+	16/147 (11)		
Treatment interruptions of ≥1 day, self-report, past month		*p*=0.003	*p*=0.08
None	27/200 (14)	1	1
Any	9/22 (41)	4.44 (1.73, 11.38)	2.77 (0.91, 8.43)
Unintentional underdosing		*p*=0.32	*p*=0.30
No	27/180 (15)	1	1
Yes	9/42 (21)	1.55 (0.67, 3.59)	1.66 (0.65, 4.24)

*32 clients with incomplete data excluded (5 missing viral loads; 13 missing pharmacy claim records); respondents with missing data were not significantly different (p>0.05) from those retained for analyses on age, sex, refugee status, and time on HAART

†Factor modelled as a linear effect (single common odds ratio presented)

††Adjusted for age group, sex, refugee status, travel in past year, time to clinic, time on HAART, time from diagnosis to HAART start, and previous regimen switch

Table 7: Final multivariate model for factors associated with unsuppressed viral load among refugees and local host community on HAART for ≥25 weeks in Kuala Lumpur, Malaysia (N=222*)

Factor	p-value, crude odds ratio (95% CI)	p-value, adjusted odds ratio (95% CI)††
Age group (years)†	*p*=0.69	*p*=0.68
18-	1	1
30-	0.90 (0.52, 1.55)	1.15 (0.60, 2.20)
40+		
Refugee status	*p*=0.19	*p*=0.60
Host	1	1
Refugee	1.59 (0.77, 3.28)	1.28 (0.52, 3.14)
Sex	*p*=0.04	*p*=0.05
Male	1	1
Female	0.41 (0.16, 1.04)	0.39 (0.14, 1.05)
Time on HAART (years)†	*p*=0.79	*p*=0.53
0-	1	1
1-	1.06 (0.68, 1.67)	1.17 (0.69, 1.96)
2+		
Time from diagnosis to start (weeks)	*p*=0.03	*p*=0.04
0-	1	1
25-	0.61 (0.39, 0.95)	0.64 (0.41, 0.99)
50+		
Temporary migration (≥1 continuous month in past year)	*p*<0.001	*p*=0.002
No	1	1
Yes	4.21 (1.87, 9.50)	4.12 (1.70, 9.99)
Average time to clinic (hours)	*p*=0.01	*p*=0.02
0-	1	1
1+	2.88 (1.14, 7.27)	3.05 (1.09, 8.49)
Adherence, pharmacy refill schedule, HAART start or 24 months†§	*p*=0.002	*p*=0.007
0-	1	1
80-	0.45 (0.28, 0.73)	0.47 (0.27, 0.81)
95+		

*32 clients with incomplete data excluded (5 missing viral loads; 13 missing pharmacy claim records); respondents with missing data were not significantly different (p>0.05) from those retained for analyses on age, sex, refugee status, and time on HAART

†Factor modelled as a linear effect (single common odds ratio presented)

††Adjusted for all factors in table except those denoted by §. A priori factors retained: age group, refugee status, and time on HAART. Factors excluded after one iteration: previous regimen switch

§Factor not included in the final model process due to presumptive role as mediator; other final model factors were not adjusted for these designated factors

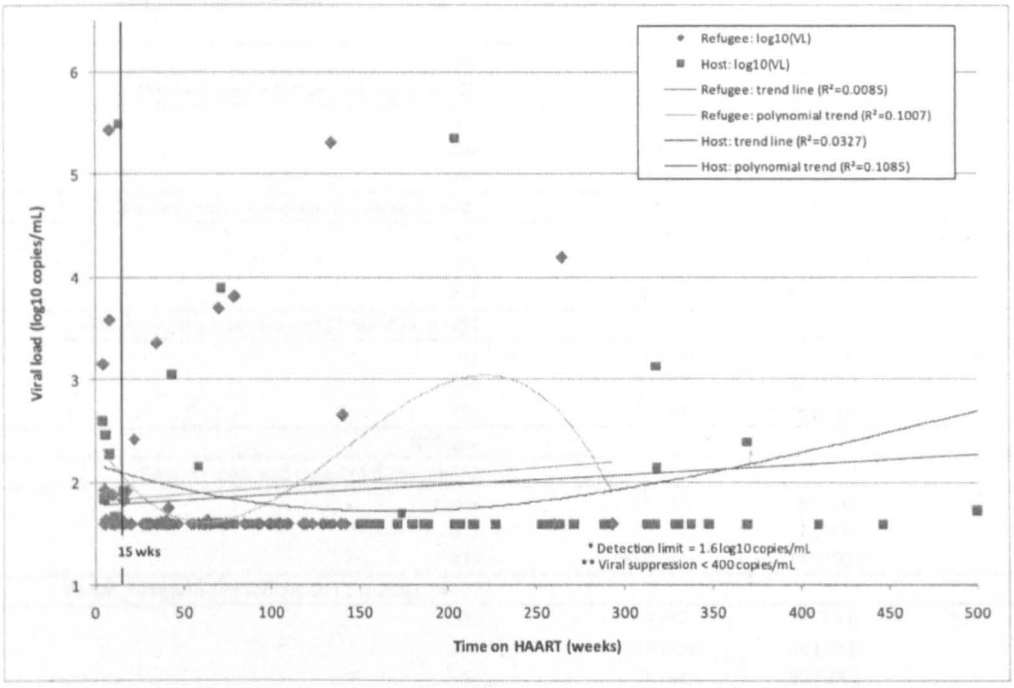
SUPPLEMENTARY MATERIAL

Table i: Comparison of interviewed and randomly sampled host community clients using data from electronic medical records*

Factor	Interviewed sample (n_1)	Random sample (n_2)	p-value
Female/transgender, n (%)	33/144 (23)	32/150 (21)	0.74††
Age in years, median (IQR) (n_1=148; n_2=150)	42 (34, 49)	39 (35, 48)	0.35‡
Marital status, n (%)			
Single	63/141 (45)	52/115 (45)	0.14†
Married	68/141 (48)	61/115 (53)	
Divorced/widowed	10/141 (7)	2/115 (2)	
Ethnicity, n (%)			
Chinese	88/145 (61)	50/140 (36)	<0.001††
Malay	36/145 (25)	56/140 (40)	
Tamil/Other	21/145 (15)	34/140 (24)	
Most recent routine viral load, copies/mL (%)			
Suppressed <40	111/146 (76)	105/139 (76)	0.92††
Not suppressed ≥40	35/146 (24)	34/139 (25)	
Recent routine CD4, median cells/μL (IQR) (n_1=144; n_2=149)	376 (248, 598)	350 (202, 486)	0.07‡
Time on HAART, median weeks (IQR) (n_1=140; n_2=130)	184 (59, 324)	134 (66, 259)	0.09‡

†Fisher's exact test ††Chi-squared test ‡Mann-Whitney test

Figure i: Scatterplot of viral load (log10 copies/mL) by time on treatment (weeks) and by refugee status



A scatterplot of viral load (log10 copies/mL) by time on treatment showed little evidence for a linear relationship between viral load and time on treatment in either the refugee (R^2=0.009, p=0.51) or host community (R^2=0.03, p=0.26) groups. Fitting a third order polynomial curve to the data yielded a slightly stronger (but still weak) relationship between viral load and time on treatment for both the refugee (R^2=0.1) and host community (R^2=0.1) groups. In the host group, the shallow U-shaped curve suggested the possibility of some acquired resistance to HAART over time. However, the best-fitted polynomial curve for the refugee population was not U-shaped, suggesting that this may not have been the case in that group.

Table ii: Viral suppression by type of adherence measurement, stratified by refugee status (≥25 weeks on treatment)

Adherence measurement	<40 copies/mL, n (%)	Total	p-value†
Host			
Dose-by-dose self-report (4 days); n=125			
0+	2 (50)	4 (100)	0.06
80+	0 (0)	0 (0)	
95+	103 (85)	121 (100)	
Visual analogue scale self-report (1 month); n=125			
0+	6 (55)	11 (100)	0.002
80+	21 (78)	27 (100)	
95+	78 (90)	87 (100)	
Pharmacy claim adherence (24 months); n=121			
0+	9 (69)	13 (100)	0.10
80+	27 (84)	32 (100)	
95+	67 (88)	76 (100)	
Refugee			
Dose-by-dose self-report (4 days); n=152			
0+	3 (50)	6 (100)	0.07
80+	1 (100)	1 (100)	
95+	94 (83)	114 (100)	
Visual analogue scale self-report (1 month); n=121			
0+	4 (57)	7 (100)	0.06
80+	18 (75)	24 (100)	
95+	76 (84)	90 (100)	
Pharmacy claim adherence (24 months); n=113			
0+	5 (56)	9 (100)	0.004
80+	17 (68)	25 (100)	
95+	69 (87)	79 (100)	

†Chi-squared test for trend (Cochran-Armitage test)

Table iii: Proportions of clients reporting specific barriers to adherence

Barrier	Refugee		Host		Total	
	Never / Rarely	Sometimes /Often	Never / Rarely	Sometimes /Often	Never / Rarely	Sometimes /Often
...Away from home	141 (94%)	9 (6%)	130 (88%)	17 (12%)	271 (91%)	26 (9%)
...Busy with other things	139 (93%)	11 (7%)	124 (84%)	24 (16%)‡	263 (88%)	35 (12%)*
...Simply forgot	141 (94%)	9 (6%)	140 (95%)	8 (5%)	281 (94%)	17 (6%)
...Have too many pills to take	149 (99%)	1 (1%)	140 (95%)	8 (5%)	289 (97%)	9 (3%)
...Want to avoid side-effects	149 (99%)	1 (1%)	139 (94%)	9 (6%)	288 (97%)	10 (3%)
...Not want others to notice you taking your meds	142 (95%)	8 (5%)	138 (93%)	10 (7%)	280 (94%)	18 (6%)
...Have a change in daily routine	145 (97%)	5 (3%)	139 (94%)	9 (6%)	284 (95%)	14 (5%)
...Feel like the drug is toxic/harmful	150 (100%)	0 (0%)	138 (93%)	10 (7%)	288 (97%)	10 (3%)
...Fall asleep/slept through dose time	142 (95%)	8 (5%)	134 (91%)	14 (9%)	276 (93%)	22 (7%)
...Feel sick or ill	149 (99%)	1 (1%)	142 (96%)	6 (4%)	291 (98%)	7 (2%)
...Feel depressed/overwhelmed	148 (99%)	2 (1%)	137 (93%)	11 (7%)	285 (96%)	13 (4%)
...Have problems taking pills at specified times	142 (95%)	7 (5%)	138 (94%)	9 (6%)	280 (95%)	16 (5%)
...Run out of pills	141 (94%)	10 (7%)	139 (94%)	9 (6%)	280 (94%)	19 (6%)
...Detained or incarcerated by the authorities	139 (94%)	9 (6%)	120 (96%)	5 (4%)	259 (95%)	14 (5%)
...Difficulty concentrating	144 (96%)	6 (4%)	136 (93%)	10 (7%)	280 (95%)	16 (5%)
...Feeling irritable/angry	145 (97%)	4 (3%)	135 (91%)	13 (9%)	280 (94%)	17 (6%)
...Less interest in daily activities	139 (93%)	10 (7%)	139 (94%)	9 (6%)	278 (94%)	19 (6%)
...Feeling that you have less skills than you had before	134 (90%)	15 (10%)†	135 (91%)	13 (9%)	269 (91%)	28 (9%)
...Having difficulty dealing with new situations	139 (93%)	11 (7%)	139 (94%)	9 (6%)	278 (93%)	20 (7%)
...Feeling unable to make daily plans	143 (95%)	7 (5%)	140 (95%)	8 (5%)	283 (95%)	15 (5%)
...Worrying too much about things	138 (93%)	11 (7%)	134 (91%)	14 (9%)	272 (92%)	25 (8%)
...Feeling hopeless about the future	139 (93%)	11 (7%)	132 (90%)	15 (10%)	271 (91%)	26 (9%)

Other reasons cited (Hosts):

Ramadan period (fast), resistant to present medication, admitted to hospital, attend wedding dinner (got drunk), centre forgot to give client, family was annoying, forgot to bring medications out, forgot to take along medication, frustration from children, got stolen, high on drugs, left meds at home, need to stay clear/alert, no confidence in meds, too stressed/happy about other things, took beer, travelling, unstable emotion, work pressure, working in Perak, confused with panadol, financial problems

Other reasons cited (Refugees):

Did not know had to take stocrin, doctor stopped medication, drunk, forget to take while going out, forgot phone alarm, missed at beginning of HAART, no money for transportation, phone alarm not working well, rain dissolved medications, warded in hospital

†Most reported barrier for refugees

‡Most reported barrier for host community

*Most reported barrier overall

Table iv: Proportions of clients reporting on food insecurity

	Refugee		Host		Total	
To what extent are the following statements true...	**Not true**	**Sometimes/ Often true**	**Not true**	**Sometimes/ Often true**	**Not true**	**Sometimes/ Often true**
...I can't afford to eat properly.	48 (31%)	105 (69%)	102 (69%)	46 (31%)	150 (50%)	151 (50%)
...I am often hungry but I don't eat because I can't afford enough food.	44 (29%)	109 (71%)	117 (79%)	31 (21%)	161 (53%)	140 (47%)
...I eat less than I think I should because I don't have enough money for food.	50 (33%)	102 (67%)	108 (73%)	40 (27%)	158 (53%)	142 (47%)
...I cannot give my child(ren) / dependents a balanced meal because I can't afford that.	15 (23%)	49 (77%)	43 (81%)	10 (19%)	58 (50%)	59 (50%)

Table v: Proportions of clients reporting satisfaction with doctor-patient relationship

	Refugee		Host		Total	
Thinking about the doctor that prescribes your medication...						
	Strongly disagree / disagree / uncertain	**Agree/ strongly agree**	**Strongly disagree / disagree / uncertain**	**Agree/ strongly agree**	**Strongly disagree / disagree / uncertain**	**Agree/ strongly agree**
...He/she offers the best medical care they can provide	27 (18%)	126 (82%)	17 (11%)	131 (89%)	44 (15%)	257 (85%)
...He/she puts your health above everything else	31 (20%)	122 (80%)	16 (11%)	132 (89%)	47 (16%)	254 (84%)
Thinking the provider that you interact with most often (if not your doctor)...						
...He/she offers the best medical care they can provide	13 (17%)	63 (83%)	4 (13%)	28 (88%)	17 (16%)	91 (84%)
...He/she puts your health above everything else	17 (22%)	59 (78%)	2 (6%)	31 (94%)	19 (17%)	90 (83%)

Table vi: Proportions of clients reporting on wait-time, obstacles to refill, and costs

	Refugee		Host		Total	
	No	**Yes**	**No**	**Yes**	**No**	**Yes**
...Left clinic due to waiting time in past three months	148 (99%)	2 (1%)	137 (93%)	10 (7%)	285 (96%)	12 (4%)
...Unable to refill HAART prescription in past three months*	138 (93%)	11 (7%)†	141 (95%)	7 (5%)‡	279 (94%)	18 (6%)
...Incur costs related to taking HAART	21 (14%)	132 (86%)	25 (17%)	123 (83%)	46 (15%)	255 (85%)

†5/11 (46%) reported stock-out; 2/11 (18%) reported costs/lack of money for transport
‡2/7 (29%) reported stock-out

Cover sheet for each 'research paper' included in a research thesis

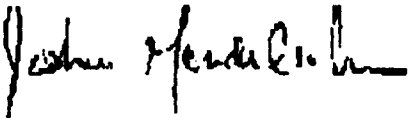
PAPER THREE: POOR TREATMENT OUTCOMES AMONG REFUGEES AND A HOST COMMUNITY ACCESSING ANTIRETROVIRAL THERAPY FROM KAKUMA REFUGEE CAMP IN NORTHWESTERN KENYA

1. For a 'research paper' prepared for publication but not yet published
   1.1. Where is the work intended to be published?
   The Lancet
   1.2. List the paper's authors in the intended authorship order
   Joshua B Mendelsohn, Paul Spiegel, Marian Schilperoord, John Wagacha Burton, Julie A Okonji, Bosco Muhindo, Patterson Njogu, Natasha Larke, Alison Grant, Ibrahim M Mohammed, Irene N Mukui, David A Ross
   1.3. Stage of publication
   Not yet submitted

2. For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)

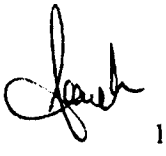
   JBM designed the research protocol, managed data collection, completed statistical analyses and interpretation of results, wrote the manuscript, and edited the manuscript according to comments from co-authors. DAR supported protocol design, statistical analyses, interpretation of results, and commented on the manuscript. MS and PS supported protocol design, interpretation of results, and commented on the manuscript. NP, JWB, and BM supported data collection, interpretation of results, and commented on the manuscript. JO managed all laboratory procedures and tests, supported interpretation of results, and commented on the manuscript. NL and AG supported statistical analyses, interpretation of results, and commented on the manuscript. IM and IM supported protocol design and commented on the manuscript.

Candidate's signature



14/8/2012

Supervisor or senior author's signature to confirm role as stated in (2)



15/8/2012

PAPER THREE

POOR TREATMENT OUTCOMES AMONG REFUGEES AND A HOST COMMUNITY ACCESSING ANTIRETROVIRAL THERAPY FROM KAKUMA REFUGEE CAMP IN NORTHWESTERN KENYA

Brief title

Poor treatment outcomes among camp-based refugees

Prospective authors, addresses, and affiliations

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1 September 2012

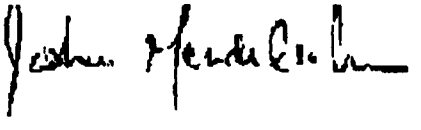
Dear Editor:

We are delighted to submit our manuscript entitled: "Adherence to HAART in refugees and host communities in a refugee camp setting: is forced displacement a barrier to adherence?" We believe that this work is germane to The Lancet and is relevant to its general audience for three main reasons:

- It is highly relevant to The Lancet expressed interest in global health research.
- We believe that your general readership will be interested in the subject matter given recent public interest in the ongoing famine and mass displacement in Somalia and eastern Kenya and recent debates about a broad approach to HIV treatment as prevention.
- It is the first work that we are aware of that systematically studies adherence in asylum-based refugees in a refugee camp, therefore its contribution is novel.
- We report extremely worrying clinical outcomes in this setting.

In the event that we are fortunate enough to have the manuscript published in the Lancet, if the editors must shorten the paper for print publication, we suggest that Tables 1-3 and 5 are retained and the remainder of tables and figures published as web extra material.

Sincerely



Joshua Mendelsohn (on behalf of co-authors)

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COMPETING INTERESTS

The authors declare that they have no conflicts of interest.

AUTHORS AND CONTRIBUTORS

JBM co-designed the research protocol, managed data collection, completed statistical analyses and interpretation of results, and wrote the manuscript. DAR supported protocol design, statistical analyses, interpretation of results, and commented on the manuscript. MS and PS supported protocol design, interpretation of results, and commented on the manuscript. NP, JWB, and BM supported data collection, interpretation of results, and commented on the manuscript. JO managed all laboratory procedures and tests, supported interpretation of results, and commented on the manuscript. NL and AG supported statistical analyses, interpretation of results, and commented on the manuscript. IM and IM supported protocol design and commented on the manuscript. All authors read, commented on, and approved the final manuscript (to be confirmed).

ABBREVIATIONS

ART: antiretroviral therapy; CI: confidence interval; DRC: Democratic Republic of the Congo; HAART: highly active antiretroviral therapy; HIV: human immune deficiency virus; IDP: internally-displaced person; KEMRI: Kenya Medical Research Institute; LSHTM: London School of Hygiene and Tropical Medicine; NNRTI: Non-nucleoside reverse transcriptase inhibitor; OR: odds ratio; PMTCT: prevention of mother-to-child transmission; Rx: adherence

to pharmacy refill schedule; UNHCR: United Nations High Commissioner for Refugees; VAS: visual analogue scale

ABSTRACT

Background. Given the near absence of data on treatment outcomes among refugees, our objective was to evaluate if refugees and the local host community attending a remote refugee camp clinic were achieving acceptable adherence and virological outcomes.

Methods. We conducted a cross-sectional survey among HAART clients (≥18 years) in Kakuma, Kenya. Data sources included structured questionnaires, a pharmacy-based measure of HAART prescription refills over 24 months prior to the study interview (Rx), and HIV viral loads. The primary outcome was unsuppressed viral load (≥1000 copies/mL).

Findings. In refugees and host clients, 86% (n=73) and 84% (n=86) of all clients not lost to follow-up participated. Compared with the host community, refugees were older (median age 36y (IQR 31, 41) v. 32y (IQR 27, 38); p=0.02), but similar with respect to the proportion of women (67% v. 66%, p=0.91) and median time on HAART (147 weeks (IQR 38, 264) v. 139 (IQR 39,225); p=0.65). Median time spent by refugees in the host country was 9.8 years (IQR 4.5,15.7). Proportions optimally adherent to Rx were 85% among refugees vs. 74% among the host community (p=0.09). Similar proportions in both groups on treatment for ≥25 weeks had an unsuppressed viral load (88% v. 89%, p=0.89). In multivariable analyses, refugee status was not associated with the outcome (OR_{adj}=0.64, 95%CI 0.20,2.08; p=0.46). Larger household sizes (OR_{adj}=0.26, 95%CI 0.11,0.61; p<0.001) were protective and there was weak evidence that underdosing (OR_{adj}=7.48, 95%CI 0.74,27.22; p=0.07) was independently associated with lack of viral suppression.

Interpretation. Virological measures were valuable for monitoring program effectiveness. The unacceptable levels of viral suppression may have resulted from previous unmeasured treatment interruptions or adherence lapses. Remedial interventions are urgently required to improve outcomes in this setting.

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INTRODUCTION

Previous studies among conflict-affected populations has reported good adherence and treatment outcomes (1-3). As a result, international guidelines now recommend provision of highly active antiretroviral therapy (HAART) to conflict-affected populations (4). However, among these groups, refugees are unique insofar as they have crossed an international border and are normally entitled to a level of health care equivalent to the standard of care for host nationals. In Kenya, where most refugees reside in remote camp settings, supporting clients on a complex chronic therapy such as HAART may be facilitated by the ability to follow them up in the relatively small area of the refugee camp. Even in urban settings, recent findings demonstrated that good, equitable adherence and virological outcomes are achievable (5). Yet, in times of financial uncertainty when allocating scarce resources to non-nationals may be contested, refugees may face questions pertaining to their ability to sustain treatment. In this context, high unemployment, lack of disposable income, and fractured support networks may be used to argue that optimal adherence and treatment outcomes will be difficult to achieve (6). The lack of data on adherence and treatment outcomes among refugees unwittingly fuels these assertions, in addition to stifling the ability of providers to assess and improve program delivery. In response to these concerns, we conducted a study of adherence and treatment outcomes with refugee and host community clients accessing HAART in Kakuma Refugee Camp, Kenya.

METHODS

Study setting

The Comprehensive Care Clinic, Kakuma (CCCK), was chosen as it presented an opportunity to study a refugee camp setting in sub-Saharan Africa with sufficient numbers of clients accessing treatment. At the time of study start (February 2011), 446,946 refugees from the Horn of Africa were registered by UNHCR in Kenya; the population of Kakuma Refugee Camp was 82,409. The Kenyan government has signed the 1951 Refugee Convention and its 1967 Protocol, and the National HIV/AIDS Strategic Plans included refugees. Access to first and second-line HAART is provided by the national program. The comparison group (local host community) was comprised primarily of the Turkana, a nomadic-pastoralist ethnic group. Although traditionally nomadic, many Turkana opt for a non-nomadic way of life, living in more permanent dwellings around established towns or settlements. The CCCK is managed by the International Rescue Committee (IRC). Biomarker testing, nutritional, and counselling services were routinely provided to all clients. At the start of the study in February 2011, 389 HIV-positive refugee and host community clients had been enrolled since the start of the HAART program. If diagnosed HIV-positive, clients were routinely counselled and started on

multivitamins and cotrimoxazole. A two week trial regimen of nevirapine-based HAART, dosed once-daily, was routinely initiated when indicated by national guidelines. Depending on tolerance, this regimen was either continued twice-daily or substituted with an efavirenz-based therapy.

Study design

A five-week cross-sectional survey was conducted at the Comprehensive Care Clinic in Kakuma Refugee Camp with a serially-recruited sample of refugee and Kenyan adults. Clients who were ≥18y, on HAART for ≥30 days, not lost to follow-up (defined as having missed six or more consecutive monthly pharmacy refills), and not exclusively on ART for prevention of mother-to-child transmission (PMTCT), were systematically recruited at the time of their regular clinic appointment or through an active recruitment protocol implemented by home-based care workers. Efforts were made to contact all known eligible HAART clients meeting the inclusion criteria at least three times by either telephone or home visit. Clients self-identified as a refugee or host community national.

Data sources

Data sources included a structured questionnaire with self-reported adherence measures, a pharmacy-based prescription refill measure, and HIV viral loads. The primary outcome was unsuppressed viral load (cut-off <1000 copies/mL). The questionnaire was translated into Kiswahili, Nga'turkana, French, Amharic, and Somali, and backwards translated into English. The back-translated and original English versions were reconciled prior to pre-testing and pilot-testing. Adherence to pharmacy refill schedule (Rx) was measured using a pharmacy-based measure of HAART prescription refills, calculated as the proportion of refills collected over the total prescribed up to 24 months prior to the interview date. Self-reported adherence was measured using both a four-day dose-by-dose recall and a general one-month visual analogue scale (VAS). HIV viral loads were collected as dried blood spots on Whatman 903 filter paper, dried and frozen at -20°C. Samples were shipped on dry ice to the Kenya Medical Research Institute HIV Laboratory in Kisumu, Kenya and analysed using the COBAS Ampliprep/Taqman platform (Roche Diagnostics Systems, Branchburg, New Jersey, USA).

Statistical methods

Socio-demographic characteristics were compared between host and refugee groups using Mann-Whitney tests for continuous variables, Chi-square or Fisher's exact test for categorical variables, and Chi-square test for trend for ordered categorical variables. The primary outcome was unsuppressed viral load (≥1000 copies/mL). Risk factors for unsuppressed viral load were evaluated using unconditional logistic regression; effect estimates were odds ratios and

corresponding 95% confidence intervals (CI). A three-level forwards, step-wise modelling approach was used to classify and order the entry of factors into the model. Drawing on social action theory (7), factors were grouped into levels representing treatment contexts such as socio-demographic, displacement-related, and treatment factors; self-change processes such as disease and medication knowledge, self-efficacy, and serostatus disclosure; and action state factors including adherence measures. Associations between unsuppressed viral load and factors from all levels were first evaluated in univariable analyses using log-likelihood ratio tests. A "treatment context model" was then fitted by adjusting for treatment context factors with $p<0.1$ in univariable analyses. A "self-change processes model" was fitted by adjusting each new factor by all retained treatment context factors, then adjusting again for any additional factors with $p<0.1$. A model evaluating the effect of "action state (adherence) factors" was adjusted for factors from previous levels only due to collinearity between adherence measures. The final multivariable logistic regression model was obtained by excluding each retained factor with the highest p-value, one at a time, until all remaining factors had $p<0.05$. Refugee status, age, and time on HAART were retained throughout all modelling. Due to their role as mediators in the causal mechanism between distal factors and treatment outcomes, factors were not adjusted for adherence in the final model to avoid over-adjustment bias (8).

Ethical approval

Ethical approval was received by the Kenya Medical Research Institute (Approval 1884) and the London School of Hygiene and Tropical Medicine Research Ethics Committee (Approval 5547).

Role of funding source

UNHCR supported this study and its representatives assisted with study design, interpretation of data, and writing of the manuscript, and approved the protocol in advance of data collection. The corresponding author had full access to all the study data and took the final decision to submit the work for publication.

RESULTS

Study population

Among those eligible, we recruited 73/85 (86%) refugees and 86/102 (84%) of the Kenyan adults. Among those not participating, nine refugees (75%) declined and 3 (25%) were not found, while 6 (38%) host community clients declined and 10 (62%) were not found. The HIV-positive clients at the Kakuma clinic from the refugee and host communities were similar in relation to the proportions of females (67% v. 66%, $p=0.91$) and median time on HAART (147

v. 139 weeks, p=0.65). Although not statistically significant, current defaulters were more prevalent among the host community (1% v. 7%, p=0.13). The refugee group was older (median age 36y v. 32y, p=0.02), had a median time in the host country of 9.8 years (IQR 4.5, 15.7), and median since registration with UNHCR of 8.5 years (IQR 2.8, 14.9) (Table 1).

[*** Table 1, p.104, near here ***]

Virological and adherence outcomes

Using a threshold of <1000 copies/mL to signify viral suppression, 11% (18/159) of surveyed clients were virologically suppressed. The proportions suppressing viral load were similarly low in both refugee 10% (7/73) and host clients 13% (11/86) (p=0.53). Even after restricting analyses to clients who had been on treatment for a minimum of 25 weeks, only 12% (7/59) of refugees and 11% (8/72) of host community clients had a suppressed viral load (p=0.89) (Table 2).

Among all clients, the four-day dose-by-dose adherence recall showed that a high proportion of refugee and host clients self-reported optimal adherence over the previous four days (86% vs. 88%, p=0.92). There was weak evidence for a difference between the groups on adherence to Rx (85% v. 74%, p=0.09). The proportions self-reporting optimal adherence on the one-month (VAS) were still lower, and a comparatively higher proportion of refugees reported optimal adherence (62% v. 28%, p=0.002). Among clients on HAART for ≥25 weeks, within each group, there was no evidence for ordered trends between proportions not suppressing viral load and adherence measured by the four-day recall (p=0.81, p=1.00) and Rx (p=0.74, p=0.91). On the VAS, there was strong evidence for a trend (p=0.02) among host nationals but not among refugees (p=0.91) (see Supp. Table ii).

[*** Table 2, p.104 and Table 3, p.105, near here ***]

Risk factors for unsuppressed virological outcomes

Unsuppressed viral load was defined as ≥1000 copies/mL. In initial analyses of contextual factors (Table 4), there was strong evidence for a protective effect of increasing household size (OR_{adj}=0.25, 95%CI 0.10, 0.62; p=0.001). Longer time between HIV diagnosis and HAART start (OR_{adj}=2.23, 95%CI 0.83, 5.98; p=0.07) increased the odds of unsuppressed viral load. There was no association between lack of viral suppression and refugee status (OR_{adj}=0.70, 95%CI 0.21, 2.34; p=0.56) after adjusting for age group, time on HAART, refugee status, household size, and time from HIV diagnosis to HAART start.

[*** Table 4, p.106-107, near here ***]

Among self-change process factors (Table 5), more reported adherence barriers resulted in more protection (OR_{adj}=0.56, 95%CI 0.30, 1.03; p=0.05). Among exposures in the action state level (Table 6), there was strong evidence that clients reporting unintentional underdosing (determined by comparing self-reported dosing schedules to commonly recommended dosing schedules) (9) were more likely to have an unsuppressed viral load (OR_{adj}=7.49, 95%CI 1.02, 55.33; p=0.03), and weak evidence for a protective effect of perfect self-reported adherence to medication schedule (OR_{adj}=0.21, 95%CI 0.02, 1.79; p=0.09). These associations were adjusted for age group, time on HAART, refugee status, household size, time from diagnosis to HAART start, and number of reported adherence barriers.

[*** Table 5, p.108 and Table 6, p.109, near here ***]

The final multivariable model (Table 7) identified strong evidence for a protective effect of increasing household size (OR_{adj}=0.26, 95%CI 0.11, 0.61; p<0.001). There was weak evidence for an association between lack of viral suppression and underdosing (OR_{adj}=7.48, 95%CI 0.74, 27.22; p=0.07). Pharmacy refill schedule was tested in the final model but no association with lack of viral suppression was found (OR_{adj}=0.96, 95%CI 0.41, 2.24; p=0.74). Refugee status was not associated with failure to suppress viral load (OR_{adj}=0.64, 95%CI 0.20, 2.08; p=0.46) after adjusting for age group, time on HAART, refugee status, and household size. Among clients on HAART for 1-3y, 83% were not suppressed, rising to 91% among those on HAART for ≥3y but no association between increasing time on treatment and outcomes was found (OR_{adj}=1.25, 95%CI 0.59, 2.64; p=0.57).

[*** Table 7, p.110, near here ***]

Discussion

Few clients on HAART attending the CCCK achieved viral suppression, a very worrying result that is inconsistent with the effectiveness of HAART. There were only minor differences, none statistically significant, in terms of pharmacy refill adherence and virological outcomes between the refugee and host community groups. Self-reported one-month adherence was worse among the host community (p=0.002) and at poor levels in both groups. Although virological data are unavailable for other non-refugee, conflict-affected groups, good treatment outcomes as measured by CD4 gains and survival have been reported (10, 11). In studies of refugees who have been resettled, virological outcomes were also good (12-16). In sub-Saharan African HIV treatment programmes as a whole, a meta-analysis of 89 studies found that 76% of clients had achieved viral suppression after six months, and 67% after 12 months on treatment (17). Although viral suppression decreased slightly between 12 and 24 months, suppression remained high at 24 months, a finding that was not replicated in the present study setting. However, other

studies have found virological failure in the presence of good self-reported and pharmacy refill adherence (18, 19), a phenomenon that may be due to the sensitivity of virological outcomes to the dynamic, time-dependent features of adherence. The adherence outcomes in the refugee group were comparable to previously reported data in conflict-affected groups. In northern Uganda, 92% of internally-displaced persons (IDPs) achieved optimal adherence (≥95%) as measured by a composite score including drug possession ratio, pharmacy refill records, and three day recall by patients or caregivers (11). In a different Ugandan study, mean self-reported adherence among IDPs was 99.5% (2) and in western Equatorial Province, Sudan, 88% of refugees and IDPs on HAART for ≥6 months self-reported ≥95% adherence (20). During active conflict in the Democratic Republic of the Congo, 99% of clients were adhering optimally as measured by pill counts (1).

Some potential explanations for the unacceptable levels of viral suppression include: poor adherence over time due to daily lapses or irregular medication refills, either not captured by the adherence proxy measures or occurring before the retrospective period that was covered by the study; poor continuity of care due to interruptions in HAART supply or poor client follow-up; accumulation of drug resistant mutations over time due to poor adherence and/or treatment interruptions; reduced potency of medications due to quality of medications, storage conditions, and/or drug-drug interactions; initial transmission of drug resistant virus; severe malnutrition; infrequent viraemia (viral "blips"); and high baseline viral load.

The adherence findings provided few clues as to the reasons for the low levels of suppression. Routine adherence of at least 95% of tablets taken as prescribed is the optimal level required for achieving and sustaining viral suppression across common triple-therapy regimens including NNRTIs (21, 22). There was a clear gap between the proportions not suppressing viral load at a threshold of <1000 copies/mL (88% and 89% for refugees and hosts on treatment for ≥25 weeks, respectively) and those self-reporting adherence of <80% of doses by four-day recall (8% and 12% among refugees and hosts, respectively), by VAS (14% in each group), and also within the pharmacy refill data (7% v. 14%, respectively). The prevalence of optimal self-reported adherence was much lower according to the self-reported one-month VAS when compared to the pharmacy refill measure, suggesting that daily adherence may have been more problematic than simply collecting the drugs as prescribed. However, the data did not show any independent associations between adherence measures and virological outcomes. Unintentional underdosing (discrepancies between self-reported dosing and routine dosing schedules), was a weak independent risk factor for unsuppressed viral load in the final model, suggesting that some of the result may have been due to confusion in dosing schedules.

Intermittent continuity of care such as interruptions in HAART supply or poor client follow-up may have led to sub-optimal adherence and/or treatment interruptions. Anecdotal reports of prescribing and stocking abnormalities during the transition from stavudine as a routine first-line drug was suggestive of difficulties that may have contributed to past adherence lapses. Of the 13% (20/157) of clients who reported an inability to refill their medications in the past three months, one-third (7/20) reported that the reason was a pharmacy stock-out. The fact that many host clients lived considerable distances away from the clinic or lead traditional nomadic lifestyles may also have contributed to irregular clinic or pharmacy attendance. However, in terms of displacement-related factors, neither travel time to clinic, previous travel in the past year, nor refugee status, were associated with virological outcomes. Only 54% of surveyed clients indicated that they either rarely or never used specific reminders to assist with daily adherence, a result that suggested intervention opportunities by using mobile phones to engage clients with adherence support (23).

The possibility that the poor viral suppression results may have been a consequence of underlying resistance patterns was indirectly supported by the lack of independent associations between unsuppressed viral load and any measure of adherence in the final model. Non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance over time appears to be the most problematic form of resistance, with mortality rates three times higher than for other regimens (24) and the majority (98%) of clients in the present setting received NNRTI-based therapy. It was plausible that very high baseline viral loads contributed to the low levels of viral suppression. In a previous study, baseline viral loads $\geq$100,000 were shown to lower the likelihood of ever achieving viral suppression over the duration of follow-up (25). There is an increased likelihood of mortality at these high baseline levels in the presence of poor adherence (26, 27). As there had been no previous viral load testing in this population, a baseline measure was unavailable. The 36%/year (95% CI 15, 45) increase in prevalence of NNRTI resistance recently observed in East Africa (28) suggests that resistance was responsible for the high levels of viraemia in the present setting. In one rural South African setting, 86% (160/187) of virological failures had $\geq$1 drug resistance mutations, compromising second-line therapy in 18% of clients (29). Thus resistance is on the rise and must be carefully monitored, however, NNRTI resistance prevalence in East Africa is still estimated at only 5.1%, eight years after ART rollout, suggesting that this explanation was unlikely in the present setting (28).

One counter-intuitive finding that emerged from the analysis of risk factors was that increasing household numbers protected against poor virological outcomes. Conventional wisdom would suggest that adherence might be compromised in crowded living environments due to fear of serostatus disclosure (30). By contrast, our findings suggested that larger household sizes may have benefitted clients in this context, perhaps through enhanced assistance and support. Half of

clients indicated that they received emotional support from family and friends (see Supp. Table vii). The extent to which larger households are integrated (e.g. the strength of ties between household members), or a greater chance that effective support networks emerge from larger households may also be important factors that merit further study.

This study had important limitations. First, some explanations for the poor outcomes, such as drug resistance, drug potency, and malnutrition, were not assessed. Food insecurity was assessed but was not associated with the outcome in multivariable analyses. Second, the single viral load sample collected invited the possibility that some unsuppressed outcomes were due to "viral blips". These fluctuations are caused by random statistical or biological variation around mean HIV-levels often as a result of sporadic release of virus from latent reservoirs (31, 32). However, given that viral blips usually occur at low levels around the detection limit (<400 copies/mL in the present study), the widespread lack of suppression in the very high ranges observed (median=4,840 copies/mL, IQR 1,920-21,100) was a consequence of treatment failure or inadequate adherence as opposed to sporadic escape. Moreover, we chose a cut-off of <1000 copies/mL for the outcome to ensure that small fluctuations around the detection limit would not lead to false positives. Third, recall and social desirability biases may have plagued adherence measurement. Pharmacy refills are good predictors of treatment outcomes in some settings (33), but this measure may not have been sufficiently sensitive to poor daily adherence to serve as a good proxy in the present setting (34). Fourth, the cross-sectional design placed limits on the study in relation to the attribution of causality and the potential exacerbation of recall biases. Lastly, clients who were defaulting for five months or more were considered lost to follow-up. Exclusion of these individuals may have introduced survivor bias by overestimating outcomes. In relation to generalisability, the comparison group (local host community) was comprised primarily of the Turkana, a nomadic-pastoralist ethnic group. Nomadic groups can also be expected to face particular adherence challenges in relation to migration and poverty.

Key study strengths included the high participation rates in both groups, a sampling frame that included the entire eligible population and efforts to mitigate recall and social desirability biases by conducting face-to-face interviews with trained local researchers. The study also aimed to triangulate multiple adherence measurements in an effort to enhance the overall validity of findings.

In summary, the very low proportion of clients who had achieved viral suppression (11% <1000 copies/mL) is highly concerning and requires immediate remedial programmatic action. Importantly, there were no differences observed between refugees and the host community on adherence or treatment outcomes. Optimal adherence was not ideal but better than the viral load results would predict. Unintentional underdosing by clients, inconsistent maintenance of

personal medication supply, poor continuity of care, and occasional daily adherence lapses may account for some of the poor clinical outcomes observed. Overall, the severe degree of failure in this HAART delivery programme was not fully captured by single or multiple factors. Clinic procedures and adherence support have been strengthened by providers since the study by enhancing routine follow-up and counselling performed by home-based care staff. These efforts will be evaluated by conducting a second round of viral load testing to confirm treatment failures and drug resistance testing for those clients. Future work will include a pre-post study to verify if these remedial measures were effective. In general, these very poor outcomes serve as a stark reminder that programs must regularly evaluate their performance and adapt, if HAART is to be scaled-up effectively and universally.

REFERENCES

1. Culbert H, Tu D, O'Brien DP, Ellman T, Mills C, Ford N, et al. HIV treatment in a conflict setting: outcomes and experiences from Bukavu, Democratic Republic of the Congo. PLoS Med. 2007 May;4(5):e129.

2. Garang PG, Odoi RA, Kalyango JN. Adherence to antiretroviral therapy in conflict areas: a study among patients receiving treatment from Lacor Hospital, Uganda. AIDS Patient Care STDS. 2009;23(9):743-7.

3. Kiboneka A, Nyatia RJ, Nabiryo C, Anema A, Cooper CL, Fernandes KA, et al. Combination antiretroviral therapy in population affected by conflict: outcomes from large cohort in northern Uganda. BMJ. 2009;338:b201.

4. Inter-agency Standing Working Group on Reproductive Health in Crises. Inter-agency Field Manual on Reproductive Health in Humanitarian Settings - 2010 Revision for Field Review. 2010 [cited 2012 13 March]; Available from: http://www.iawg.net/IAFM%202010.pdf

5. Mendelsohn JB, Spiegel P, Schilperoord M, Balasundaram S, Radhakrishnan A, Lee C, et al. Good adherence and treatment outcomes in refugee and host communities on highly active antiretroviral therapy in urban Kuala Lumpur, Malaysia. In Preparation.

6. UNHCR, Southern African HIV Clinicians Society. Clinical Guidelines for Antiretroviral Therapy Management for Displaced Populations - Southern Africa. Geneva: UNHCR; 2007.

7. Ewart C. Social-action theory for a public health psychology. Am Psychol. 1991 Sep;46(9):931-46.

8. Schisterman EF, Cole SR, Platt RW. Overadjustment bias and unnecessary adjustment in epidemiologic studies. Epidemiology. 2009 Jul;20(4):488-95.

9. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1 infected adults and adolescents. 2012 [cited 30 July 2012]; Available from: http://www.aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf

10. O'Brien DP, Venis S, Greig J, Shanks L, Ellman T, Sabapathy K, et al. Provision of antiretroviral treatment in conflict settings: the experience of Médecins Sans Frontières. Confl Health. 2010;4:12.

11. Kiboneka A, Wangisi J, Nabiryo C, Tembe J, Kusemererwa S, Olupot-Olupot P, et al. Clinical and immunological outcomes of a national paediatric cohort receiving combination antiretroviral therapy in Uganda. AIDS (London, England). 2008 Nov 30;22(18):2493-9.

12. Blood E, Beckwith C, Bazerman L, Cu-Uvin S, Mitty J. Pregnancy among HIV-infected refugees in Rhode Island. AIDS Care. 2009 Feb;21(2):207-11.

13. Krentz H, Gill MJ. The five-year impact of an evolving global epidemic, changing migration patterns, and policy changes in a regional Canadian HIV population. Health Policy. 2009 May;90(2-3):296-302.

14. Moreno A, Crosby S, Labelle C, Sullivan M, Samet JH. Health assessment of HIV-infected refugees. Journal of acquired immune deficiency syndromes (1999). 2003 1 Oct;34(2):251-4.

15. Nisbet SM, Reeve AM, Ellis-Pegler RB, Woodhouse AF, Ingram RJ, Roberts SA, et al. Good outcome in HIV-infected refugees after resettlement in New Zealand: population study. Intern Med J. 2007 May;37(5):290-4.

16. Rutta E, Gongo R, Mwansasu A, Mutasingwa D, Rwegasira V, Kishumbu S, et al. Prevention of mother-to-child transmission of HIV in a refugee camp setting in Tanzania. Glob Public Health. 2008;3(1):62-76.

17. Barth RE, van der Loeff MF, Schuurman R, Hoepelman AI, Wensing AM. Virological follow-up of adult patients in antiretroviral treatment programmes in sub-Saharan Africa: a systematic review. Lancet Infect Dis. 2010 Mar;10(3):155-66.

18. Bisson GP, Rowh A, Weinstein R, Gaolathe T, Frank I, Gross R. Antiretroviral failure despite high levels of adherence: discordant adherence-response relationship in Botswana. Journal of acquired immune deficiency syndromes (1999). 2008 Sep 1;49(1):107-10.

19. Trotta MP, Pierro P, Marconi P, Sette P, Zaccarelli M, Acinapura RA, et al. With current ARV treatments virological failure mostly occurs in the context of optimal self-reported adherence. Infection. 2011 Mar;39:S27-S8.

20. Salami O, Buzu A, Nzeme C. High level of adherence to HAART among refugees and internally displaced persons on HAART in western equatorial region of Southern Sudan. J Int AIDS Soc. 2010;13(Suppl4):123.

21. Lima VD, Harrigan R, Murray M, Moore DM, Wood E, Hogg RS, et al. Differential impact of adherence on long-term treatment response among naive HIV-infected individuals. AIDS. 2008 Nov 12;22(17):2371-80.

22. Low-Beer S, Yip B, O'Shaughnessy MV, Hogg RS, Montaner JS. Adherence to triple therapy and viral load response. J Acquir Immune Defic Syndr (1999). 2000 Apr 1;23(4):360-1.

23. Lester RT, Ritvo P, Mills EJ, et al. Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya1): a randomised trial. Lancet. 2010;376(9755):1838-45.

24. Hogg RS, Bangsberg DR, Lima VD, Alexander C, Bonner S, Yip B, et al. Emergence of drug resistance is associated with an increased risk of death among patients first starting HAART. PLoS Med. 2006 Sep;3(9):e356.

25. Wood E, Hogg RS, Yip B, Harrigan PR, Montaner JS. Why are baseline HIV RNA levels 100,000 copies/mL or greater associated with mortality after the initiation of antiretroviral therapy? J Acquir Immune Defic Syndr (1999). 2005 Mar 1;38(3):289-95.

26. Wood E, Hogg RS, Yip B, Quercia R, Harrigan PR, O'Shaughnessy MV, et al. Higher baseline levels of plasma human immunodeficiency virus type 1 RNA are associated with increased mortality after initiation of triple-drug antiretroviral therapy. J Infect Dis. 2003 Nov 15;188(10):1421-5.

27. Wood E, Hogg RS, Yip B, Moore D, Harrigan PR, Montaner JS. Impact of baseline viral load and adherence on survival of HIV-infected adults with baseline CD4 cell counts > or = 200 cells/microl. AIDS. 2006 May 12;20(8):1117-23.

28. Gupta RK, Jordan MR, Sultan BJ, Hill A, Davis DH, Gregson J, et al. Global trends in antiretroviral resistance in treatment-naive individuals with HIV after rollout of antiretroviral treatment in resource-limited settings: a global collaborative study and meta-regression analysis. Lancet. 2012 Jul 20.

29. Manasa J, McGrath N, Lessells R, Skingsley A, Newell ML, de Oliveira T. High levels of drug resistance after failure of first-line antiretroviral therapy in rural South Africa: impact on standardised second-line regimens (TUAB0304 - Oral Abstract). IAC2012. Washington DC; 2012.

30. Stirratt MJ, Remien RH, Smith A, Copeland OQ, Dolezal C, Krieger D. The role of HIV serostatus disclosure in antiretroviral medication adherence. AIDS Behav. 2006 Sep;10(5):483-93.

31. Nettles RE, Kieffer TL, Kwon P, Monie D, Han Y, Parsons T, et al. Intermittent HIV-1 viremia (Blips) and drug resistance in patients receiving HAART. JAMA. 2005 Feb 16;293(7):817-29.

32. Zhang S, van Sighem A, Gras L, Reiss P, Smit C, Kroon F, et al. Clinical significance of transient HIV type-1 viraemia and treatment interruptions during suppressive antiretroviral treatment. Antivir Ther. 2010;15(4):555-62.

33. Bisson GP, Gross R, Bellamy S, Chittams J, Hislop M, Regensberg L, et al. Pharmacy refill adherence compared with CD4 count changes for monitoring HIV-infected adults on antiretroviral therapy. PLoS Med. 2008 May 20;5(5):e109.

34. McMahon JH, Jordan MR, Kelley K, Bertagnolio S, Hong SY, Wanke CA, et al. Pharmacy adherence measures to assess adherence to antiretroviral therapy: review of the literature and implications for treatment monitoring. Clin Infect Dis. 2011 Feb 15;52(4):493-506.

TABLES AND FIGURES

Research in context

Systematic review

See Mendelsohn et al. Adherence to highly active antiretroviral therapy in forcibly displaced populations – a systematic review [if published or in print in advance]

Interpretation

We report very poor treatment outcomes among both refugees and the local host communities accessing services from a remote clinic in Northwestern Kenya.

Table 1: Baseline socio-demographic and treatment factors interviewed host community (n=86) and refugee clients (n=73)

Factor	Host	Refugee	p-value
Female, n (%)	57 (66)	49 (67)	0.91†
Age in years, median (IQR)	32 (27, 38)	36 (31, 41)	0.02††
Unemployed, n (%)	70 (81)	63 (86)	0.41†
Educational status, n (%)			
None	38 (44)	28 (38)	0.50†
Any primary	39 (45)	33 (45)	
Any secondary or above	9 (11)	12 (16)	
Marital status, n (%)			
Single	47 (55)	44 (60)	0.48††
Married/relationship	39 (45)	29 (40)	
Nationality			
Kenyan	86 (100)	0 (0)	<0.001†††
Somali, Ethiopian, Eritrean	0 (0)	36 (49)	
Sudanese	0 (0)	20 (27)	
Rwandese, Congolese, Burundian	0 (0)	17 (23)	
Current defaulters, n (%)§	6 (7)	1 (1)	0.13†††
Viral load, copies/mL (IQR)	5875 (2120, 28500)	3580 (1810, 12800)	0.14††
Most recent routine CD4, median cells/μL (IQR)‡	308 (192, 439)	254 (141, 472)	0.57††
CD4 at HAART program start, cells/μL‡‡	198 (119, 289)	196 (136, 320)	0.28††
Time on HAART, median weeks (IQR)	139 (39, 225)	147 (38, 264)	0.65††
Time since HIV diagnosis, median weeks (IQR)	182 (83, 265)	212 (87, 288)	0.22††
Time in host country, median weeks (IQR)	NA	507 (234, 814)	NA
Time since refugee status approval, median weeks (IQR)	NA	440 (143, 774)	NA

§1-5 consecutive months without pharmacy refill at time of survey interview

†Chi-square test ††Mann-Whitney test †††Fisher's exact test

‡n_1=76, n_2=61 ‡‡n_1=55, n_2=48

Table 2: Comparison of virological outcomes in host community and refugee clients

Time on HAART (weeks)	Group	≥1000 copies/mL, n (%)	Total, n (%)	p-value
All	Host	75 (87)	86 (100)	0.53†
	Refugee	66 (90)	73 (100)	
< 25	Host	11 (79)	14 (100)	0.22††
	Refugee	14 (100)	14 (100)	
≥ 25	Host	64 (89)	72 (100)	0.89†
	Refugee	52 (88)	59 (100)	

†Chi-square test ††Fisher's exact test

Table 3: Adherence in host community and refugee clients

Adherence measure	Host, n (%)	Refugee, n (%)	p-value†
Dose-by-dose self-report (4 days)	(N=86)	(N=72)	0.92
0+	10 (12)	6 (8)	
80+	0 (0)	4 (6)	
95+	76 (88)	62 (86)	
Visual analogue scale self-report (1 month)	(N=86)	(N=73)	0.002
0+	12 (14)	10 (14)	
80+	50 (58)	18 (25)	
95+	24 (28)	45 (62)	
Pharmacy claim adherence (24 months)§	(N=86)	(N=73)	0.09
0+	12 (14)	5 (7)	
80+	10 (12)	6 (8)	
95+	64 (74)	62 (85)	

†Chi-square test for trend (Cochran-Armitage test) §Since started on HAART to a maximum of 24 months

Table 4: Association of contextual factors with unsuppressed viral load among refugees and local host community on HAART for ≥25 weeks in Kakuma, Kenya (N=128*)

Factor	Prevalence ≥1000 copies/mL, n/N (%)†	p-value, crude odds ratio (95% CI)	p-value, adjusted odds ratio (95% CI)††
Age group (years)†		*p*=0.89	*p*=0.66
18-	28/31 (90)	1	1
30-	54/63 (86)	1.05 (0.50, 2.24)	1.20 (0.52, 2.77)
40+	31/34 (91)		
Refugee status		*p*=0.86	*p*=0.56
Host	63/71 (89)	1	1
Refugee	50/57 (88)	0.91 (0.31, 2.67)	0.70 (0.21, 2.34)
Time on HAART (years)†		*p*=0.58	*p*=0.41
0-	18/20 (90)	1	1
1-	34/41 (83)	1.22 (0.60, 2.48)	1.40 (0.64, 3.07)
3+	61/67 (91)		
Sex		*p*=0.50	*p*=0.82
Male	40/44 (91)	1	1
Female	73/84 (87)	0.66 (0.20, 2.22)	0.86 (0.23, 3.21)
Travel (≥1 continuous month in past year)		*p*=0.97	*p*=0.61
No	90/102 (88)	1	1
Yes	23/26 (89)	1.02 (0.27, 3.93)	0.67 (0.15, 3.00)
Nationality		*p*=0.21	*p*=0.33
Kenyan	63/71 (89)	1	1
Somali, Ethiopian, Eritrean	27/28 (96)	3.43 (0.41, 28.77)	2.26 (0.23, 22.12)
Sudanese	14/18 (78)	0.44 (0.12, 1.69)	0.47 (0.11, 2.09)
Rwandese, Congolese, Burundian	9/11 (82)	0.57 (0.10, 3.13)	0.44 (0.07, 2.83)
Household size†		*p*=0.001	*p*=0.001
1-	44/45 (98)	1	1
5-	51/58 (88)	0.28 (0.12, 0.65)	0.25 (0.10, 0.62)
9+	18/25 (72)		
Living children		*p*=0.14	*p*=0.25
No	24/25 (96)	1	1
Yes	89/103 (86)	0.27 (0.03, 2.12)	0.30 (0.03, 2.93)
Average time to clinic (hours)		*p*=0.85	*p*=0.83
0-	25/28 (89)	1	1
1+	88/100 (88)	0.88 (0.23, 3.36)	0.19 (0.25, 5.65)
Personal income		*p*=0.12	*p*=0.18
None	83/91 (91)	1	1
Any income	30/37 (81)	0.41 (0.14, 1.24)	0.42 (0.12, 1.48)
Time from HIV diagnosis to HAART start (weeks)†		*p*=0.07	*p*=0.07
0-	74/87 (85)	1	1
25-	13/14 (93)	2.16 (0.82, 5.69)	2.23 (0.83, 5.98)
50+	26/27 (96)		
HAART regimen, dosing		*p*=0.27	*p*=0.19
NVP-based, twice-daily	84/97 (87)	1	1
EFV-based, twice-daily/others	29/31 (94)	2.24 (0.48, 10.55)	2.78 (0.53, 14.64)
Any symptom or side-effect, past 4 weeks		*p*=0.53	*p*=0.45
No	91/102 (89)	1	1
Yes	22/26 (85)	0.67 (0.19, 2.29)	0.57 (0.14, 2.35)
Cotrimoxazole prescription		*p*=0.77	*p*=0.92
No	10/11 (91)	1	1
Yes	103/117 (88)	0.74 (0.09, 6.19)	1.13 (0.09, 13.63)
Regimen switch, ever		*p*=0.29	*p*=0.41
No	59/69 (86)	1	1
Yes	54/59 (92)	1.83 (0.59, 5.70)	1.69 (0.48, 5.92)

Table 4: Association of contextual factors with unsuppressed viral load among refugees and local host community on HAART for ≥25 weeks in Kakuma, Kenya (N=128*)

Factor	Prevalence ≥1000 copies/mL, n/N (%)†	p-value, crude odds ratio (95% CI)	p-value, adjusted odds ratio (95% CI)††
Unable to refill prescription, past 3 months		*p*=1.00	*p*=0.95
No	98/111 (88)	1	1
Yes	15/17 (88)	1.00 (0.20, 4.85)	0.94 (0.16, 5.59)
Food security‡		*p*=0.63	*p*=0.76
Secure	29/32 (91)	1	1
Insecure	84/96 (88)	0.72 (0.19, 2.75)	0.80 (0.19, 3.44)
Satisfaction with primary health care provider, mean score‡‡	Mean= 3.66; SE=0.05	*p*=0.38; 0.61 (0.18, 2.02)	*p*=0.50; 0.67 (0.19, 2.31)

*3 clients with incomplete data excluded

†Factor modelled as a linear effect (common odds ratios presented)

††Unless otherwise noted

†††Adjusted for age group, refugee status, time on HAART, household size, time from HIV diagnosis to HAART start

‡Item constructed from 3 questions, each measured on a 3-point Likert scale. An endorsement of "some of the time" or " all of the time" on any of the three questions was scored as "insecure"

‡‡Item constructed from 2 questions, each measured on a 5-point Likert scale; ascending score was consistent with greater satisfaction

Table 5: Association of self-change factors with unsuppressed viral load among refugees and local host community on HAART for ≥25 weeks in Kakuma, Kenya (N=128*)

Factor	Prevalence ≥1000 copies/mL, n/N (%)†	p-value, crude odds ratio (95% CI)	p-value, adjusted odds ratio (95% CI)††
Adherence self-efficacy (self-rated ability to take medications as prescribed over previous month)		*p*=0.57	*p*=0.42
Excellent/very good	59/68 (87)	1	1
Good/fair/poor/very poor	54/60 (90)	1.37 (0.46, 4.11)	1.76 (0.44, 7.02)
Serostatus disclosure to partner		*p*=0.37	*p*=0.60
No	20 /25 (80)	1	1
Yes	67/75 (89)	2.09 (0.62, 7.12)	2.04 (0.44, 9.40)
No partner	26/28 (93)	3.25 (0.57, 18.52)	2.52 (0.31, 20.46)
Serostatus disclosure to community		*p*=0.37	*p*=0.16
No	87/100 (87)	1	1
Yes	26/28 (93)	1.94 (0.41, 9.17)	3.56 (0.51, 24.77)
Alcohol use		*p*=0.92	*p*=0.82
Never in past month	99/112 (88)	1	1
Once or more in past month	14/16 (88)	0.92 (0.19, 4.51)	0.81 (0.13, 4.86)
Use of illegal/harmful substances, past 6 months		*p*=0.86	*p*=0.69
No	104/118 (88)	1	1
Yes	9/10 (90)	1.21 (0.14, 10.30)	0.60 (0.06, 6.50)
No. of reported barriers to adherence†		*p*=0.55	*p*=0.05
0	30/33 (91)	1	1
1+	31/35 (89)	0.87 (0.54, 1.39)	0.56 (0.30, 1.03)
3+	20/23 (87)		
5+	32/37 (87)		
Knowledge of HIV and AIDS (% correct of 4 questions)		*p*=0.78	*p*=0.62
0+	34/38 (90)	1	1
100+	79/90 (88)	0.85 (0.25, 2.84)	0.70 (0.16, 3.02)

*3 clients with incomplete data excluded

†Factor modelled as a linear effect (common odds ratios presented)

††Adjusted for age group, refugee status, time on HAART, household size, time from HIV diagnosis to HAART start, and number of reported barriers to adherence

Table 6: Association of action state (adherence) factors with unsuppressed viral load among refugees and local host community on HAART for ≥25 weeks in Kakuma, Kenya (N=128*)

Factor	Prevalence ≥1000 copies/mL, n/N (%)	p-value, crude odds ratio (95% CI)	p-value, adjusted odds ratio (95% CI)††
Adherence to medication schedule, self-reported		*p*=0.14	*p*=0.09
Less than all of the time	24/25 (96)	1	1
All of the time	89/103 (86)	0.27 (0.03, 2.12)	0.21 (0.02, 1.79)
Adherence, visual analogue scale self-report, past month (%)		*p*=0.23	*p*=0.21
0-	64/70 (91)	1	1
95+	49/58 (85)	0.51 (0.17, 1.53)	0.43 (0.11, 1.63)
Adherence, dose-by-dose self-report, past 4 days (%)†		*p*=0.94	*p*=0.93
0-	11/12 (92)	1	1
80-	2/3 (67)	0.97 (0.38, 2.43)	0.96 (0.35, 2.61)
95+	100/113 (89)		
All daily doses missed, self-report, past 4 days		*p*=0.49	*p*=0.64
0	99/113 (88)	1	1
1+	14/15 (93)	1.98 (0.24, 16.24)	1.68 (0.17, 16.29)
Adherence, pharmacy refill schedule, HAART start or 24 months†		*p*=0.91	*p*=0.74
0-	13/15 (87)	1	1
80-	14/15 (93)	0.96 (0.43, 2.14)	0.86 (0.36, 2.07)
95+	86/98 (88)		
Treatment interruptions of ≥2 days, self-report, past 6 months		*p*=0.41	*p*=0.19
0	88/101 (87)	1	1
1+	25/27 (93)	1.85 (0.39, 8.73)	2.94 (0.51, 16.88)
Unintentional underdosing		*p*=0.37	*p*=0.03
No	87/100 (87)	1	1
Yes	26/28 (93)	1.94 (0.41, 9.17)	7.49 (1.02, 55.33)

*3 clients with incomplete data excluded

†Factor modelled as a linear effect (single common odds ratio presented)

††Adjusted for age group, refugee status, time on HAART, household size, time from HIV diagnosis to HAART start, and number of reported barriers to adherence

Table 7: Final multivariate model for factors associated with unsuppressed viral load among refugees and local host community on HAART for ≥25 weeks in Kakuma, Kenya (N=128*)

Factor†	p-value, crude odds ratio (95% CI)	p-value, adjusted odds ratio (95% CI)††
Age group (years)†	*p*=0.89	*p*=0.54
18-	1	1
30-	1.05 (0.50, 2.24)	1.30 (0.56, 3.00)
40+		
Refugee status	*p*=0.86	*p*=0.46
Host	1	1
Refugee	0.91 (0.31, 2.67)	0.64 (0.20, 2.08)
Time on HAART (years)†	*p*=0.58	*p*=0.57
0-	1	1
1-	1.22 (0.60, 2.48)	1.25 (0.59, 2.64)
2+		
Household size†	*p*=0.001	*p*<0.001
1-	1	1
5-	0.28 (0.12, 0.65)	0.26 (0.11, 0.61)
9+		
Unintentional underdosing§	*p*=0.37	*p*=0.07
No	1	1
Yes	1.94 (0.41, 9.17)	7.48 (0.74, 27.22)
Adherence, pharmacy refill schedule, HAART start or 24 months†§	*p*=0.91	*p*=0.74
0-	1	1
80-	0.96 (0.43, 2.14)	0.96 (0.41, 2.24)
95+		

*3 clients with incomplete data excluded

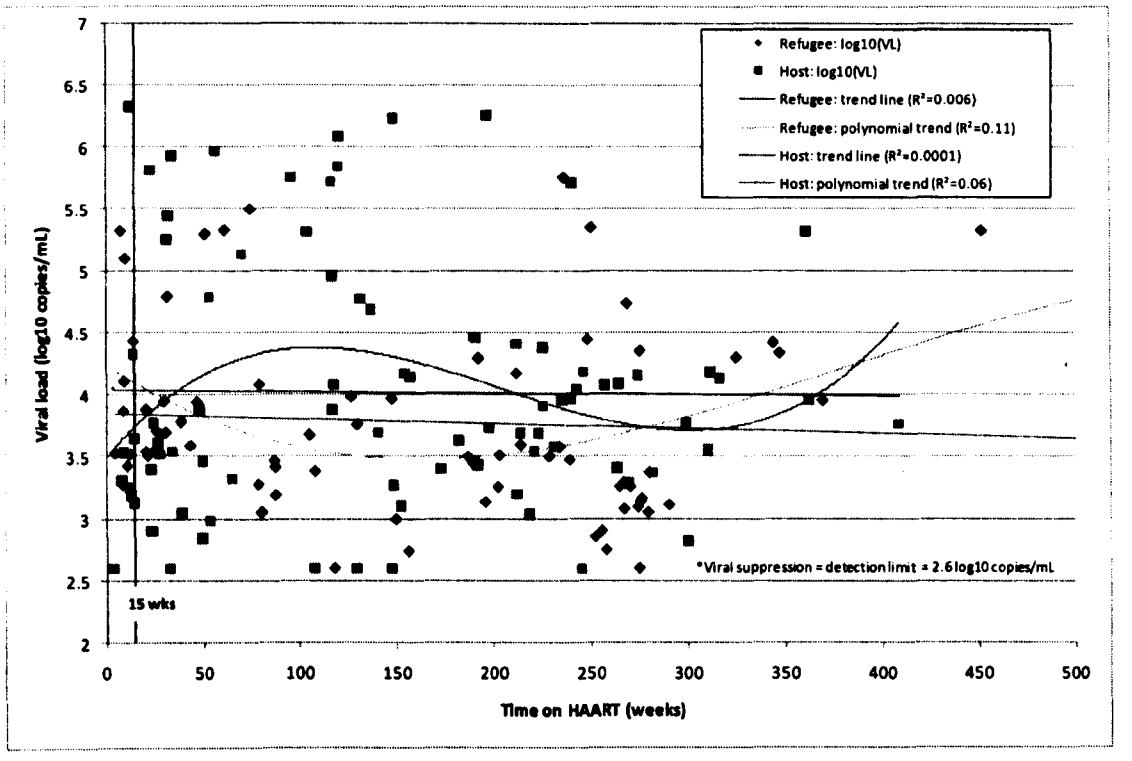
†Factor modelled as a linear effect (single common odds ratio presented)

††Adjusted for all factors in table except those denoted by §. A priori factors retained: age group, refugee status, time on HAART, and adherence to pharmacy refill schedule. Factors excluded after two iterations: number of reported barriers to adherence; time from HIV diagnosis to HAART start

§Factor not included in the final model process due to presumptive role as mediator; other final model factors were not adjusted for these designated factors

SUPPLEMENTARY MATERIAL

Figure i: Scatterplot of viral load (log10 copies/mL) by time on treatment (weeks) and by refugee status



A scatterplot of viral load (log10 copies/mL) by time on treatment (see Appendix A, Figure i), did not show any evidence of a relationship between viral load and time on treatment in both the host community (R^2=0.0001, p=0.91) and refugee (R^2=0.006, p=0.47) groups. Fitting a third order polynomial curve to the data yielded a slightly stronger relationship between viral load and time on treatment for both the host community (R^2=0.06) and the refugee groups (R^2=0.11). In the refugee group, the U-shaped curve suggested the possibility of some acquired resistance to HAART over time. However, the best-fitted polynomial curve for the host population was not U-shaped.

Table I: Virological outcomes by type of adherence measurement, stratified by refugee status

Adherence measurement	≥1000 copies/mL, n (%)	Total	p-value†
Host			
Dose-by-dose self-report (4 days) ; n=86			
0+	9 (90)	10 (100)	0.78
80+	0 (0)	0 (0)	
95+	66 (87)	76 (100)	
Visual analogue scale self-report (1 month) ; n=86			
0+	12 (100)	12 (100)	0.08
80+	44 (88)	50 (100)	
95+	19 (79)	24 (100)	
Pharmacy claim adherence (24 months) ; n=86			
0+	10 (83)	12 (100)	0.88
80+	10 (100)	10 (100)	
95+	55 (86)	64 (100)	
Refugee			
Dose-by-dose self-report (4 days); n=72			
0+	6 (100)	6 (100)	0.71
80+	3 (75)	4 (100)	
95+	56 (90)	62 (100)	
Visual analogue scale self-report (1 month); n=73			
0+	10 (100)	10 (100)	0.73
80+	15 (83)	18 (100)	
95+	41 (91)	45 (100)	
Pharmacy claim adherence (24 months); n=73			
0+	5 (100)	5 (100)	0.70
80+	5 (83)	6 (100)	
95+	56 (90)	62 (100)	

†Chi-squared test for trend (Cochran-Armitage test)

Table ii: Virological outcomes by type of adherence measurement, stratified by refugee status (≥25 weeks on treatment)

Adherence measurement	≥1000 copies/mL, n (%)	Total	p-value†
Host			
Dose-by-dose self-report (4 days) ; n=72			
0+	8 (89)	9 (100)	1.00
80+	(0)	0 (0)	
95+	56 (89)	63 (100)	
Visual analogue scale self-report (1 month) ; n=72			
0+	10 (100)	10 (100)	0.02
80+	40 (93)	43 (100)	
95+	14 (74)	19 (100)	
Pharmacy claim adherence (24 months) ; n=72			
0+	10 (83)	12 (100)	0.91
80+	10 (100)	10 (100)	
95+	44 (88)	50 (100)	
Refugee			
Dose-by-dose self-report (4 days); n=58			
0+	4 (100)	4 (100)	0.81
80+	2 (67)	3 (100)	
95+	45 (88)	51 (100)	
Visual analogue scale self-report (1 month); n=59			
0+	7 (100)	7 (100)	0.91
80+	10 (77)	13 (100)	
95+	35 (90)	39 (100)	
Pharmacy claim adherence (24 months); n=59			
0+	3 (100)	3 (100)	0.74
80+	5 (83)	6 (100)	
95+	44 (88)	50 (100)	

†Chi-squared test for trend (Cochran-Armitage test)

Table ii: Proportions of clients reporting satisfaction with doctor-patient relationship

	Refugee		Host		Total	
Thinking about the doctor that prescribes your medication...						
	Not at all/ A little	**Quite a bit/ Extremely**	**Not at all/ A little**	**Quite a bit/ Extremely**	**Not at all/ A little**	**Quite a bit/ Extremely**
...He/she offers the best medical care they can provide	1 (1%)	85 (99%)	8 (11%)	65 (89%)	9 (6%)	150 (94%)
...He/she puts your health above everything else	1 (1%)	84 (99%)	8 (11%)	65 (89%)	9 (6%)	150 (94%)
Thinking the provider that you interact with most often (if not your doctor)...						
...He/she offers the best medical care they can provide	2 (14%)	12 (86%)	1 (6%)	16 (94%)	3 (10%)	28 (90%)
...He/she puts your health above everything else	1 (7%)	13 (93%)	2 (11%)	15 (89%)	3 (10%)	28 (90%)

Table iii: Proportions of clients reporting on satisfaction clinic and patient autonomy

	Refugee		Host		Total	
Please tell us how you agree with the following statements...	**Agree/ Strongly agree**	**Uncertain/ Disagree/ Strongly disagree**	**Agree/ Strongly agree**	**Uncertain/ Disagree/ Strongly disagree**	**Agree/ Strongly agree**	**Uncertain/ Disagree/ Strongly disagree**
...I am treated justly and with respect during my visits to the clinic	64 (88%)	9 (12%)	81 (94%)	5 (6%)	145 (91%)	14 (9%)
...When I go for medical care, they are careful to check everything when treating and examining me	63 (88%)	9 (12%)	80 (93%)	6 (7%)	143 (91%)	15 (9%)
...Sometimes I wonder if the provider's tests and treatments are correct	28 (38%)	45 (62%)	31 (36%)	55 (64%)	59 (37%)	100 (63%)
...I was given a choice concerning the type of treatment that was prescribed to me†	37 (51%)	36 (49%)	43 (50%)	43 (50%)	80 (50%)	79 (50%)

†The high proportion of clients endorsing this idea may be linked to the validity of the question: clients may have understood the question as asking if they believe they are making a choice whether or not to take the medications, as opposed to asking if they felt they had a choice of regimens

Table iv: Proportions of clients reporting on wait-time, obstacles to refill, and costs

	Refugee		Host		Total	
	No	**Yes**	**No**	**Yes**	**No**	**Yes**
...Left clinic due to waiting time in past three months	66 (93%)	5 (7%)	77 (91%)	8 (9%)	143 (92%)	13 (8%)
...Unable to refill HAART prescription in past three months	64 (90%)	7 (10%)	73 (85%)	13 (15%)	137 (87%)	20 (13%)*
...Incur costs related to taking HAART†	41 (56%)	32 (44%)	58 (67%)	28 (33%)	99 (63%)	60 (38%)

*7/21 (33%) reported reason was stock-out; 6/21 (29%) reported reason was wait time

† This could be an explanatory factor, but the small sample size placed limitation on sub-group analyses. Costs may have included transport or food that clients felt were needed to sustain HAART

Table v: Proportions of clients reporting on food insecurity

	Refugee		Host		Total	
To what extent are the following statements true...	**Not true**	**Sometimes/ Often true**	**Not true**	**Sometimes/ Often true**	**Not true**	**Sometimes/ Often true**
...I can't afford to eat properly.	13 (18%)	59 (82%)	17 (20%)	69 (80%)	30 (19%)	128 (81%)
...I am often hungry but I don't eat because I can't afford enough food.	7 (10%)	65 (90%)	5 (6%)	81 (94%)	12 (8%)	146 (92%)
...I eat less than I think I should because I don't have enough money for food.	2 (3%)	70 (97%)	1 (1%)	85 (99%)	3 (2%)	155(98%)
...I cannot give my child(ren) / dependents a balanced meal because I can't afford that.	2 (4%)	55 (96%)	8 (10%)	74 (90%)	10 (7%)	129 (93%)

Table vi: Proportions of clients reporting specific barriers to adherence

Barrier	Refugee		Host		Total	
	Never/Rarely	Sometimes/ Often	Never/Rarely	Sometimes/ Often	Never/Rarely	Sometimes/ Often
...Away from home	68 (93%)	5 (7%)	73 (85%)	13 (15%)‡	141 (89%)	18 (11%)
...Busy with other things	71 (97%)	2 (3%)	81 (94%)	5 (6%)	152 (96%)	7 (4%)
...Simply forgot	67 (92%)	6 (8%)	85 (99%)	1 (1%)	152 (96%)	7 (4%)
...Have too many pills to take	69 (95%)	4 (5%)	82 (95%)	4 (5%)	151 (95%)	8 (5%)
...Want to avoid side-effects	71 (97%)	2 (3%)	82 (95%)	4 (5%)	153 (96%)	6 (4%)
...Not want others to notice you taking your meds	71 (97%)	2 (3%)	80 (93%)	6 (7%)	151 (95%)	8 (5%)
...Fall asleep/slept through dose time	68 (93%)	5 (7%)	82 (95%)	4 (5%)	150 (94%)	9 (6%)
...Feel sick or ill	62 (85%)	11 (15%)	82 (95%)	4 (5%)	144 (91%)	15 (9%)
...Feel depressed/overwhelmed	59 (81%)	14 (19%)†	82 (95%)	4 (5%)	141 (89%)	18 (11%)
...Have problems taking pills at specified times	66 (90%)	7 (10%)	81 (94%)	5 (6%)	147 (92%)	12 (8%)
...Run out of pills	66 (90%)	7 (10%)	72 (84%)	14 (16%)‡	138 (87%)	21 (13%)*
...Detained or incarcerated by the authorities	69 (95%)	4 (5%)	85 (99%)	1 (1%)	154 (97%)	5 (3%)
...Difficulty concentrating	67 (92%)	6 (8%)	85 (99%)	1 (1%)	152 (96%)	7 (4%)
...Feeling irritable/angry	60 (82%)	13 (18%)	80 (93%)	6 (7%)	140 (88%)	19 (12%)
...Less interest in daily activities	66 (90%)	7 (10%)	84 (98%)	2 (2%)	150 (94%)	9 (6%)
...Feeling that you have less skills than you had before	67 (92%)	6 (8%)	83 (96%)	3 (4%)	150 (94%)	9 (6%)
...Having difficulty dealing with new situations	66 (90%)	7 (10%)	82 (95%)	4 (5%)	148 (93%)	11 (7%)
...Worrying too much about things	67 (92%)	6 (8%)	82 (95%)	4 (5%)	149 (94%)	10 (6%)
...Feeling hopeless about the future	67 (92%)	6 (8%)	83 (98%)	2 (2%)	150 (95%)	8 (5%)
...Want to be free of medicines	69 (95%)	4 (5%)	84 (98%)	2 (2%)	153 (96%)	6 (4%)
...Financial constraints	56 (77%)	17 (23%)†	81 (94%)	5 (6%)	137 (86%)	22 (14%)*
...Other illnesses	58 (79%)	15 (21%)†	84 (98%)	2 (2%)	142 (89%)	17 (11%)
...Felt fine/healthy	65 (89%)	8 (11%)	85 (99%)	1 (1%)	150 (94%)	9 (6%)
...Decreased quality of life	67 (92%)	6 (8%)	84 (98%)	2 (2%)	151 (95%)	8 (5%)
...Uncertainty	64 (89%)	8 (11%)	82 (95%)	4 (5%)	146 (92%)	12 (8%)
...Disruptions/chaotic routine	64 (88%)	9 (12%)	74 (86%)	12 (14%)‡	138 (87%)	21 (13%)*

†Top three most reported barriers for refugees
‡Top three most reported barriers for host community
*Top three most reported barriers overall

Table vii: Proportions of clients reporting specific facilitators of adherence

Facilitator	Refugee		Host		Total	
	Never/Rarely	Sometimes/ Often	Never/Rarely	Sometimes/ Often	Never/Rarely	Sometimes/ Often
...Meds take priority over substance or alcohol abuse	14 (19%)	59 (81%)	8 (9%)	78 (91%)	22 (14%)	137 (86%)
...I have accepted my HIV status and learned to manage it	1 (1%)	71 (99%)	1 (1%)	85 (99%)	2 (1%)	156 (99%)
...My HAART gives me good results	3 (4%)	69 (96%)	3 (4%)	83 (96%)	6 (4%)	152 (96%)
...I understand why I must adhere to HAART	1 (1%)	71 (99%)	3 (4%)	83 (96%)	4 (3%)	155 (97%)
...I believe that HAART works	3 (4%)	70 (96%)	6 (7%)	80 (93%)	9 (6%)	150 (94%)
...My HAART regimen is simple	7 (10%)	66 (90%)	13 (15%)	73 (85%)	20 (13%)	139 (87%)
...My routine is fixed	20 (27%)	53 (73%)	12 (14%)	74 (86%)	32 (20%)	127 (80%)
...I use reminders like my phone alarm	47 (65%)†	25 (35%)	39 (45%)‡	47 (55%)	86 (54%)*	72 (46%)
...I live for someone (child, spouse, etc.)	22 (30%)	51 (70%)	15 (17%)	71 (83%)	37 (23%)	122 (77%)
...I was part of the decision to start HAART	12 (16%)	61 (84%)	8 (9%)	78 (91%)	20 (13%)	139 (87%)
...My family and/or friends remind me to take HAART	51 (70%)†	22 (30%)	38 (45%)‡	47 (55%)	89 (56%)*	69 (44%)
...My family and/or friends support me emotionally	41 (56%)	32 (44%)	36 (42%)‡	50 (58%)	77 (49%)	82 (52%)
...My family and/or friends support me financially	59 (81%)†	14 (19%)	44 (51%)‡	42 (49%)	103 (65%)*	56 (35%)
...I respect my doctor and listen to their advice	2 (3%)	71 (97%)	0 (0%)	86 (100%)	2 (1%)	157 (99%)
...People know I am HIV+ so I have nothing to lose	27 (37%)	46 (63%)	29 (34%)	57 (66%)	56 (35%)	103 (65%)
...I trust in my ability to take my HAART	2 (3%)	70 (97%)	3 (4%)	83 (96%)	5 (3%)	153 (97%)
...I have a bright future ahead	5 (7%)	68 (93%)	12 (14%)	74 (86%)	17 (11%)	142 (89%)

†Top three least reported facilitators for refugees
‡Top three least reported facilitators for host community
*Top three least reported facilitators overall

Cover sheet for each 'research paper' included in a research thesis

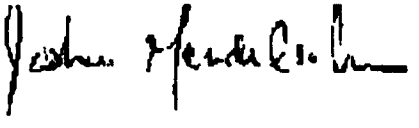
PAPER FOUR: ADHERENCE TO ANTIRETROVIRAL THERAPY AMONG REFUGEES AND LOCAL HOST COMMUNITIES: PATIENT PERSPECTIVES FROM KENYA AND MALAYSIA

1. For a 'research paper' prepared for publication but not yet published
   1.1. Where is the work intended to be published?
   AIDS Care
   1.2. List the paper's authors in the intended authorship order
   Joshua B Mendelsohn, Tim Rhodes, Marian Schilperoord, John Wagacha Burton, Susheela Balasundaram, Chunting Wong, Paul Spiegel, David A Ross
   1.3. Stage of publication
   Not yet submitted

2. For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)

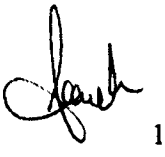
   JBM designed and implemented the data collection strategy, conducted the primary analyses and interpretation of results, wrote the first draft of the manuscript, and edited the manuscript according to comments from co-authors. DAR reviewed the research design and data collection instruments, assisted with analyses and interpretation of results, and suggested revisions in the draft manuscript. MS and PS reviewed research design and commented on the manuscript. TR contributed to the research design, supported interpretation of results, and commented on the manuscript. JWB facilitated data collection in Kenya and supported interpretation of results. SB facilitated data collection in Malaysia, supported interpretation of results, and commented on the manuscript. CW supported data analysis and interpretation of results, and commented on the manuscript.

Candidate's signature



14/8/2012

Supervisor or senior author's signature to confirm role as stated in (2)



15/8/2012

PAPER FOUR

ADHERENCE TO ANTIRETROVIRAL THERAPY AMONG REFUGEES AND LOCAL HOST COMMUNITIES: PATIENT PERSPECTIVES FROM KENYA AND MALAYSIA

Brief title

Adherence to ART among refugees in Kenya and Malaysia

Prospective authors, addresses, and affiliations

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Format

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Max word count: 5000 not including abstract, tables and references

Current word count: 5128

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AIDS Care
Taylor and Francis

1 September 2012

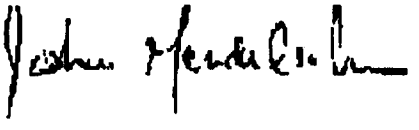
Dear Editor:

We are pleased to submit our manuscript entitled: "Adherence to antiretroviral therapy in refugees and local host communities: a qualitative study of patient perspectives in two host countries."

We believe that this work will be valuable to the readership of Social Science and Medicine as the topics of adherence to antiretroviral medicines and forced displacement will be of interest to range of social scientists, policymakers, and medical professionals who practice or are interested in humanitarian settings. Moreover, it is the first qualitative work that we are aware of that systematically studies adherence issues in asylum-based refugees.

We are grateful for your consideration of our manuscript.

Sincerely



Joshua Mendelsohn (on behalf of co-authors)

ABSTRACT

Refugees may face challenges maintaining adherence to highly active antiretroviral therapy (HAART). However, there is little research exploring how such challenges are navigated or how they may differ to local host communities or across refugee settings. We therefore sought to document refugee and host community accounts of threats, barriers and facilitators related to HAART adherence in urban and camp settings. We conducted semi-structured interviews in a purposive sample of refugees (n=14) and local host participants (n=11) in a public, urban clinic in Kuala Lumpur, Malaysia (July-September 2010), and similar groups (n=12 and n=6, respectively) in a camp-based clinic in Northwestern Kenya (February-March 2011). We used framework methods, process-tracing, and between-case comparison to analyse and interpret the data, with a view to delineating social factors influencing adherence. Food insecurity, treatment delivery insecurity, stigma and discrimination, economic hardship, and lack of social support were typically reported barriers, accentuated in the Kenyan camp setting. The urban Malaysian accounts shared thematic similarities; however, the resulting treatment outcomes were considerably better in this group. We found evidence of resilience among refugees and host communities in the face of difficult conditions, and while refugees experienced some unique barriers in both settings such as crossing borders and integrating into treatment systems, these were seldom linked to treatment interruptions. We drew on levels of influence and the concept of "bounded agency" to argue that relative success of individual efforts to transcend social and environmental threats to adherence were important determinants of adherence behaviours and treatment success. Easing food insecurity, treatment delivery insecurity, and the threat of treatment discontinuity for refugees upon arrival in asylum – while bolstering treatment support for clients who experience intensive stigma and discrimination, should provide strong intervention opportunities.

KEYWORDS

Highly active antiretroviral therapy, adherence, refugees, Kenya, Malaysia, qualitative methods

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

ROLE OF FUNDING SOURCE

Financial support was provided by UNHCR, CIHR, and the Parkes Foundation. UNHCR assisted in study design, interpretation of results, and drafting of the manuscript.

AUTHORS' CONTRIBUTIONS

JBM designed and implemented the data collection strategy, conducted the primary analyses and interpretation of results, and wrote the first draft of the manuscript. DAR reviewed the research design and data collection instruments, assisted with analyses and interpretation of results, and suggested revisions in the draft manuscript. MS and PS reviewed research design and commented on the manuscript. TR contributed to the research design, supported interpretation of results, and commented on the manuscript. JBW facilitated data collection in Kenya and supported interpretation of results. SB facilitated data collection in Malaysia, supported interpretation of results, and commented on the manuscript. CW supported data analysis and interpretation of results, and commented on the manuscript. All authors edited the manuscript for intellectual content and approved the final manuscript (to be confirmed).

ABBREVIATIONS

ART: antiretroviral therapy; cART: combination antiretroviral therapy; DRC: Democratic Republic of the Congo; HAART: highly active antiretroviral therapy; HR: hazard ratio; HIV: human immune deficiency virus; IDP: internally displaced person; MSF: Médecins Sans Frontières; OR: odds ratio; UNHCR: United Nations High Commissioner for Refugees

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INTRODUCTION

There is now general agreement that, as a public health and humanitarian issue, forcibly-displaced and conflict-affected persons who clinically require highly active antiretroviral therapy (HAART) for HIV, ought to receive it (The Sphere Project, 2011), although this had not always been the case (The Sphere Project, 2004). Assertions have been made about the potential consequences of displacement for adherence, often in the absence of empirical evidence (UNHCR & Southern African HIV Clinicians Society, 2007). Adherence to HAART is a modifiable determinant of HIV treatment outcomes but must be consistently excellent to prevent treatment failure and drug resistance (Lima et al., 2008). Among the few studies of HAART adherence among forcibly-displaced populations, encouraging estimates of 87-99.5% were reported (Mendelsohn, Schilperoord, Spiegel, & Ross, Submitted).

Many research models of adherence are premised on a highly "individuated" conception of health behaviour (Fisher, Fisher, Amico, & Harman, 2006; Weinstein, 1993). By contrast, alternative accounts seek to capture adherence as a product of social condition and action and often emphasise an interplay of factors exogenous to individuals that mediate individual-environment interactions, thereby creating the specific contexts which constrain or enable individual decision-making and action (Ewart, 1991; Rhodes, 2002). Advocates of these social models of HIV prevention and treatment (Blankenship, Bray, & Merson, 2000; Gupta, Parkhurst, Ogden, Aggleton, & Mahal, 2008; Wolfe, Carrieri, & Shepard, 2010) have stressed an interplay of macro-level forces (legal, political, and economic), meso-level forces (institutional, system, network effects), and micro-level forces (interpersonal relationships and social interactions) (Rhodes, Singer, Bourgois, Friedman, & Strathdee, 2005). Recent discussion has specifically called for more focus on social influences in studies of adherence to HAART (Castro, 2005; Krusi, Wood, Montaner, & Kerr, 2010; Wolfe et al., 2010). Qualitative research is well-positioned in this regard (Pope & Mays, 1995), however, a recent review found that few qualitative studies had critically examined the role of social and structural factors in shaping adherence (Vervoort, Borleffs, Hoepelman, & Grypdonck, 2007). Of the limited qualitative work among internally-displaced groups, social barriers to adherence included travel, insecurity in attending clinics, food insecurity, distance to health centres, and inadequate planning for the return phase of the displacement cycle (Garang, Odoi, & Kalyango, 2009; Olupot-Olupot et al., 2008; Wilhelm-Solomon, 2009).

Among forcibly-displaced groups, refugees are particular in that they have crossed an international border, are unable to return to their home country, and have been granted an internationally-recognised legal status that entitles them to public relief, including health care, on an equivalent basis to host nationals. Given this imperative to provide refugees with a

locally-acceptable standard of care, our investigation aimed to examine the opportunities and limitations afforded by the treatment "system" in which HAART was delivered and the comparative experiences of refugee and host community participants within these systems and between two different settings. Two recent surveys of refugees and local host communities by our research team found a marked difference in outcomes (measured as the proportion with viral suppression, defined as <1000 copies/mL) between a camp-based population in Kenya (11% suppressed) and an urban population in Malaysia (91% suppressed) (Mendelsohn, Schilperoord, Spiegel, Burton et al., In Preparation; Mendelsohn, Spiegel et al., In Preparation). Drawing on participant accounts from these two studies, we sought to consider how social and environmental factors may structure threats and barriers to adherence and treatment outcome.

METHODS

Research design and case selection

We adopted a case study approach, selecting an urban public hospital in Kuala Lumpur, Malaysia and a refugee camp clinic in Kakuma, Kenya. These settings were different from each other in terms of their geography, remoteness, and attributes of the treatment facility (Table 1). We hypothesized that any differences in treatment outcomes, if observed, would be related to aspects of this contextual variation.

[***Table 1, p.140, near here***]

Participants and sampling

Interview candidates were drawn from a sampling frame of refugee and host community clients who had recently participated in a structured survey interview focused on adherence to HAART (Mendelsohn, Schilperoord, Spiegel, Burton et al., In Preparation; Mendelsohn, Spiegel et al., In Preparation). Participants were purposively sampled with respect to sex, refugee status, and their self-reported HAART adherence over the past month. The target number of participants was 24 in Malaysia and 18 in Kenya. Refugees and sub-optimal adherers were intentionally over-sampled. "Refugees" were defined as individuals claiming a statutory designation as defined by the Refugee Convention and Protocol (UN General Assembly, 28 July 1951, 31 January 1967). Eligible clients were at least 18 years of age, had been on HAART for at least 30 days, and were willing to give informed consent.

Interviews were conducted with 26 refugees and 17 host community clients (N=43). This broke down into 12 refugee and 6 local host participants in Kenya, and 14 refugee and 11 local host participants in Malaysia (Table 2). The median age of the Kenyan sample was 33 years (IQR 30, 41) and 61% were women. In the Malaysian sample, the median age was 34 years (IQR 31, 42)

and 44% were women. The median self-reported adherence score among the interview participants was 86% (IQR 76, 98) in Kenya and 94% (IQR 81, 100) in Malaysia, while the proportions who had achieved viral suppression (defined as <1000 copies/mL) were 17% in Kenya and 68% in Malaysia among the qualitative study participants. Tables 2 and 3 further summarise key characteristics of the participants.

[***Table 2, p.140, and Table 3, p.141-142, near here***]

Case study settings

At the start of the study (April 2010), over 91,985 individuals were registered by UNHCR as refugees and asylum seekers in Malaysia. Most had fled the protracted internecine conflict in Burma. The Malaysian government has not signed the Refugee Convention; however, the Ministry of Health issued a circular in 2006 that permitted refugees to access public health services, including HAART. The study recruited both refugee and host study participants receiving HAART from Sungai Buloh Hospital, the national reference hospital for HIV located on the outskirts of Kuala Lumpur (Malaysia). At the start of the study, there were 315 HIV-positive refugees registered with UNHCR, 171 of whom were listed as on HAART (98% Burmese). The Malaysian host community is composed primarily of Malays, Chinese, and Tamils. For host nationals, the national treatment program fully subsidised first-line treatment and virological monitoring; second-line treatment was partially subsidised. For refugees, the national program fully subsidised first-line fixed-dose treatments but more expensive first and second-line drugs (e.g. efavirenz; lopinavir/ritonavir) and virological monitoring are supported by UNHCR. Expensive first and second-line drugs were collected form an alternative private pharmacy. Financial assistance was provided by UNHCR for travel to the clinic and pharmacy to refugees on a case-by-case basis (similar support is not provided to host nationals).

In Kenya, the study recruited refugee and host community clients accessing services at the "Comprehensive Care Clinic", Kakuma (CCCK), a clinic managed by a non-governmental organisation in Kakuma refugee camp, located in a remote, arid part of Northwestern Kenya. When the study started in February 2011, 446,946 refugees were registered by UNHCR in Kenya as a whole, and the population of Kakuma refugee camp was 82,409. The Kenyan government has signed the Refugee Convention and Protocol and access to first- and second-line HAART is provided by the national program to all clients who meet national clinical eligibility criteria. The local host community is primarily Turkana, a nomadic-pastoralist ethnic group. CD4 counts, nutritional support, and counselling services were routinely provided, but virological monitoring was not available to either group. Prior to the study period, 389 clients had been enrolled since the start of the HAART program in 2004.

Interviews

Data were collected from semi-structured interviews administered by trained interviewers, and facilitated by a topic guide translated into local languages, back-translated into English, and reconciled with the original English versions by two independent translators. Interviewers were trained to probe in-depth when they felt this would yield detailed accounts. Interviews were audio-recorded, lasted between 30 and 120 minutes, and were usually conducted in a language shared by the interviewer and participant. Where this was not possible, a third-party interpreter was used. Interviews were conducted in Kuala Lumpur from July-September 2010 and in Kakuma from February-March 2011.

Analyses

All the interviews were transcribed verbatim, translated into English, and uploaded into NVivo 9.2 for coding. The framework method, a systematic process of sorting and charting data according to key themes, was employed to analyse the data (Ritchie & Spencer, 1994). Between-case comparisons and within-case process-tracing methods that aim to identify causal mechanisms, were used to assist with interpretation (George & Bennett, 2005). Coding began with an initial scheme and novel themes were allowed to emerge from the data. Sub-themes were refined and aggregated into higher-order themes during analyses. In the initial coding scheme, we distinguished themes on the basis of social levels of influence in relation to adherence (macro, meso, micro) to explore links between environment and individual agency. When accounting, participants often evoked barriers to adherence without directly describing an actual adherence lapse or interruption. We therefore also attempted to distinguish between potential threats to adherence as "imagined future possibilities" (Evans, 2007), barriers that were directly linked to reported treatment interruptions, and facilitators of adherence. To this end, we sought to uncover the continuum of threats and barriers, and the countervailing techniques employed by participants.

Ethical approval

Ethical approvals were received from the London School of Hygiene and Tropical Medicine (Approval 5547); the Kenya Medical Research Institute (Approval 1884); and the Malaysian Medical Research and Ethics Committee and Clinical Research Centre (Approval 3275). All participants consented to their anonymous participation, to the audio-recording of their interviews, and to the use of their anonymous quotations in reports. Participants' reported names are pseudonyms. Participants were offered refreshments during the interview and a small cash incentive was provided to offset travel costs and the approximate cost of one meal. Counselling referrals were facilitated upon request.

RESULTS

Analyses of refugee and host community interview accounts (N=43) yielded multiple interacting factors risking or precipitating adherence interruptions, clustering thematically as follows: crossing borders, integration upon arrival, food insecurity, treatment delivery insecurity, stigma and discrimination, economic hardship, social support and resilience.

Crossing borders

Adherence threats were reported in some refugees' experiences of crossing borders. For example, Keren, a Chin refugee who was originally diagnosed with HIV and treated in Burma, eventually sought treatment across the border in India and reported a close call when returning home, before she opted to flee Burma for good.

> "My CD4 was about 200 at that time...I was questioned by the soldiers at the border on my way back home...Since I was carrying a lot of medicines, I told them that I was hospitalized at Lamka [capital of Churachandpur district in Manipur state, India]...When I was asked what sickness I had, I just showed my book because there were many others with me being questioned and I do not want those people to know about me...They asked me how much money I had with me...their senior said there was not enough money and it would not be possible to give [my medications] back. I begged them to give me back the medicines telling them that the medicines might not be that useful for them while if I did not take the medicines I would not be able to live...They...let me go with my medicines bag. They also swore to me that...I would have much more trouble if I went there again." (Keren, refugee, Malaysia, 25)

Similarly, Jeffrey told of a treatment interruption resulting from the crossing of borders in search of asylum.

> "I did not come with medication because I fled, but I tried to run away with an empty bottle of medication that I used before. I did not even manage to come with my treatment record. I think that I stopped for at least one month...when I went to Ethiopia...they allowed me to pick-up my medication from their clinic..." (Jeffrey, refugee, Kenya, 36)

Integration upon arrival

In Malaysia, worry was a pervasive theme in refugee accounts of their early experiences in asylum, especially among refugees who had started HAART prior to their arrival. Integration into the health system occasionally resulted in "close calls" in relation to treatment continuity, but also did not result in any actual reported interruptions.

"They [UNHCR] asked me to go to the hospital and collect my HAART medication, but the hospital had not received any instructions...I had to go to hospital every day, morning and evening and had to argue..." (Khun, refugee, Malaysia, 31)

By contrast, Aye described how, on account of perceived bureaucratic obstacles, she delayed re-engagement with treatment that she had started before displacement.

"...they told me that I had to go to Hospital. To go to Hospital was difficult as I did not have a [UNHCR] identity card then, so I just prolonged the time due to my difficulty and did not go to Hospital. When September/October came I could not take it anymore. I was ill and feeling very, very weak." (Aye, refugee, Malaysia, 33)

Understanding their new treatment "infrastructure" was problematic and caused some refugees to temporarily interrupt their treatment. For example, many participants accessed a portion of their HAART regimen from an alternative pharmacy. For some, this led to confusion and resulted in treatment interruptions.

"One kind of tablet was given to me for two weeks only while the other two were given for one month...when the medicine I was given for two weeks was finished...I did not take it for two [more] weeks." (Maung, refugee, Malaysia, 32)

Food insecurity and hunger

Food insecurity and hunger were identified by many participants as common difficulties often underlying other threats and barriers, and echoed by host nationals most intensively in Kenya. The feeling that HAART required sustenance in order to tolerate the medication, or that it caused an increase in appetite, was typical but most commonly reported among the camp-based participants in Kenya.

"...this medicine is bringing appetite...so I can eat a lot and sometimes if there is no food what are you going to do? If the ration we receive is finished I cannot get power or energy." (Sarah, refugee, Kenya, 31)

For some, food security concerns were not merely threats to adherence but had resulted in a treatment interruption. For example, Leila identified hunger as the main reason why she missed her medications for three days, while hunger galvanised Samson to migrate to Nairobi in search of employment, which eventually led to a depletion in his personal medication stock and a long-term treatment interruption.

"...if your stomach is empty the drug will make you dizzy but if you take the drug with food it is OK. I did not have food." (Leila, refugee, Kenya, 21)

"After I started [HAART] I felt better and I went to Nairobi...when I got a job I did not have any one here to send me [medications] and I quit for one year. We did not have enough food here and we cannot get money." (Samson, refugee, Kenya, 33)

Concerns relating to food insecurity were also typical among host community participants in the Kenyan setting. During the interview of a participant who had been lost to follow-up, he initially indicated that he failed to return to the clinic on account of having lost his clinic card. Later in the interview, however, his account suggested that hunger had informed his decision to halt treatment.

"It is hunger, hunger [is the reason]. When you take this drug you cannot even go to work...because I feel like falling sometimes. When I have eaten nothing...you stop [HAART] only to stop for a long period." (Peter, host, Kenya, 30)

Treatment delivery insecurity

Refugees in both settings experienced a number of health system threats to adherence linked to disrupted provider networks and pharmacy stock-outs. For example, while living in "protection" (refugee housing with augmented security), one participant became dependent on a provider who subsequently left. This abrupt change in provider arrangements was the source of a threat to adherence.

"When Sid [pseudonym for doctor who no longer works at clinic] was at the clinic, I was told to stay there [in protection]...they will go and pick me up, take blood and take me back, but when Sid left all things became problems." (Christine, refugee, Kenya, 35)

Similarly, the interaction of a physical disability with the departure of a treatment supporter created a barrier to treatment reported by a refugee participant in Kakuma.

"There is no medicine that time because the person who used to collect for me...went to Nairobi." (John, physically-disabled refugee, Kenya, 47)

Meanwhile, limited availability of medication stocks at the pharmacy forced some clients to disrupt their refill schedule. For some, this led to treatment interruptions.

"...sometimes the HAART I am taking will not be available or maybe the types of medicines will be changed...I will be given for a week or three days, and I will be told to come back after three days to confirm if [my] HAART is available... [or sometimes] they will give me another type in order to wait [for] those which were finished..." (Sarah, refugee, Kenya, 31)

Though not commonly reported, we also found evidence of treatment interruptions brought about by tensions between traditional and biomedical approaches to treatment. For example, one refugee described how he ceased HAART on the advice of a group that claimed to possess a cure for HIV.

> "People came with other drugs and said that those drugs can heal HIV/AIDS...when I heard that people are being healed I stopped the treatment which I took from the clinic...they told us to stop the treatment that we have received from CCCK [clinic]..." (Jeffrey, refugee, Kenya, 36)

Stigma and discrimination

Refugees in both settings faced stigma and discrimination of different kinds. In Malaysia, refugees described an interplay of threats and barriers to adherence that were linked to arrest or fear of arrest on their journeys between their home and the clinic or in search of employment to help offset treatment-related costs.

> "Even with the [refugee] card, I was arrested on my way back from Hospital...I showed them [police] my card but to no avail. They took 30 Ringgit...There is no guarantee in our life, anything can happen. [He continues] If I go to the hospital for a check up, I have to pay administrative costs every time. I will have to earn the costs first. Work is available but I have to be careful where I am going." (Saw, refugee, Malaysia, 44)

In Kenya, stigma and discrimination typically originated from within participants' own families and ethnic communities constituting threats for some, but insurmountable obstacles for others, especially in the camp setting.

> "...when my family found out that I am HIV-positive, they chased me [out] and I was not able to take my drugs...I faced problems with my family, that is the reason I stopped taking medication, because of stress." (Leila, refugee, Kenya, 21)

> "...if [you] go to fetch water maybe you will quarrel with somebody... I am getting a lot of abusive words in the community, so with all of that you forget to take your medicine." (Sarah, refugee, Kenya, 31)

Stigma and discrimination was often reported in the context of an interplay of systemic factors that also included food insecurity, especially in the camp setting. For example, Imara described an array of challenges but it was ultimately an armed raid on her home that forced her to abandon her medication supply.

> "The biggest challenge that I am going through is the distance from my home to where I am supposed to take my HAART...footing up to that place, sleeping two

days on the way, and lack of food at home, insecurity from my place of stay...sometimes raids occur where you have to run away from home and the drugs remain back [at home]..." (Imara, host, Kenya, 18)

Economic hardship

Both refugees and host community participants reported economic hardships. Efforts at finding employment were often derailed due to a prevailing fear of arrest in Malaysia, while others lamented their inability to afford basics like a watch to act as an adherence reminder.

"We receive financial aid [from the UNHCR]...We have to struggle to survive. When my son arrived, he worked with friends, but as there were many arrests, he stopped working." (Shwin, refugee, Malaysia, 39)

"...It would be a bit easier [to remember dosing time] if I had an alarm. Now that I do not have a small watch and do not know how to buy one, it becomes difficult." (Hajima, refugee, Malaysia, 31)

Social support

Participants often linked improved adherence and better relations with friends and family to the visible benefits of HAART. Perseverance was often linked to the presence of children in the family.

"... my kids are young and if I died, what would the kids do? If the mother has it [HIV] and not the father, it wouldn't be so bad, but when both parents have it then if they pass away, who will look after the kids?" (Hajima, refugee, Malaysia, 31)

Moreover, some participants who had disclosed their HIV status to their partners or their community reported benefits in the form of moral or financial support and feelings of self-empowerment.

"When others know your status you can make consequential decisions as to the kind of life you would like to lead." (Samson, refugee, Kenya, 33)

In turn, improvement in health resulting from good adherence acted as a prominent facilitator of continued treatment engagement across all groups.

"Just imagine when my CD4 went down from 500 to 11. I was really very sad about this...At least due to my medication my health has improved. I made a determined effort to take my medication regularly." (Shwin, refugee, Malaysia, 39)

Personal resilience

Personal resilience and problem-solving skills were commonly mentioned in both settings and consisted of a range of "self-help" techniques including "strong will", contingency planning,

and the use of medication reminders. Reminders varied widely and consisted of techniques rooted in individual and social experience such as phone alarms, linking treatment to regular religious activities, and the use of treatment supporters.

> "He [doctor] asked me to take Combivir with another medicine which caused my body to break out in a rash and get itchy and swollen...I was feeling dizzy and was burning inside...but I decided that I would take the medication whether I lived or died..." (Mya Mya, refugee, Malaysia, 29)

> "I never missed or defaulted...When my medication was half way (15 days) I used to start sourcing for medicines... (Khun, refugee, Malaysia, 31)

> "...what reminds me of my medication time is the morning prayer just before day break. I wake up, pray, and then take my medicine... (Aziza, refugee, Kenya, 46)

Individuals' resilience was also demonstrated through strategies of coping to navigate perceived systemic and social threats to adherence. For instance, in navigating perceived social stigma some participants strategically concealed their HIV status while other participants reported drawing on their community networks for support. These support networks helped participants obviate threats and barriers.

> "Always in the morning they come they gave me tea and mandazi [donuts]...they tell me to take this medicine always...And one day another mother came to tell me we are here [in the refugee camp] 20 years, why are you giving up?" (Samson, refugee, Kenya, 33)

> "There was a neighbour who had been in Malaysia about 3 to 4 years. We got a lot of help from them since we arrived. They looked for a job for us and took us to the work place.....Then three of us went to the hospital." (Keren, refugee, Malaysia, 25)

Discussion

Recent estimates indicated that at the end of 2010, 6.6 million people or 47% of those eligible, were receiving HAART in low- and middle income-countries (UNAIDS, 2011). These numbers on HAART are encouraging in a context of global efforts to maximise "universal access" but run the risk of obscuring the diversity of treatment experiences in different social settings. Noting the dearth of qualitative research describing such experiences especially among refugees in asylum settings, we sought to describe the social and environmental factors linked to treatment adherence in refugee and host community interviews. We focused specifically on

adherence threats and barriers and the limits they placed on agency, as well as on factors identified by participants as enabling adherence in spite of constraints.

Initially, we set out to explore how differences in adherence outcome might be attributable to variation in the two settings in relation to national context, remoteness, or treatment delivery systems. We envisaged that camp-based refugees would be easier to follow-up within the confines of the camp environment, and might therefore have better treatment outcomes. However, the camp-based population in Kenya did considerably worse than their urban counterparts in Malaysia in quantitative assessments. Following Evans (2007), highly structured environments can be associated with reduced capacity for individual agency, wherein individuals' "bounded agency" describes situations where experience is *influenced but not entirely determined* by social environments. Our findings supported this framing by uncovering extensive accounts of social and environmental threats and barriers, while revealing how participants used countervailing strategies towards facilitating their treatment in spite of these challenges. Resilience occurs when adverse outcomes are mitigated by effective personal coping (Bonanno & Mancini, 2008). In Kenya, however, it appeared that social and environmental factors such as food insecurity, treatment delivery insecurity, stigma and discrimination hindered the maintenance of adherence over time, revealing how an interplay among various systemic and social factors can lead to adherence lapses or interruptions.

Refugee status, and linked processes such as border crossings and integration to the treatment system upon arrival in asylum were factors of concern in both settings. These incidents, however, were experienced as threats more often than as barriers to treatment continuity. Although not emerging directly from participant accounts, differences between the Kenyan and Malaysian national contexts were important insofar as they helped to condition the systemic factors experienced by participants and their ability to overcome them. Moreover, many threats and barriers experienced by refugees in either setting were also shared by host communities, highlighting the importance of local context for adherence.

Importantly, camp-based participants in Kenya reported intensive food insecurity. In previous studies, food insecurity had adverse effects on adherence (Franke et al., 2011), morbidity, patterns of healthcare utilisation (Weiser et al., 2012), and virological outcomes, lowering them by as much as 77% (Weiser et al., 2009). Previous studies have identified a number of mechanisms linking food insecurity to non-adherence or treatment interruptions (Weiser et al., 2010). The links between hunger, food insecurity, and adherence suggested that this challenge has the potential to contribute to frequent and/or longer duration treatment interruptions over time.

The disruptions in provider support networks reported in the camp clinic in Kenya echoed findings from South Africa (Nachega et al., 2006) and conflict-affected Uganda (Wilhelm-Solomon, 2009). In the present study, reported disruptions of support networks were usually related to HIV-related stigma and discrimination or the departure of treatment supporters, as opposed to disruptions in personal support networks resulting from original episodes of forced displacement (UNHCR & Southern African HIV Clinicians Society, 2007). Refugees in both settings elaborated how their social support networks were important for assisting them with medication collection and daily adherence, but were sometimes contingent on the visible and public success of treatment. However, consistent with the deep cultural embeddedness of HIV-related stigma in sub-Saharan Africa (Mbonu, van den Borne, & De Vries, 2009) and Kenya in particular (Izugbara & Wekesa, 2011), the stigma and abuse experienced by many participants in the camp setting was intensive, often overwhelming positive support networks and individual resilience.

Refugees reported "close calls" in relation to their adherence during and immediately after cross-border displacement. However, there were few reports linking these experiences to actual treatment interruptions, suggesting that many participants remained resilient during these periods of disruption. In Malaysia, refugees faced the threat of confrontation with law enforcement, especially during their lengthy transit times to the clinic. Discrimination was therefore situated within these overlapping landscapes of health care and law enforcement, and conditioned on the contested role of immigration in society. Given the harmful consequences of intentional treatment holidays or unstructured interruptions (Li et al., 2005; Oyugi et al., 2007; Parienti et al., 2004), awareness of the dynamics of cross-border displacement, integration into treatment systems and local travel away from treatment centres, are critical for managing treatment for newly arrived refugees, or for assisting refugee and host community clients with contingency arrangements.

Validity, relevance, and future research

One limitation of this study was the need for translation of the interviews. To minimize this, experienced translators were used and regularly debriefings were conducted with interviewers in order to gain their interpretations of participant accounts independent from translations. Furthermore, we experienced challenges in fully interviewing until saturation given the high levels of ethnic diversity in the refugee and local populations. Nonetheless, purposive sampling attempted to represent as many members of each community as possible.

The relevance of this work was enhanced by producing new knowledge through an approach that leveraged within and between-case analyses of two distinct groups (refugees and host communities), in two common refugee environments (urban and camp), and in two different

geographical locations (East Africa and Southeast Asia). Given the dearth of qualitative research focusing on how refugee experiences shape treatment adherence, further study is needed to delineate the relationships between the processes of refugee experience and systems of HIV treatment delivery.

Conclusion

Prior to this work, no previous qualitative data of refugee experiences on HAART were available. Rather than envisaging adherence as primarily a product of individual decision-making, we considered it in relation to a "bounded agency" where individual behaviours are influenced but not entirely determined by social context. We found that, while both refugee and host community participants faced systemic threats to adherence, most were able to navigate these obstacles through resilient coping strategies. We also outlined the constraining effects of settings upon agency, which helped to explain variation in treatment outcome. We therefore argue that relative differences in the success of individual efforts to transcend social and environmental threats and barriers to adherence were important determinants of adherence and treatment success in the study settings. These factors in the Kenyan refugee camp setting proved to be more extensive and difficult to overcome and ought to be urgently addressed to ensure that the clinical and public health benefits of HAART are realised. Overall, interventions are needed that will reduce systemic barriers linked to food insecurity, treatment delivery insecurity, stigma and discrimination, treatment discontinuity for refugees upon their arrival in asylum, and to bolster personal resilience through treatment support for high risk individuals, such as those experiencing intensive stigma and discrimination. In scaling-up HAART or transitioning to a treatment-as-prevention strategy in challenging settings, social and environmental threats and barriers should be critically assessed in all programmatic stages including planning, initiation, and maintenance.

REFERENCES

Blankenship, K. M., Bray, S. J., & Merson, M. H. (2000). Structural interventions in public health. *AIDS, 14*, S11-S21.

Bonanno, G. A., & Mancini, A. D. (2008). The human capacity to thrive in the face of potential trauma. *Pediatrics, 121*(2), 369-375.

Castro, A. (2005). Adherence to antiretroviral therapy: merging the clinical and social course of AIDS. *PLoS Medicine, 2*(12), e338.

Evans, K. (2007). Concepts of bounded agency in education, work, and the personal lives of young adults. *International Journal of Psychology, 42*(2), 85-93.

Ewart, C. (1991). Social-action theory for a public health psychology. *American Psychologist, 46*(9), 931-946.

Fisher, J. D., Fisher, W. A., Amico, K. R., & Harman, J. J. (2006). An information-motivation-behavioral skills model of adherence to antiretroviral therapy. *Health Psychology, 25*(4), 462-473.

Franke, M. F., Murray, M. B., Munoz, M., Hernandez-Diaz, S., Sebastian, J. L., Atwood, S., et al. (2011). Food insufficiency is a risk factor for suboptimal antiretroviral therapy adherence among HIV-infected adults in urban Peru. *AIDS and Behavior, 15*(7), 1483-1489.

Garang, P. G., Odoi, R. A., & Kalyango, J. N. (2009). Adherence to antiretroviral therapy in conflict areas: a study among patients receiving treatment from Lacor Hospital, Uganda. *AIDS Patient Care STDS, 23*(9), 743-747.

George, A. L., & Bennett, A. (2005). *Case Studies and Theory Development in the Social Sciences*. London: MIT Press.

Gupta, G. R., Parkhurst, J. O., Ogden, J. A., Aggleton, P., & Mahal, A. (2008). Structural approaches to HIV prevention. *Lancet, 372*(9640), 764-775.

Izugbara, C. O., & Wekesa, E. (2011). Beliefs and practices about antiretroviral medication: a study of poor urban Kenyans living with HIV/AIDS. *Sociology of Health and Illness, 33*(6), 869-883.

Krusi, A., Wood, E., Montaner, J., & Kerr, T. (2010). Social and structural determinants of HAART access and adherence among injection drug users. *International Journal of Drug Policy, 21*(1), 4-9.

Li, X. H., Margolick, J. B., Conover, C. S., Badri, S., Riddler, S. A., Witt, M. D., et al. (2005). Interruption and discontinuation of highly active antiretroviral therapy in the multicenter AIDS cohort study. *Journal of Acquired Immune Deficiency Syndromes, 38*(3), 320-328.

Lima, V. D., Harrigan, R., Murray, M., Moore, D. M., Wood, E., Hogg, R. S., et al. (2008). Differential impact of adherence on long-term treatment response among naive HIV-infected individuals. *AIDS, 22*(17), 2371-2380.

Mbonu, N. C., van den Borne, B., & De Vries, N. K. (2009). Stigma of people with HIV/AIDS in Sub-Saharan Africa: a literature review. *Journal of Tropical Medicine, 2009*, 145891.

Mendelsohn, J. B., Schilperoord, M., Spiegel, P., Burton, J. W., Okonji, J. A., Muhindo, B., et al. (In Preparation). Poor treatment outcomes among both refugees and host community accessing Highly Active Antiretroviral Therapy (HAART) from Kakuma refugee camp in Northwestern Kenya.

Mendelsohn, J. B., Schilperoord, M., Spiegel, P., & Ross, D. A. (Submitted). Adherence to antiretroviral therapy and treatment outcomes in conflict-affected and forcibly displaced populations: a systematic review. *Conflict and Health*.

Mendelsohn, J. B., Spiegel, P., Schilperoord, M., Balasundaram, S., Radhakrishnan, A., Lee, C., et al. (In Preparation). Good adherence and treatment outcomes in refugee and host communities on highly active antiretroviral therapy in urban Kuala Lumpur, Malaysia.

Nachega, J. B., Knowlton, A. R., Deluca, A., Schoeman, J. H., Watkinson, L., Efron, A., et al. (2006). Treatment supporter to improve adherence to antiretroviral therapy in HIV-infected South African adults - A qualitative study. *Journal of Acquired Immune Deficiency Syndromes, 43*, S127-S133.

Olupot-Olupot, P., Katawera, A., Cooper, C., Small, W., Anema, A., & Mills, E. (2008). Adherence to antiretroviral therapy among a conflict-affected population in Northeastern Uganda: A qualitative study. *AIDS, 22*(14), 1882-1884.

Oyugi, J. H., Byakika-Tusiime, J., Ragland, K., Laeyendecker, O., Mugerwa, R., Kityo, C., et al. (2007). Treatment interruptions predict resistance in HIV-positive individuals purchasing fixed-dose combination antiretroviral therapy in Kampala, Uganda. *AIDS, 21*, 965-971.

Parienti, J. J., Massari, V., Descamps, D., Vabret, A., Bouvet, E., Larouze, B., et al. (2004). Predictors of virologic failure and resistance in HIV-Infected patients treated with nevirapineor efavirenz-based antiretroviral therapy. *Clinical Infectious Diseases, 38*(9), 1311-1316.

Pope, C., & Mays, N. (1995). Reaching the parts other methods cannot reach: an introduction to qualitative methods in health and health services research. *BMJ, 311*(6996), 42-45.

Rhodes, T. (2002). The 'risk environment': a framework for understanding and reducing drug-related harm. *International Journal of Drug Policy, 13*(3), 85-94.

Rhodes, T., Singer, M., Bourgois, P., Friedman, S. R., & Strathdee, S. A. (2005). The social structural production of HIV risk among injecting drug users. *Social Science and Medicine, 61*(5), 1026-1044.

Ritchie, J., & Spencer, L. (1994). Qualitative data analysis for applied policy research. In A. Bryman & R. G. Burgess. (Eds.), *Analyzing Qualitative Data* (pp. 173-194). London: Routledge.

The Sphere Project. (2004). *The Sphere Handbook: Humanitarian Charter and Minimum Standards in Humanitarian Response* (2 ed.). Geneva, Switzerland. Retrieved 10 September 2012 from http://ocw.jhsph.edu/courses/refugeehealthcare/PDFs/SphereProjectHandbook.pdf.

The Sphere Project. (2011). *The Sphere Handbook: Humanitarian Charter and Minimum Standards in Humanitarian Response* (3 ed.). Rugby, UK. Retrieved 10 September 2012 from http://www.spherehandbook.org/

UN General Assembly. (28 July 1951, Entry into force 22 April 1954, in accordance with article 43). *Convention relating to the Status of Refugees*. Retrieved 26 June 2012, from http://www.unhcr.org/refworld/docid/3be01b964.html

UN General Assembly. (31 January 1967, Entry into force 4 Oct 1967). *Protocol Relating to the Status of Refugees*. Retrieved 13 March 2012, from http://www.unhcr.org/refworld/docid/3ae6b3ae4.html

UNAIDS. (2011). *UNAIDS World AIDS Day Report 2011*. Geneva.

UNHCR, & Southern African HIV Clinicians Society. (2007). *Clinical Guidelines for Antiretroviral Therapy Management for Displaced Populations - Southern Africa*. Geneva: UNHCR.

Vervoort, S. C., Borleffs, J. C., Hoepelman, A. I., & Grypdonck, M. H. (2007). Adherence in antiretroviral therapy: a review of qualitative studies. *AIDS, 21*(3), 271-281.

Weinstein, N. D. (1993). Testing four competing theories of health-protective behavior. *Health Psychology, 12*(4), 324-333.

Weiser, S. D., Frongillo, E. A., Ragland, K., Hogg, R. S., Riley, E. D., & Bangsberg, D. R. (2009). Food insecurity is associated with incomplete HIV RNA suppression among homeless and marginally housed HIV-infected individuals in San Francisco. *Journal of General Internal Medicine, 24*(1), 14-20.

Weiser, S. D., Tsai, A. C., Gupta, R., Frongillo, E. A., Kawuma, A., Senkungu, J., et al. (2012). Food insecurity is associated with morbidity and patterns of healthcare utilization among HIV-infected individuals in a resource-poor setting. *AIDS, 26*(1), 67-75.

Weiser, S. D., Tuller, D. M., Frongillo, E. A., Senkungu, J., Mukiibi, N., & Bangsberg, D. R. (2010). Food insecurity as a barrier to sustained antiretroviral therapy adherence in Uganda. *PLoS One, 5*(4), e10340.

Wilhelm-Solomon, M. (2009). Social networks and sustainable antiretroviral provision to displaced communities in northern Uganda. *Tropical Medicine and International Health, 14*(Suppl2), 35-36.

Wolfe, D., Carrieri, M. P., & Shepard, D. (2010). Treatment and care for injecting drug users with HIV infection: a review of barriers and ways forward. *Lancet, 376*(9738), 355-366.

TABLES AND FIGURES

Table 1: Case characteristics

Characteristic	Malaysia	Kenya
% viral suppression <1000 copies/mL)†	91%	11%
Setting	Urban	Remote (refugee camp)
Payment for first-line HAART	National program	National program
Payment for second-line HAART	Mixed (national program, client, NGOs)	Mixed (national program, UNHCR, NGOs)
Cost of treatment to client	Free	Free
Most common HAART regimen†	AZT+ 3TC + NVP BID (63%)	AZT + 3TC + EFV BID (36%)
Routine laboratory monitoring	Immunological + Virological	Immunological
Clinic implementer	Ministry of Health	Non-governmental organisation
Refugee Convention and Protocol	Not signed	Signed and ratified
Communities accessing clinical services	Refugees and host community	Refugees and host community
% travelling ≥1 hour to the clinic†	66%	80%
Ethnic Diversity	Highly varied (>6 groups)	Highly varied (>6 groups)

†Figures derived from full surveys of 159 adults in Kenya and 301 adults in Malaysia (Mendelsohn, Schilperoord, Spiegel, Burton et al., In Preparation; Mendelsohn, Spiegel et al., In Preparation)
AZT=zidovudine; 3TC=lamivudine; NVP=nevirapine; EFV=efavirenz

Table 2: Summary characteristics of refugee and host community participants

	Malaysia			Kenya		
Factor	**Refugee**	**Host**	**Total**	**Refugee**	**Host**	**Total**
Total, n (%)	14 (56)	11 (44)	25 (100)	12 (67)	6 (33)	18 (100)
Women, n (%)	6/14 (43)	5/11 (46)	11/25 (44)	8 (73)	3 (50)	11/18 (61)
Age in years, median (IQR)	33 (31, 41)	38 (31, 47)	34 (31, 42)	34 (30, 43)	32 (30, 34)	33 (30, 41)
Unemployed, n (%)	9/14 (64)	3/11 (27)	12/25 (48)	10/12 (83)	4/5 (80)	14/17 (82)
Married/relationship, n (%)	8/14 (57)	4/11 (36)	12/25 (48)	3/5 (60)	4/12 (33)	7/17 (41)
Self-reported adherence, median % (IQR)	90 (81, 100)	94 (79, 100)	94 (81, 100)	91 (83, 99)	76 (61, 89)	86 (76, 98)
Pharmacy refill adherence, median % (IQR)	100 (93, 100)	100 (100, 100)	100 (96, 100)	100 (87, 100)	92 (79, 92)	94 (83, 100)
Viral load, (% suppressed, <1000 copies/mL)	9/14 (64)	8/11 (73)	17/25 (68)	2/12 (17)	1/5 (20)	3/17 (17)
Most recent routine CD4, median cells/uL (IQR)	304 (135, 423)	337 (190, 436)	325 (183, 430)	232 (141, 480)	309 (290, 399)	290 (170, 471)
Time on HAART, median weeks (IQR)	69 (41, 139)	155 (67, 298)	79 (66, 155)	140 (27, 256)	225 (32, 269)	192 (29, 192)
Time in host country, median weeks (IQR)	191 (111, 374)	NA	NA	273 (58, 510)	NA	NA
Time since UNHCR registration, median weeks (IQR)	102 (62, 165)	NA	NA	273 (56, 482)	NA	NA

Table 3: Detailed individual participant characteristics

Setting	Pseudonym	Refugee/ Host	Age	Sex	Country of birth	Ethnicity	Time on HAART (weeks)	Study viral load (copies/mL)	Most recent CD4s (chronological from earliest, cells/μL)	Adherence to pharmacy refills (max 24 months, %)	Self-reported adherence (past month, %)
Kenya	Aziza	Refugee	46	Female	Somalia	Somali Bantu	31	61,400	26	100	54
Kenya	John	Refugee	47	Male	Sudan	Shilluk	451	213,000	547	79	85
Kenya	Aisha†	Refugee	18	Female	Ethiopia	Oromo	9	7,480	133	100	95
Kenya	Sarah	Refugee	31	Female	Sudan	Nuer	257	561	121;154;232	100	98
Kenya	Leila	Refugee	21	Female	Somalia	Somali	192	19,700	415	100	76
Kenya	Ayana	Refugee	43	Female	Somalia	Somali Bantu	87	2,600	149	94	99
Kenya	Louise	Refugee	43	Female	Burundi	Tutsi	29	8,890	NA	88	100
Kenya	Samson	Refugee	33	Male	Eritrea	Asmara	250	224,000	NA	83	99
Kenya	Ruth	Refugee	33	Female	Rwanda	Tutsi	12	3,330	NA	21	31
Kenya	Jeffrey	Refugee	36	Male	Rwanda	Hutu	325	19,900	NA	100	85
Kenya	Innocent	Refugee	26	Male	DRC	Bembe	21	3,210	NA	100	100
Kenya	Christine	Refugee	35	Female	Sudan	Bari	255	806	433;545	100	86
Kenya	David	Host	60	Male	Kenya	Turkana	269	1,940	409;309	92	61
Kenya	Peter	Host	30	Male	Kenya	Turkana	LTFU††	NA	NA	NA	NA
Kenya	Chris	Host	34	Male	Kenya	Turkana	12	2,120,000	NA	100	54
Kenya	Liz	Host	31	Female	Kenya	Turkana	225	8,190	371;262;270	92	89
Kenya	Imara	Host	18	Female	Kenya	Turkana	32	<400	NA	40	90
Kenya	Samara	Host	33	Female	Kenya	Turkana	316	13,600	489	79	76
Malaysia	Min	Refugee	44	Male	Burma	Arakan	139	<40	509;546	100	81
Malaysia	Aung	Refugee	19	Male	Burma	Kachin	67	<40	279;423	100	99
Malaysia	Aye	Refugee	33	Male	Burma	Chin	4	1,410	NA	100	83
Malaysia	Saw	Refugee	44	Male	Burma	Arakan	64	57	482;407	92	100
Malaysia	Frankie	Refugee	41	Male	Burma	Rohingya	134	205,000	640;101	60	0
Malaysia	Khun	Refugee	31	Male	Burma	Chin	180	941,000	83;37	100	100
Malaysia	Suu	Refugee	41	Female	Burma	Chin	41	56	365;304	NA	94
Malaysia	Maung	Refugee	32	Male	Burma	Chin	22	260	135	100	50
Malaysia	Keren	Refugee	25	Female	Burma	Chin	145	8170	388;423	93	100
Malaysia	Kyi	Refugee	33	Female	Burma	Kachin	107	<40	280	100	85

Table 3: Detailed individual participant characteristics

Setting	Pseudonym	Refugee/ Host	Age	Sex	Country of birth	Ethnicity	Time on HAART (weeks)	Study viral load (copies/mL)	Most recent CD4s (chronological from earliest, cells/μL)	Adherence to pharmacy refills (max 24 months, %)	Self-reported adherence (past month, %)
Malaysia	Saing	Refugee	34	Male	Burma	Chin	70	4980	201	100	75
Malaysia	Shwin	Refugee	39	Female	Burma	Burman	35	<40	74	60	100
Malaysia	Mya Mya	Refugee	29	Female	Burma	Chin	150	<40	211;341	100	97
Malaysia	Hajima	Refugee	31	Female	Burma	Burman	66	<40	573	100	86
Malaysia	Suresh	Host	49	Male	Malaysia	Tamil	313	<40	161;183	100	95
Malaysia	Selvi	Host	46	Female	Malaysia	Tamil	298	150,000	235;196	67	0
Malaysia	Nurul	Host	30	Female	Indonesia	Malay	173	<40	431	100	79
Malaysia	Denise	Host	38	Female	Malaysia	Chinese	66	<40	491;525	100	94
Malaysia	Mohammed	Host	42	Male	Malaysia	Malay	238	<40	58;135	100	69
Malaysia	Henry	Host	31	Male	Malaysia	Chinese	67	143,000	183	100	90
Malaysia	Ponmani	Host	47	Female	Malaysia	Tamil	473	<40	5541;563	100	100
Malaysia	Ganesh	Host	40	Male	Malaysia	Tamil	79	<40	204;313	100	100
Malaysia	Mimi	Host	33	Female	Malaysia	Malay	12	<40	265;337	100	100
Malaysia	Lawrence	Host	28	Male	Malaysia	Chinese	155	<40	630;440	100	82
Malaysia	Abdul Haqq	Host	28	Male	Malaysia	Malay	71	7,740	340;430	93	100

†Participant self-defined as an asylum-seeker, indicating they had registered with UNHCR but had yet to undergo a Refugee Status Determination. She was included in the study

††LTFU=lost to follow-up

SUPPLEMENTARY MATERIAL

Figure i and Table i highlights the range of thematic overlap among refugee and host community participants and between participants in the different field settings based on initial coding.

Table i: Sub-thematic congruency between clients groups and settings (Legend for Figure 2)

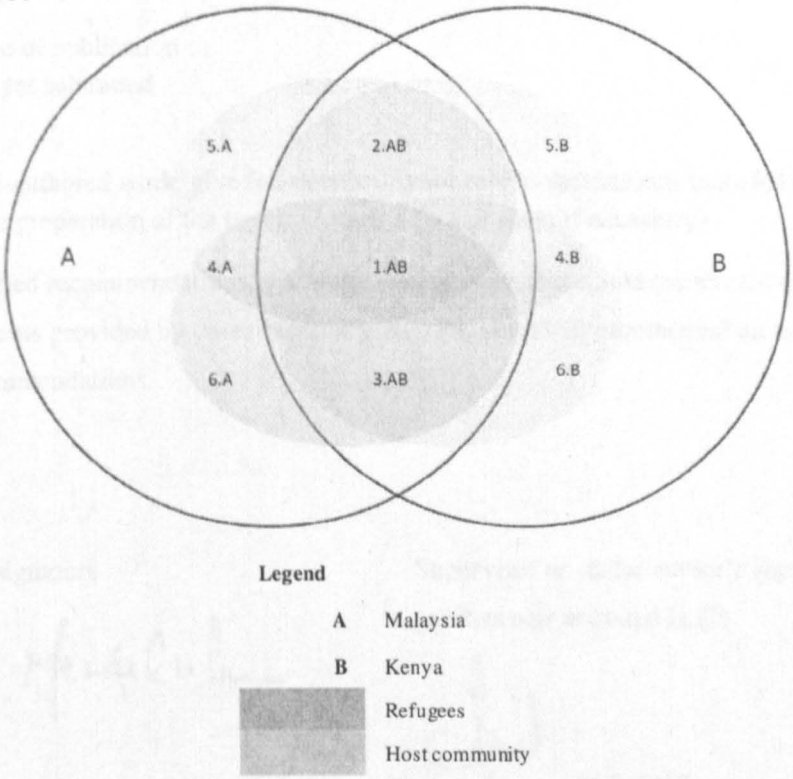
Designator in Figure 2	Thematic overlap	Barriers	Threats	Facilitators
1AB	Themes shared by all groups	Food insecurity/hunger; lack of support/disrupted support network; lack of reminders	Distance to clinic/travel costs; food insecurity/hunger; symptoms/side-effects	Positive provider relations; serostatus disclosure/concealment; social support; avoidance of poor health; good health/improvement of health; hope and optimism; planned integration of HAART into daily schedule; resilient coping strategies†
2AB	Themes shared by refugees in A and B	Pharmacy error/stock-out; cross-border displacement; lack of employment/financial hardship; psychological distress; disrupted dosing schedules (e.g. during holidays or work); substance use; side-effects	Stigma/discrimination/abuse; difficulty accessing health services; pharmacy stock-outs; family/marriage duties and tensions; employment/financial hardships; lack of support; planned travel; hiding HIV status; substance use; denial of HIV status; psychological distress; personal dosing management	Food security/eating well; reminders
3AB	Themes shared by host communities in A and B	Distance to clinic/travel costs; family /childcare duties; travel within country; traditional lifestyle/alternative therapies; privacy/hiding of HIV status		Absence of HAART side-effects
4A	Themes shared by refugees and host community in A	Prescription sharing; lack of employment/financial hardship; psychological distress; disrupted dosing schedules (e.g. during holidays or work); lack of faith in HAART; privacy/hiding of HIV status; regimen confusion; pill burden; side-effects	Stigma/discrimination/abuse; difficulty accessing health services; family/marriage duties and tensions; employment/financial hardships; living arrangements; hiding HIV status; substance use; loss of hope/uncertainty about future; personal dosing management; religion/superstition	Assisted administration of HAART; knowledge; obligation; reminders; food security/eating well
4B	Themes shared by refugees and host community in B	Family/childcare duties; travel within country; traditional lifestyle/alternative therapies	Lack of support	Absence of HAART side-effects
5A	Themes unique to refugees in A	Arrest or detention ; Dissatisfaction with provider; renewal or receipt of refugee document	Fear of arrest/security issues; cross-border displacement; fear of lifelong treatment; lack of HIV/HAART knowledge; lack of reminder device	Back-up sources of HAART; rapid pathway to care on arrival in asylum
5B	Themes unique to refugees in B	Stigma/discrimination/abuse		Normalisation of HIV in the community; employment/finances; luck
6A	Themes unique to	HAART stopped by physician; forgetful; feel healthy		Normalisation of HIV in the community; employment/finances; role

Table i: Sub-thematic congruency between clients groups and settings (Legend for Figure 2)

Designator in Figure 2	Thematic overlap	Barriers	Threats	Facilitators
	hosts in A			model for others
6B	Themes unique to hosts in B	Clinic transfer; security to clinic		

†including isolation, avoidance, positive philosophies, personal shrines, religion and prayer, education, determination, problem solving, positive affect, on account of children, overcoming language difficulty, overcoming symptoms/side-effects, acceptance of condition, self-reliance, care for others

Figure i: Overlapping thematic codes ("thematic congruency") by group and setting



Cover sheet for each 'research paper' included in a research thesis

PAPER FIVE: REFUGEES, ANTIRETROVIRALS, AND EQUITY: THE PUBLIC HEALTH AND HUMAN RIGHTS ARGUMENTS

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PAPER FIVE

REFUGEES, ANTIRETROVIRALS, AND EQUITY: THE PUBLIC HEALTH AND HUMAN RIGHTS ARGUMENTS

Brief title

Refugees, antiretrovirals, and equity

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Dear Editor:

We are pleased to submit our manuscript entitled: "Refugees, antiretrovirals, and equity: the public health and human rights arguments and evidence from recent studies."

We believe that this work is germane to your Policy Forum section for three reasons:

- We outline a debate regarding provision of treatment for a key vulnerable group (forcibly displaced persons). Discussion of this group is currently under-represented in the health science literature.
- We issue a proposal and recommendations on the basis of recently published, controversial findings, including extremely worrying viral outcomes in one setting.
- The proposal is novel and not published elsewhere.

We are grateful for your consideration and hopeful that this piece can find a place in your journal.

Sincerely,

Joshua Mendelsohn (on behalf of co-authors)

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COMPETING INTERESTS

The authors declare that they have no competing interests.

ABBREVIATIONS

ART: antiretroviral therapy; CI: confidence interval; HAART: highly active antiretroviral therapy; HIV: human immune deficiency virus; HTC: HIV testing and counselling; IDP: internally-displaced person; OR: odds ratio; OR_{adj}: adjusted odds ratio; PMTCT: prevention of mother-to-child transmission; UNHCR: United Nations High Commissioner for Refugees

AUTHOR CONTRIBUTIONS

JBM, MS, PS, and DAR developed the idea for the paper, interpreted findings, and drafted recommendations. JBM wrote the first manuscript. MS, NC, PS, and DAR commented on the manuscript. All authors read, commented on, and approved the final manuscript (to be confirmed).

BOX: SUMMARY POINTS

- Refugees and host communities achieve similar outcomes where services are equitable
- Acceptable outcomes are achievable in a range of settings serving refugees and local host communities
- Triangulating multiple indicators for routine adherence monitoring will help improve monitoring and treatment outcomes in these groups
- Future work among refugees and local host communities should focus on strengthening adherence monitoring and implementing low-cost, evidence-based support interventions

BACKGROUND

Desperate to secure antiretroviral therapy (ART) that she could not access in her native Chin State, Burma, Ning (alias) and her husband crossed the border to Manipur State, India, and travelled onwards in search of medicine. After finding a clinic willing to provide her with treatment and seeing her husband detained by police, she set off for home only to have her ARTs confiscated by officials at the India-Burma border. After borrowing bribe money from a local merchant, Ning successfully pleaded with the officials to return her medication, but was warned never to return. Unable to afford ARTs in Burma, she later became one of 10.6 million global refugees who reside in asylum countries [1]. ARTs can achieve HIV viral suppression provided optimal levels of adherence (≥95% of doses taken on time) can be sustained long-term [2]. Globally, less than two-thirds of ART clients report ≥90% adherence [3]. Refugees share adherence barriers in common with other groups, while facing the threat of additional barriers unique to their social and environmental contexts [4,5,6]. This policy forum describes recent issues in relation to HIV treatment and care for refugees and makes recommendations for ensuring that refugees and their host community counterparts initiate treatment in a timely way and sustain optimal adherence and treatment outcomes.

Refugees, health care, and the policy environment

The humanitarian and public health communities have debated the merits of ART provision among conflict-affected populations, echoing earlier discussions on the wisdom of rapid scale-up in resource-limited settings [7,8]. Four key arguments may be advanced in favour of providing refugees with access to ARTs. First, principles of fairness ought to govern decisions when faced with scarcity [9,10]. Second, from a public health perspective, the evidence of clinical benefit, reduced transmission, and cost-effectiveness argue for expanding access to ARTs for all individuals in need, regardless of their nationality [11,12,13]. Third, the right to health including access to essential medicines is codified in international human rights law and supports provision of ARTs as a life-saving, non-optional intervention for HIV-positive persons, including refugees [14,15,16]. Finally, international humanitarian law includes the requirement for host countries to provide refugees with a standard of medical care equivalent to that routinely available to host nationals [17].

However, countries do not uniformly provide access to ART for refugees [18], and where ART is provided, there may be financial obstacles to providing the monitoring and support that is necessary for optimising treatment outcomes. This deficit often originates at the level of the National Strategic Plan (NSP) and is reflected in proposals to the Global Fund. In 33 African countries with ≥10,000 refugees, 48% of NSPs failed to mention refugees, while only 21% referenced refugees in conjunction with explicit activities. Similarly, in 30 African Global Fund

proposals from rounds 1-8, 47% failed to mention refugees at all, while only 11% referenced specific activities for refugees [19]. In Asian countries, 45% of NSPs explicitly mentioned refugees, while only 18% spelled out specific activities for them. Positive developments in Asia have included improvement in access to key HIV services and equitable ART program coverage for refugees in all countries hosting ≥10,000 that routinely offer treatment to host communities [20]. The low proportion of NSPs that include specific activities for refugees may place them lower on the agenda when it comes to drafting Global Fund proposals.

Evidence on adherence and treatment outcomes

Refugees are found in specific refugee camps, or are dispersed in rural or urban settings, with trends towards more urbanisation, increased life expectancies, and increased prevalence of chronic non-communicable conditions [6]. A recent systematic review revealed a scarcity of data on adherence to ART and treatment outcomes comparing refugees and their host communities in different settings [21]. Acceptable outcomes were reported among refugees in high-income countries, but delayed treatment initiation occurred [22,23,24,25]. High levels of adherence, good survival probabilities, and the expected associations between poor adherence and mortality were found among IDPs [26,27]. Studies among mixed IDP/refugee and other conflict-affected groups also reported acceptable levels of adherence, positive CD4 gains, and good survival probabilities [28,29,30,31,32]. No differences between groups were found in comparisons between refugees or other conflict-affected groups and local communities [22,25,26]. Less encouraging findings came from western Kenya, where 16% of clients reported a treatment interruption during the period of post-election violence (PEV) in 2008, compared with 10% in the comparison period [33] and increased mortality in HIV-positive IDPs when compared with mortality prior to PEV in the same catchment area [34]. Overall, no studies were found that compared refugees and host communities on adherence indicators and treatment outcomes in asylum settings.

In response, we conducted cross-sectional studies in urban and camp-based settings where HIV-positive refugees and host population were accessing HIV services from shared clinics. In an urban setting (Kuala Lumpur, Malaysia), similar proportions of refugee and host community groups on treatment for ≥25 weeks had achieved viral suppression (81% v. 84%, p=0.54) while proportions optimally adhering to treatment were also similar according to the pharmacy's refill records (74% v. 66%, p=0.15) and self-reported one-month recall (72% v. 70%, p=0.79) [35]. By contrast, in a camp-based setting (Kakuma, Kenya) we found that very few refugee or host clients who had been on treatment for ≥25 weeks had a suppressed viral load (12% v. 11%, p=0.89) despite acceptable pharmacy-based adherence estimates (85% v. 74%, p=0.09) and in the presence of low levels of self-reported optimal adherence (62% v. 28%, p=0.002) [36]. At

first glance, this discrepancy was counterintuitive but not unique [37,38] and interpretable in the context of treatment outcomes that are sensitive to long-term adherence dynamics that are difficult to capture in cross-sectional studies [39]. Refugee status itself was not independently associated with virological outcomes in either setting. In the urban setting, men and clients who had suboptimal adherence to pharmacy refills, clients who had temporarily migrated for ≥1 month in the past year, had shorter times between diagnosis and treatment initiation and those experiencing longer transit times to clinic were less likely to have a suppressed viral load. In the camp setting, there was weak evidence for a harmful effect of suboptimal dosing (measured by comparing self-reported dosing with recommended guidelines) and good evidence for a protective effect of larger household sizes. Parallel qualitative interviews with clients drew attention to the impacts on adherence of crossing borders, integration into the treatment system upon arrival in asylum, food insecurity and hunger, treatment delivery insecurity, economic hardship, stigma and discrimination, social support and the notion that personal resilience may be overwhelmed by extensive social and environmental barriers present in local contexts.

Importantly, many studies among forcibly displaced populations on ARTs have been conducted among relatively stable refugee groups attending HIV clinics after periods of acute instability and displacement. Very few (if any) studies have examined the barriers to adherence experienced during displacement, when treatment has already been initiated. If sufficient medication supplies are obtained prior to transit, the period of displacement is short, and ARTs are made available quickly in asylum, then the threat of treatment interruptions resulting from personal stock-outs will be reduced and the greatest threat to adherence will be retaining sufficient supplies of medication and sustaining daily adherence. Yet, when one or more of these three conditions do not occur, there may be a greater risk of poor treatment outcomes, as was found in the studies of PEV in Kenya where displaced people on treatment appeared to have significant problems during the actual period of instability. Responding rapidly to treatment interruptions is critical as longer interruptions and lower "coverage times" (proportion of time with sufficient drug concentrations) have been associated with increased odds of having a detectable viral load [40].

These results suggest that refugees can achieve excellent outcomes if they are provided with consistent access to ARTs and effective support. In some settings, both refugees and host communities may experience the same barriers that may result in inferior outcomes. However, when in stable settings, refugees do as well (or as badly) as host communities. These findings echo previous work that reported successful treatment outcomes among the very poor in settings where structural barriers were properly addressed and minimised [41]. Policy for forcibly displaced and conflict-affected people is now catching up. A recent update to the Sphere Handbook, the most widely accepted guidelines for humanitarian assistance, recommended

provision of ART to these groups, in a change from the previous view that ART was not feasible in such settings [42,43,44]. The public health benefits of ART provision cannot be realised without sustained access, monitoring, and support. To this end, the challenge for donors, implementers and host countries is how to simultaneously increase access and effective support. In short, how can we secure the best possible outcomes?

RECOMMENDATIONS

For the clinical and public health benefits of HAART to be realised, it is essential to expand access to ARTs for all clients meeting national guidelines for when to start treatment. Host countries should include refugees in their NSPs and Global Fund proposals and detail specific results-oriented activities with them. By engaging in partnerships with humanitarian organisations through commitments to expand access to ARTs, forward looking host countries will be in a position to leverage funding for the benefit of refugees and host nationals, particularly in rural and underserviced areas. Expanding access requires continued scale-up of HIV testing and counselling (HTC) among refugees so that those who are unaware of their status are given a chance to initiate ART at the optimal time [45]. This will save lives and costs through better survival outcomes and reduced transmission [11,46,47]. Some countries are reluctant to provide HAART to illegal migrants, economic migrants and even asylum seekers, fearing additional costs or that starting them on HAART will make it difficult to expel them. However, international humanitarian law clearly entitles refugees to the routine standard of medical care available to the host population in the asylum country. The global population of 14.7 million IDPs [1] share similar entitlements to protection and standards of care as refugees. It is therefore important that NSPs and Global Fund proposals are explicit in which types of migrant are or are not entitled to HAART and which agencies will be responsible [48,49].

Refugees have been forcibly displaced and may travel again for purposes of repatriation, resettlement, or family reunion. Similarly, host community members are mobile when seeking employment, visiting family, or when living a traditional nomadic lifestyle. Both groups may experience unstructured treatment interruptions that have been shown to increase the risk of death, opportunistic infections virological failure, development of drug resistance, while slowing immunological recovery [50]. Therefore, preparing for onwards movement and implementing best practices for managing continuation or re-initiation of treatment for new arrivals in a program is essential to the continuity and sustainability of ART in any group [51]. For refugees, this will require active responses in all phases of the displacement cycle where ART is accessed [52,53]. Distance to clinic and associated transportation costs are also crucial as longer travel times or higher costs may increase the chance of treatment interruptions [33,54,55,56]. In response, efforts to minimise costs and bridge distances have been helpful

[27,57], and provide valuable lessons for refugee settings. Refugees in urban settings also require freedom of movement without fear of arrest or detention when travelling for routine appointments or medication refills. To this end, awareness interventions within the police and other law enforcement institutions of the rights accorded to refugees, IDPs and asylum-seekers is an urgent step for host countries to undertake [58].

As our recent findings from Kenya demonstrated and others have pointed out [59], there are dangers in providing ART in under-resourced settings, yet few would argue that this is a reason to limit access. Inferior outcomes should serve as a call to fix programs that are not achieving acceptable results. At the implementation level, adherence monitoring and support are crucial for achieving optimal, consistent treatment outcomes. The feasibility of delivering ART in unstable settings has been demonstrated in relatively well-resourced programs. In the absence of expensive laboratory support and motorcycle-equipped treatment monitors, a basic package of support and monitoring can be effective [60]. To this end, thorough adherence monitoring should be implemented in all refugee settings as a minimum indicator [27,61] including pharmacy-based adherence measures and client self-reports as has been recommended for low-income settings [62]. Self-reported measures are feasible, have been significantly associated with virological outcomes in most studies [63], and encourage client self-assessment while usefully revealing adherence patterns. Pharmacy-based measures are objective, have been strongly associated with virological outcomes in most studies [64], and are better than CD4 changes at predicting virological outcomes in the first 12 months of treatment [65]. Triangulating multiple indicators for routine adherence monitoring will help to promote valid monitoring by overcoming the limitations of any single measure. Supporting routine adherence monitoring with integrated electronic medical and pharmacy records, where feasible, will be an important tool for optimising treatment outcomes. Although adherence intervention trials have typically shown small and transitory effects [66], proven support interventions such as mobile phone text messaging [67], enhanced counselling [68] and peer-support [69] ought to be implemented and evaluated at the clinic level. Operational research among refugees and host communities should aim to assess the acceptability and effectiveness of low-cost adherence support interventions. With a few exceptions [70,71], most research on adherence and treatment outcomes in conflict-affected populations has focused on adults, highlighting a need for studies focused on young people. Further recommendations may be found in Table 1-3.

[*** Table 1, p.154-155, Table 2, p.156, near here ***]

In summary, equitable and acceptable HIV treatment outcomes have been shown to be achievable in a range of challenging settings serving forcibly displaced clients including refugees. Refugees have a right to equal access to HIV treatment based on principles of fairness

and human rights, in addition to the individual and population-based public health benefits. Since HIV-positive individuals on HAART with good adherence will rarely transmit HIV to their sexual partners [11], it is also in the enlightened self-interest of host country governments to support HIV programs that serve HIV-positive refugees and host clients equally and to a high standard. Since an average refugee spends 17 years in asylum [52], there is an obvious public health and humanitarian interest in guaranteeing access to ART and promoting optimal adherence among this group.

Table 1: Key recommendations for providers and implementers

Theme	Recommendation
Access	Provide treatment on an equitable basis to refugees and local host communities, leveraging national and international resources to achieve good treatment outcomes and reduced transmission of HIV.
Adherence	Upgrade community health and counselling teams to ensure uninterrupted personal HAART supply, rigorous progress monitoring, and optimal adherence.
	Consider providing small personal grants to subsidise transport and meals for a monthly clinic trip for medication pick-up or doctor's appointment.
	Given that refugee counsellors are often refugees themselves, each counsellor should partner with a back-up counsellor such that if the primary counsellor goes on leave or is resettled their duties to specific clients are effectively handed over.
	Where appropriate, counsellors should deliver medication directly to clients who are disabled, or who do not regularly attend the clinic due to stigma, prohibitive costs, or other reasons.
	Consider pilot-testing a mobile phone SMS intervention to facilitate daily adherence reminders and monthly medication refill reminders, especially for clients at higher risk of erratic adherence.
	Monitor gender and other sub-group differences in adherence and treatment outcomes, to ensure services are distributed consistently and equitably.
	Where feasible, encourage clients to join support groups, so they may benefit from support in relation to ensuring consistent pharmacy claims and mitigating local adherence challenges as they arise.
	Consider using small personal grants to subsidise transport and meals for a monthly or bi-monthly clinic trip for medication pick-up or doctor appointment.
	Assess future travel plans at regular nursing or refill appointments and conduct risk assessments for clients who travel for any reason. Provide contingency plans and emergency hotlines. Partnerships among pharmacies in major centres might facilitate access in the event that an emergency prescription refill is required.
Pharmacy	Install or upgrade the electronic medical record (EMR) such that pharmacy records are linked to the main medical record and adherence data may be easily extracted so that clients who begin to default from clinic appointments or pharmacy refills are identified and traced by home-based care workers. Remove any existing barriers between medical and pharmacy records.
	Manage changes in treatment guidelines such that a transitional overlap is allowed between the discontinuation of old regimens and the implementation of new ones. In this period, consider purchasing both regimens to avoid situations where stock-outs or the threat of stock-outs

Table 1: Key recommendations for providers and implementers

Theme	Recommendation
	leads to forced alteration of client pick-up schedules and treatment interruptions.
	Implement routine adherence monitoring using a combination of a counsellor-administered or self-administered self-report using a visual analogue instrument, pharmacy refill measures (where feasible), and feedback results to providers and clients. The system should be rights-based (voluntary consent required for participation).
	Consider issuing extended supplies of HAART for those who live far from the hospital, have difficulty attending, and are otherwise in good health. Distribute HAART through partnerships with a single provider where possible.
	Ensure that medications are disbursed with clear prescription guidelines that may be understood across multiple languages and cross-culturally. Ideally this should be provided in writing as well as verbally. Pictorial instructions illustrating dose times and tablet numbers may be helpful.
Training and turnover	Consider formal training of designated nursing and/or home-based care staff in adherence counselling.
	Implement appropriate plans to manage staff turnover, which occurs often in humanitarian and fragile settings.
Food security	Evaluate food security. Where supplementary rations are provided, consider adjusting them based on the total number of household members (clients who live in group settings may be expected to share their supplementary rations across the household leading to shortages and food insecurity).
Operational research	Support operational research assessing adherence and treatment outcomes over time.
	Pilot-test interventions such as enhanced face-to-face counselling and mobile-phone based communications that support adherence and solicit feedback from clients.

Table 2: Key recommendations for host country Ministries of Health and donors

Theme	Recommendation
Access	Expand HIV treatment and scale-up treatment support on an equitable basis to refugees and local host communities.
	Provide awareness to the police and other law enforcement institutions of the rights accorded to refugees and other displaced persons to ensure that access to medical care is not interrupted.
National Strategic Plans (NSPs) and Global Fund	Include refugees in national strategic plans and Global Fund proposals with specific activities noted for them.
	Distinguish between different types of displaced groups in NSPs and Global Fund proposals.
	Formalize responsibilities for refugees in NSPs, identifying all stakeholders with national governments and Ministries of Health, and non-governmental actors including UNHCR and implementing partner non-governmental organisations.
	Leverage national and international resources to achieve good treatment outcomes and reduced transmission of HIV among both refugee and host community groups.
Funding	Fund enhanced community health and counselling teams and adherence interventions to ensure uninterrupted personal HAART supply, rigorous progress monitoring and optimal adherence.
	Fund and support the development and implementation of routine adherence monitoring systems.
	Fund an intensive package of adherence interventions for groups at high risk of sub-optimal adherence and/or loss to follow-up.
	Manage changes in treatment guidelines such that transitions do not lead to stock-outs or the threat of stock-outs.
	Consider augmented training for designated nursing and home-based care staff in adherence counselling.
	Support operational research assessing adherence and treatment outcomes over time, acceptability and effectiveness of low-cost adherence support, such as mobile-phone based interventions.

References

1. UNHCR (2011) Statistical Yearbook 2010. Geneva: UNHCR.
2. Martin M, Del Cacho E, Codina C, Tuset M, De Lazzari E, et al. (2008) Relationship between adherence level, type of the antiretroviral regimen, and plasma HIV type 1 RNA viral load: a prospective cohort study. AIDS Res Hum Retroviruses 24: 1263-1268.
3. Ortego C, Huedo-Medina TB, Llorca J, Sevilla L, Santos P, et al. (2011) Adherence to highly active antiretroviral therapy (HAART): a meta-analysis. AIDS Behav 15: 1381-1396.
4. International Federation of Red Cross and Red Crescent Societies (2008) World Disaster Report 2008: Focus on HIV and AIDS. Geneva. pp. 118-141.
5. Porter M, Haslam N (2005) Predisplacement and postdisplacement factors associated with mental health of refugees and internally displaced persons - a meta-analysis. JAMA 294: 602-612.
6. Spiegel PB, Checchi F, Colombo S, Paik E (2010) Health-care needs of people affected by conflict: future trends and changing frameworks. Lancet 375: 341-345.
7. Ford N (2009) Treating AIDS in complex emergencies: the need for clear policy consensus. Progress in Development Studies 9: 55-61.
8. Mills EJ, Ford N, Singh S, Eyawo O (2009) Providing antiretroviral care in conflict settings. Curr HIV/AIDS Rep 6: 201-209.
9. Leaning J, Spiegel P, Crisp J (2011) Public health equity in refugee situations. Confl Health 5: 6.
10. Persad G, Wertheimer A, Emanuel EJ (2009) Principles for allocation of scarce medical interventions. Lancet 373: 423-431.
11. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, et al. (2011) Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med 365: 493-505.
12. Nosyk B, Montaner JS (2012) The evolving landscape of the economics of HIV treatment and prevention. PLoS Med 9: e1001174.
13. Nachega JB, Mills EJ, Schechter M (2010) Antiretroviral therapy adherence and retention in care in middle-income and low-income countries: current status of knowledge and research priorities. Curr Opin HIV AIDS 5: 70-77.
14. Pillay N (2008) Right to health and the Universal Declaration of Human Rights. Lancet 372: 2005-2006.
15. UN (1966) International Covenant on Economic, Social, and Cultural Rights (ICESCR). New York.
16. UN Economic and Social Council (2000) Committee on on Economic, Social, and Cultural Rights: general comments. New York.
17. UN General Assembly (28 July 1951) Convention relating to the Status of Refugees. In: United Nations, editor. Treaty Series (vol 189, p 137).
18. Trippayya V (2005) Botswana: Refugees not entitled to same services as citizens. HIV AIDS Policy Law Rev 10: 27-28.
19. Spiegel PB, Hering H, Paik E, Schilperoord M (2010) Conflict-affected displaced persons need to benefit more from HIV and malaria national strategic plans and Global Fund grants. Confl Health 4: 2.
20. Burton A (2010) HIV, refugees and conflict-affected populations in Asia. Forced Migration Review.

21. Mendelsohn JB, Schilperoord M, Spiegel P, Ross DA (Submitted) Adherence to antiretroviral therapy and treatment outcomes in conflict-affected and forcibly displaced populations: a systematic review. Confl Health.

22. Beckwith CG, DeLong AK, Desjardins SF, Gillani F, Bazerman L, et al. (2009) HIV infection in refugees: a case-control analysis of refugees in Rhode Island. Int J Infect Dis 13: 186-192.

23. Moreno A, Crosby S, Labelle C, Sullivan M, Samet JH (2003) Health assessment of HIV-infected refugees. J Acquir Immune Defic Syndr 34: 251-254.

24. Nisbet SM, Reeve AM, Ellis-Pegler RB, Woodhouse AF, Ingram RJ, et al. (2007) Good outcome in HIV-infected refugees after resettlement in New Zealand: population study. Intern Med J 37: 290-294.

25. Krentz H, Gill MJ (2009) The five-year impact of an evolving global epidemic, changing migration patterns, and policy changes in a regional Canadian HIV population. Health Policy 90: 296-302.

26. Garang PG, Odoi RA, Kalyango JN (2009) Adherence to antiretroviral therapy in conflict areas: a study among patients receiving treatment from Lacor Hospital, Uganda. AIDS Patient Care STDS 23: 743-747.

27. Kiboneka A, Nyatia RJ, Nabiryo C, Anema A, Cooper CL, et al. (2009) Combination antiretroviral therapy in population affected by conflict: outcomes from large cohort in northern Uganda. BMJ 338: b201.

28. O'Brien DP, Mills C, Hamel C, Ford N, Pottie K (2009) Universal access: the benefits and challenges in bringing integrated HIV care to isolated and conflict affected populations in the Republic of Congo. Confl Health 3: 1.

29. O'Brien DP, Venis S, Greig J, Shanks L, Ellman T, et al. (2010) Provision of antiretroviral treatment in conflict settings: the experience of Médecins Sans Frontières. Confl Health 4: 12.

30. Culbert H, Tu D, O'Brien DP, Ellman T, Mills C, et al. (2007) HIV treatment in a conflict setting: outcomes and experiences from Bukavu, Democratic Republic of the Congo. PLoS Med 4: e129.

31. Salami O, Buzu A, Nzeme C (2010) High level of adherence to HAART among refugees and internally displaced persons on HAART in western equatorial region of Southern Sudan. J Int AIDS Soc 13: 123.

32. McCarthy K, Chersich MF, Vearey J, Meyer-Rath G, Jaffer A, et al. (2009) Good treatment outcomes among foreigners receiving antiretroviral therapy in Johannesburg, South Africa. Int J STD AIDS 20: 858-862.

33. Pyne-Mercier LD, John-Stewart GC, Richardson BA, Kagondu NL, Thiga J, et al. (2011) The consequences of post-election violence on antiretroviral HIV therapy in Kenya. AIDS Care 23: 562-568.

34. Feikin DR, Adazu K, Obor D, Ogwang S, Vulule J, et al. (2010) Mortality and health among internally displaced persons in western Kenya following post-election violence, 2008: novel use of demographic surveillance. Bull World Health Organ 88: 601-608.

35. Mendelsohn JB, Spiegel P, Schilperoord M, Balasundaram S, Radhakrishnan A, et al. (In Preparation) Good adherence and treatment outcomes in refugee and host communities on highly active antiretroviral therapy in urban Kuala Lumpur, Malaysia.

36. Mendelsohn JB, Schilperoord M, Spiegel P, Burton JW, Okonji JA, et al. (In Preparation) Poor treatment outcomes among both refugees and host community accessing Highly

Active Antiretroviral Therapy (HAART) from Kakuma refugee camp in Northwestern Kenya

37. Bisson GP, Rowh A, Weinstein R, Gaolathe T, Frank I, et al. (2008) Antiretroviral failure despite high levels of adherence: discordant adherence-response relationship in Botswana. J Acquir Immune Defic Syndr 49: 107-110.

38. Trotta MP, Pierro P, Marconi P, Sette P, Zaccarelli M, et al. (2011) With current ARV treatments virological failure mostly occurs in the context of optimal self-reported adherence. Infection 39: S27-S28.

39. Tesoriero J, French T, Weiss L, Waters M, Finkelstein R, et al. (2003) Stability of adherence to highly active antiretroviral therapy over time among clients enrolled in the treatment adherence demonstration project. J Acquir Immune Defic Syndr 33: 484-493.

40. Genberg BL, Wilson IB, Bangsberg DR, Arnsten J, Goggin K, et al. (2012) Patterns of antiretroviral therapy adherence and impact on HIV RNA among patients in North America. AIDS 26: 1415-1423.

41. Farmer PE, Nizeye B, Stulac S, Keshavjee S (2006) Structural violence and clinical medicine. PLoS Med 3: 1686-1691.

42. The Sphere Project (2011) The Sphere Handbook: Humanitarian Charter and Minimum Standards in Humanitarian Response (3ed). Rugby, UK.

43. The Sphere Project (2011) What is new in the Sphere Handbook 2011 edition.

44. Inter-agency Standing Working Group on Reproductive Health in Crises (2010) Inter-agency Field Manual on Reproductive Health in Humanitarian Settings - 2010 Revision for Field Review. Geneva.

45. Spiegel PB (2009) The effects of antiretroviral therapy on HIV prevalence in conflict situations: not yet there. AIDS 23: 541-542.

46. Kitahata MM, Gange SJ, Abraham AG, Merriman B, Saag MS, et al. (2009) Effect of early versus deferred antiretroviral therapy for HIV on survival. N Engl J Med 360: 1815-1826.

47. Garnett GP, Becker S, Bertozzi S (2012) Treatment as prevention: translating efficacy trial results to population effectiveness. Curr Opin HIV AIDS 7: 157-163.

48. UNHCR (2006) Note on HIV/AIDS and the protection of refugees, IDPs and other persons of concern. Geneva: United Nations High Commissioner for Refugees.

49. Inter-agency Standing Committee (IASC) (2010) Handbook for the Protection of Internally Displaced Persons. Geneva: UNHCR.

50. Kranzer K, Lewis JJ, Ford N, Zeinecker J, Orrell C, et al. Treatment interruption in a primary care antiretroviral therapy program in South Africa: cohort analysis of trends and risk factors. J Acquir Immune Defic Syndr 55: e17-23.

51. Veenstra N, Whiteside A, Lalloo D, Gibbs A (2010) Unplanned antiretroviral treatment interruptions in southern Africa: how should we be managing these? Global Health 6: 4.

52. UNHCR (2007) Antiretroviral Medication Policy for Refugees. Geneva: UNHCR.

53. Wilhelm-Solomon M (2010) Challenges for antiretroviral provision in northern Uganda. Forced Migr Rev.

54. Olupot-Olupot P, Katawera A, Cooper C, Small W, Anema A, et al. (2008) Adherence to antiretroviral therapy among a conflict-affected population in Northeastern Uganda: A qualitative study. AIDS 22: 1882-1884.

55. Tuller DM, Bangsberg DR, Senkungu J, Ware NC, Emenyonu N, et al. (2010) Transportation costs impede sustained adherence and access to HAART in a clinic population in southwestern Uganda: a qualitative study. AIDS Behav 14: 778-784.

56. Hardon AP, Akurut D, Comoro C, Ekezie C, Irunde HF, et al. (2007) Hunger, waiting time and transport costs: time to confront challenges to ART adherence in Africa. AIDS Care 19: 658-665.

57. Mukherjee JS, Ivers L, Leandre F, Farmer P, Behforouz H (2006) Antiretroviral therapy in resource-poor settings: Decreasing barriers to access and promoting adherence. J Acquir Immune Defic Syndr 43 Suppl 1: S123-S126.

58. de Waal A (2010) Reframing governance, security and conflict in the light of HIV/AIDS: a synthesis of findings from the AIDS, security and conflict initiative. Soc Sci Med 70: 114-120.

59. Harries AD, Zachariah R, van Oosterhout JJ, Reid SD, Hosseinipour MC, et al. (2010) Diagnosis and management of antiretroviral-therapy failure in resource-limited settings in sub-Saharan Africa: challenges and perspectives. Lancet Infect Dis 10: 60-65.

60. Mugyenyi P, Walker AS, Hakim J, Munderi P, Gibb DM, et al. (2010) Routine versus clinically driven laboratory monitoring of HIV antiretroviral therapy in Africa (DART): a randomised non-inferiority trial. Lancet 375: 123-131.

61. Spiegel P, Sheik M, Gotway-Crawford C, Salama P (2002) Health programmes and policies associated with decreased mortality in displaced people in postemergency phase camps: a retrospective study. Lancet 360: 1927-1934.

62. Thompson MA, Mugavero MJ, Amico KR, Cargill VA, Chang LW, et al. (2012) Guidelines for improving entry into and retention in care and antiretroviral adherence for persons With HIV: evidence-based recommendations from an International Association of Physicians in AIDS Care panel. Ann Intern Med 156: 817-33.

63. Simoni JM, Kurth AE, Pearson CR, Pantalone DW, Merrill JO, et al. (2006) Self-report measures of antiretroviral therapy adherence: a review with recommendations for HIV research and clinical management. AIDS Behav 10: 227-245.

64. McMahon JH, Jordan MR, Kelley K, Bertagnolio S, Hong SY, et al. (2011) Pharmacy adherence measures to assess adherence to antiretroviral therapy: review of the literature and implications for treatment monitoring. Clin Infect Dis 52: 493-506.

65. Bisson GP, Gross R, Bellamy S, Chittams J, Hislop M, et al. (2008) Pharmacy refill adherence compared with CD4 count changes for monitoring HIV-infected adults on antiretroviral therapy. PLoS Med 5: e109.

66. Simoni JM, Amico KR, Smith L, Nelson K (2010) Antiretroviral adherence interventions: translating research findings to the real world clinic. Curr HIV/AIDS Rep 7: 44-51.

67. Horvath T, Azman H, Kennedy GE, Rutherford GW (2012) Mobile phone text messaging for promoting adherence to antiretroviral therapy in patients with HIV infection. Cochrane Database Syst Rev 3: CD009756.

68. Chung MH, Richardson BA, Tapia K, Benki-Nugent S, Kiarie JN, et al. (2011) A randomized controlled trial comparing the effects of counseling and alarm device on HAART adherence and virologic outcomes. PLoS Med 8: e1000422.

69. Simoni JM, Nelson KM, Franks JC, Yard SS, Lehavot K (2011) Are peer interventions for HIV efficacious? A systematic review. AIDS Behav 15: 1589-1595.

70. Vreeman RC, Nyandiko WM, Sang E, Musick BS, Braitstein P, et al. (2009) Impact of the Kenya post-election crisis on clinic attendance and medication adherence for HIV-infected children in western Kenya. Confl Health 3: 5.

71. Kiboneka A, Nyatia RJ, Nabiryo C, Olupot-Olupot P, Anema A, et al. (2008) Pediatric HIV therapy in armed conflict. AIDS 22: 1097-1098.

GENERAL CONCLUSIONS

Prior to this work, very few studies had been conducted among conflict-affected and forcibly displaced groups. Those that had been done suggested that consistent adherence to HAART and acceptable treatment outcomes were possible. All studies of internally-displaced persons (IDPs) were conducted in resource-limited settings. However, most studies of refugees were conducted among those claiming asylum or resettled to high-income countries. Only one study compared outcomes among refugees in asylum and local host communities but this study limited its comparison to self-reported adherence [1]. Therefore, the primary aim of this thesis was to assess and compare HAART adherence and treatment outcomes among refugees and host communities attending the same HIV treatment clinic in one urban setting in Southeast Asia (Kuala Lumpur, Malaysia, *Paper Two*) and one camp setting in rural East Africa (Kakuma, Kenya, *Paper Three*). Secondary objectives sought to explore factors associated with viral suppression in each study setting, to understand client perspectives on sustaining adherence over time, and on the basis of these findings, to make recommendations for policy. From these aims, four research questions were proposed. Table 1 links the research questions to the sub-study, thesis paper, and methods employed.

Table 1: Research questions linked to thesis papers and methods

	Research question	Thesis paper(s)	Method(s)
1	Do refugees adhere to treatment and achieve viral suppression while in asylum at levels that are comparable to local host communities?	Paper Two (Malaysia) Paper Three (Kenya)	Structured questionnaire on adherence Pharmacy refill adherence Viral load
2	If differences in treatment outcomes between refugees and local host communities exist, why do the outcomes vary? What are the risk factors for lack of viral suppression in the study settings?	Paper Two (Malaysia) Paper Three (Kenya)	Structured questionnaire on adherence Pharmacy refill adherence Viral load
3	How do refugees and host nationals experience their treatment and what do they perceive to be the major threats, barriers, and facilitators of adherence?	Paper Four (Kenya and Malaysia)	Semi-structured interviews
4	What policies can improve adherence to HAART in clinics shared by refugee and host community groups?	Paper Five (Kenya and Malaysia)	All data collected

SUMMARY OF FINDINGS

Do refugees adhere to treatment and achieve viral suppression while in asylum at levels that are comparable to local host communities?

The initial hypothesis was that refugees would adhere to prescribed regimens and achieve viral suppression, but at lower levels than the local host community. In both study settings, there were no differences between groups in the proportions virologically suppressed and very few differences between the groups in levels of adherence to HAART. In the urban, Southeast Asian setting (Kuala Lumpur, Malaysia, *Paper Two*), similar proportions of refugee and host community groups on treatment for ≥25 weeks achieved viral suppression (81% v. 84%, p=0.54) while proportions optimally adhering to treatment were also not statistically significantly different according to pharmacy refill records (74% vs. 66%, p=0.15) and self-reported one-month recall (72% v. 70%, p=0.79). By contrast, in the camp-based setting in East Africa (Kakuma, Kenya, *Paper Three*) we found that very few refugee or host clients who had been on treatment for ≥25 weeks had a suppressed viral load (12% v. 11%, p=0.89). This was despite acceptable pharmacy-based adherence estimates (85% v. 74%, p=0.09) and in the presence of low levels of self-reported optimal adherence, which were poor in both groups but significantly worse in hosts (62% v. 28%, p=0.002). In multivariable analyses, refugee status itself was not independently associated with virological outcomes in either setting. In contrast to the Malaysian setting, the very poor Kenyan outcomes were stark and surprising in light of the presumption that, since refugees in camp settings may be viewed as "captive audiences", management of their treatment ought to have been easier relative to those living in urban areas. Proportions optimally adhering to pharmacy refill were not ideal in this setting, however self-reported one-month recall findings were clearly low, especially so among the host community. When taken together with the moderate proportions of clients who were collecting their prescriptions refills in an optimal manner, these findings were indicative of routine adherence difficulties. However, each measure alone was not independently associated with lack of viral suppression. The proportions of unsuppressed virological outcomes that were not explained by sub-optimal adherence echoed previous studies [2,3], and may be interpretable in the context of long-term adherence dynamics that are difficult to capture in cross-sectional studies using proxy adherence measures [4].

If differences in treatment outcomes between refugees and local host communities exist, why do the outcomes vary? What are the risk factors for lack of viral suppression in the study settings?

Consistent with the plethora of previous studies on the effect of adherence on virological outcomes, the expectation was that sub-optimal adherence would be a strong independent risk

factor for poor virological outcomes in this study. Initially, we thought that other important risk factors might include serostatus disclosure and recent travel.

The findings showed that, in the urban Southeast Asian setting *(Paper Two)*, women, and clients with longer times between diagnosis and treatment initiation were less likely to have an unsuppressed viral load, while suboptimal pharmacy refill records, temporary migration for one month or more in the past year and longer transit times to clinic were associated with lack of viral suppression. In the East African camp setting *(Paper Three)*, there was only one statistically significant association with failure to suppress the viral load. There was strong evidence for an association between smaller household sizes and lack of viral suppression and weak evidence (p=0.09) for an association between underdosing (measured by comparing self-reported dosing with routine guidelines) and the outcome. In contrast to the Malaysian study, in the camp-based East African setting neither sub-optimal adherence measured by pharmacy refills and self-reports, nor reported serostatus disclosure, recent travel or temporary migration were independently associated with this key outcome. The main covariate of interest, refugee status, was not independently associated with virological outcomes in either setting. In Malaysia, adherence to pharmacy refill schedule was better than the self-reported measures of adherence at predicting inadequate suppression *(Paper Three)*. In Kenya, none of the adherence measures were associated with the virological outcomes; however the weak evidence for the association with client underdosing in relation to routine prescriptions suggested that clients were often not having sufficient coverage time by HAART. Possible explanations include simple misunderstandings of required dosing abetted by changes from once-daily to twice-daily nevirapine on the basis of initial assessments of tolerability and/or refill prescriptions being given to the patients without clear dosing instructions. Moreover, at the time of the study, many home-based care workers had been laid off and there was dissatisfaction among the remaining team suggesting that active follow-up and engagement may have been lacking for many of the patients. There was no direct evidence to support or refute these assertions. The finding that the pharmacy refill measure of adherence was not significantly linked to the virological outcome suggested that in spite of the fact that the majority of clients were collecting their HAART prescriptions at optimal levels, either their comprehension of the recommended dosing schedule or daily adherence had indeed been problematic. However, self-reported proxy measures of adherence were not able to capture this dynamic. Clients may also have developed drug resistance or medication potency may have been adversely affected by storage conditions or less likely but still possible, by drug counterfeiting. Again, there was no direct evidence to verify or refute these possibilities.

How do refugees and host nationals experience their treatment and what do they perceive to be the major threats, barriers, and facilitators of adherence?

In advance of qualitative interviews, we hypothesised that semi-structured interviews with clients would show that a key adherence challenges in both settings would include stigma and discrimination. The qualitative interviews suggested that, for refugees, crossing borders and integration upon arrival (in asylum) were important threats, while food insecurity, treatment delivery insecurity, stigma and discrimination, and economic hardship were experienced in both settings and by both groups. Social support and personal resilience were important facilitators of adherence for participants across the settings. Stigma and discrimination seemed less intensive (but was still present) among the Kenyan host community. Clients in both settings reported using a variety of adherence support strategies and demonstrated resilience and personal agency in response to challenges; however, when compared to the urban Malaysian group, treatment agency in the Kenyan camp-based group appeared to be "bounded" (ie. constrained) by the extent of the systemic challenges they faced. This was perhaps also worsened for refugees by an underlying lack of hope as resettlement to a high-income country is uncommon in Kenya, and more common in the Malaysian setting.

What policies can improve adherence to HAART in clinics shared by refugee and host client groups?

The initial working hypotheses were that earlier initiation of therapy, better adherence monitoring programs and access to appropriate counselling services would help to optimise future treatment outcomes. There was no evidence from this study to support an effect of earlier initiation of therapy on virological outcomes despite observational findings that earlier treatment start increases life expectancy [5,6]. The effect of earlier initiation of therapy on virological outcomes, mediated by adherence, could work in both directions. Earlier therapy may lead to treatment fatigue that compromises adherence and outcomes or earlier initiation could lead to tighter linkages with care that would positively impact adherence and outcomes. The START study will be the first randomised controlled trial to examine the optimal time to start antiretroviral therapy [7]. Other trials such as HPTN052 and TEMPRANO are also addressing the issue. The findings from the present study supported our more modest initial hypothesis that better adherence monitoring and counselling services might help to mitigate adherence barriers, improving adherence and treatment outcomes. The findings were elaborated into the following recommendations, addressed to different levels of the treatment system.

For UNHCR and implementing partners:

In Kakuma, Kenya:

1) Urgently investigate the reasons for the high proportion of clients lacking viral suppression including the clinic and pharmacy systems, storage of medications, effectiveness of community-based health workers, whether clients are drug selling or sharing.
   - Once the investigation is complete and remedial measures have been implemented, collect a second viral load sample to confirm treatment failures and perform drug resistance testing to identify the proportion of treatment failures that are due to resistance. Adjust treatment and care accordingly.

In general:

2) Access to HAART
   - Continue to provide treatment on an equitable basis to refugees and local host communities, leveraging national and international resources to achieve good treatment outcomes and reduced transmission of HIV among both groups.
3) Direct adherence support
   - Where possible, introduce and provide adequate support to community-based health workers to ensure uninterrupted personal HAART supply, rigorous progress monitoring and optimal adherence.
   - Each community health worker or counsellor should be responsible for tracking medication collections and adherence for a defined list of clients. Each counsellor should partner with a back-up counsellor so that, if the primary person goes on leave, their duties to specific clients are covered effectively.
   - Counsellors should deliver medication directly to clients who are disabled, who do not regularly attend the clinic due to stigma, prohibitive costs or for other reasons.
   - Pilot-test adherence support interventions, such as mobile phone SMS intervention, to facilitate daily adherence reminders and monthly medication refill reminders especially for clients at higher risk of inconsistent adherence.
4) Pharmacy support
   - Install or upgrade the electronic medical record (EMR) such that pharmacy records are linked to the main medical record and adherence data may be easily extracted so that clients who begin to default from clinic appointments or pharmacy refills may be quickly identified and traced by home-based care workers. Remove any existing disconnections between medical and pharmacy records. If records remain paper-based, devise a system that routinely assesses pharmacy records while identifying and following-up clients who have failed to collect their prescriptions.

- Manage the ordering of drug supplies when treatment guidelines are changed such that an appropriate transitional overlap is allowed between the discontinuation of the supply of the old regimen and the start of the supply of the new regimen. In this period, both regimens should be ordered to avoid situations where stock-outs or the threat of stock-outs leads to forced alteration of client drug collection schedules and increased risk of treatment interruptions.
- Implement a routine adherence monitoring using a combination of self-reports measured using visual analogue instruments and pharmacy refill measures, where feasible. The monitoring system should be used to give regular feedback to providers and clients. To protect human rights, voluntary consent from the clients should be required for participation through an opt-out approach.
- Consider issuing extended supplies of HAART for those who live far from the hospital and have difficulty attending. Distribute routine HAART through partnerships with a single provider where possible. Promote linkages among a network of regional pharmacies to facilitate contingency access in the event that an emergency prescription refill is required.
- Ensure that medications are disbursed with clear prescription guidelines that may be understood across multiple languages and cross-culturally. Ideally these should be provided in writing as well as verbally. Pictorial instructions illustrating dose times and tablet numbers may be helpful.

5) Peer support
   - Encourage clients to join active support groups, so they may benefit from support in relation to ensuring consistent pharmacy claims and mitigating adherence challenges as they arise.

6) Food support
   - Evaluate food security. Where supplementary rations are provided, consider adjusting them based on the total number of household members (clients who live in group settings are likely to share their supplementary rations across the household leading to shortages and food insecurity).

7) Travel support
   - Consider providing small personal grants to subsidise transport and meals for monthly medication refills or doctor's appointment.
   - Assess travel plans at regular doctor appointments and conduct risk assessments for those clients who might travel for any reason. Develop contingency plans in partnership with clients. This could include emergency hotlines.

8) Health care providers

- Consider advanced formal training of designated nursing and/or home-based care staff in adherence counselling.
- Implement appropriate plans to manage staff turnover especially in camp settings. Enhance the role of the home-based care system to provide continuity when staff members depart.

For Ministries of Health and Donors:

1) Access to HAART
   - Expand HIV treatment and scale-up treatment support on an equitable basis to refugees and local host communities.
   - Provide awareness interventions within the police and other law enforcement institutions of the rights accorded to refugees, IDPs and asylum-seekers.
2) National Strategic Plans and Global Fund
   - Include refugees in national strategic plans (NSPs) and Global Fund proposals with specific activities related to their treatment and care described and budgeted.
   - Distinguish between different types of displaced groups in NSPs and Global Fund proposals.
   - Formalize responsibilities for refugees in NSPs, identifying all stakeholders within national governments and Ministries of Health, and non-governmental actors including UNHCR and implementing partner NGOs.
   - Leverage national and international resources to achieve good treatment outcomes and reduced transmission of HIV among and between refugees and host communities.
3) General support to the treatment system
   - Support enhancement of home-based care and adherence interventions to ensure uninterrupted personal HAART supply, rigorous progress monitoring and optimal adherence.
   - Support the development and implementation of routine adherence monitoring systems.
   - Support a basic package of adherence interventions, and a more intensive package for groups at high risk of adherence lapses and loss to follow-up.
   - Manage changes in treatment guidelines such that transitions do not lead to stock-outs or the threat of stock-outs.
   - Fund additional training for nurses and home-based care staff in adherence counselling.
   - Support operational research for assessing adherence and treatment outcomes over time, acceptability and effectiveness of low-cost adherence support interventions.

ETHICS AND UNDUE INDUCEMENT

This research was conducted with highly vulnerable clients. An incentive was offered in exchange for participation, which amounted to a stipend to offset transport costs and the value of approximately one meal. Clients with greater transport needs were offered additional money to offset their costs. Although acceptable to all Ethics Committees with jurisdiction over the project, these ethical issues are nonetheless important to re-examine in detail. Among ethical violations, Emanuel and colleagues (2005) distinguish three which are most relevant here: undue inducement, coercion, and unfortunate circumstances. In general, inducement itself is an acceptable means to affect a personal judgment with respect to study participation, provided clients are fairly able to make effective judgments. If no sort of inducement were ethical, no incentive would be appropriate in research, thus compromising the ability to affect improvements in health on the basis of evidence. Undue inducement refers to situations that meet all of the following criteria: an individual is offered a valuable good to incentivise an action; the offer is so excessive as to be irresistible in the context; the offer leads to poor judgment in an important decision; the poor judgment leads to a high risk of serious harm against their interests [8]. Coercion refers to the threat of an outcome that is worse than the status quo, if a choice is made by a participant not to engage in the incentivised action (e.g. your money or your life). Unfortunate circumstances denote an ethical situation where a combination of vulnerable circumstances and tempting offers compromise autonomy. Therefore, the first question that ought to be asked is: does the incentive structure actually give participants no choice at all; in other words, are participants effectively being coerced? Second, is the incentive large enough so as to encourage reasonable people to accept excessive risks that far outweigh the benefits of participation? Third, are circumstances sufficiently abject as to render almost any incentive unethical? The distinction is also reflected in proposed remedies. For coercion, the remedy is to remove the threat; for undue inducement the solution is to reduce the incentive [8]; while for unfortunate circumstances, the answer is presumably not to undertake the research or, more controversially, not to give any incentive. In the present study, a sceptic would be hard-pressed to argue that participants were subject to undue inducement. Complete information is necessary, but not sufficient, to avoid undue inducement. In the consent procedure, detailed information on potential risks and benefits was offered at the outset. The variation in the languages spoken among clients created a risk that some participants would not fully understand the information. To control this, the protocol directed enumerators to read the information sheet and the consent form aloud at each interview, in order to ensure that illiteracy did not preclude participants from having complete information. Clients were then asked questions to ensure they understood the content. If, in the judgment of the interviewer, a client was not sufficiently fluent in the language, the interview was rescheduled with an interpreter. The potential harms in

participation were largely related to discomfort in giving a blood sample, and the possibility of anxiety or emotional discomfort while providing responses relating to illness and treatment. These risks were not considered substantial, nor were the potential harms considered extremely serious [9]. All appropriate precautions were taken to minimise discomfort and medical risk in blood sampling. Efforts included the use of professional phlebotomists in Malaysia and close training and supervision of research assistants who took the dried-blood spot samples in Kenya. In the event that a participant became emotionally distressed, our protocol instructed enumerators to discontinue the interview. In the event of such incidents or upon request, follow-up counselling was made available.

In relation to coercion, a choice to abstain from participation in the study would not have created an unfair choice, as there was no threat to the routine standard of care. In essence, abstention from the study did not affect a participant's status quo. In the event that participants were invited, arrived, but later deemed ineligible for the study, they were still provided with the incentive. A sceptic might press the argument that such research is structurally unethical, to the extent that participant's abject circumstances result in the impossibility that any participation choice could be construed as fair. To press this argument is to advance a view that research among vulnerable individuals who live amidst the deepest structural violence is either an ethical impossibility or ethical only under the most restrictive conditions [8]. However, there are objective and subjective (as participants perceive them) benefits to research that are contingent neither on the presence of incentivised participation, nor on the full realisation of benefits by participants alone. Ideally, the benefits of research accrue to participants by improving their outcomes; however, participants may also see value in research that may not benefit them directly but will help people who may eventually suffer from their condition. The reasonable view is that ethical decisions must balance these legitimate concerns in an effort to avoid undue inducement, such that incentives do not interact with unfortunate circumstances and compromised judgment to create a "a seriously unfavourable risk-benefit ratio that threatens fundamental interests" of the participant [9,10]. Among refugees, HIV-positive individuals, and other vulnerable groups such as conflict-affected and forcibly displaced persons, this balanced view is most appropriate given the value and benefit of research. For forcibly-displaced and conflict-affected groups, a proposed ethical framework has set key benchmarks for ensuring that research is conducted to the highest possible ethical standard [11].

ONGOING WORK AND NEXT STEPS

After the very worrying findings in Kakuma, UNHCR responded by initiating remedial efforts to improve staffing levels, adherence counselling and support, and client follow-up in advance of potential regimen switches. Decisions to switch regimens will be based on algorithms

provided in the *Kenya National Clinical Manual for ART Providers* that use viral load and serial CD4 measurements to govern switching decisions. According to this algorithm, clients with a viral load ≥10,000 copies/mL will have their adherence reviewed and changed to second line treatment. After implementing remedial measures in the program including enhancement of adherence support and client follow-up, UNHCR has agreed to confirm treatment failures with a second viral load and to fund drug resistance tests among these clients. Led by the HIV Laboratory at the KEMRI (Kisumu), this additional work will elucidate which resistance mutations, if any, are causing the widespread treatment failure and will assist with the choice of second line regimens. Phylogenetic work will also be undertaken in order to shed light on the relatedness of circulating viral sub-types and to check the possibility that resistance was disproportionately transmitted, rather than acquired.

The candidate also conducted in-depth interviews with providers that have not been analysed or presented for the thesis. They will be analysed as soon as possible, with the aim of examining provider perspectives on the challenges faced by the study groups in relation to adherence.

In addition to this ongoing work, I recommend that interventions to improve the proportion successfully achieving viral suppression in Kakuma are documented and evaluated in detail within a before-after study that also assesses adherence. This would involve administering a new questionnaire to assess self-reported adherence, risk factors and taking a further set of viral load samples to confirm treatment failures.

FINAL THOUGHTS

This was a complex project in logistical terms and four of these complications deserve to be outlined for future researchers who may pursue related questions. First, UNHCR's logistical and financial support for this project was essential. However, there were trade-offs in collaboration, and these were made more acute given the nature and objectives of the PhD when contrasted with professional assessments or evaluations. UNHCR's programme evaluations are usually short-term and aim for sufficiency. On the other hand, a PhD requires a depth study that consists of components of an evaluation, but much more detail and depth than a typical programmatic evaluation would include. All stakeholders were very keen that the work should include studies in more than one setting, and were concerned about the time commitments involved. In retrospect, preparation time, ethics procedures, research clearances, ethics approvals and preparatory work in two settings using a mixed methods approach, was excessively time consuming; however, little could be done to rectify this situation without taking undue risks in relation to the rigour and thoroughness of the work.

As much as the study methods were reasonably straight forward, the politics and logistics were not. From the PhD perspective, the post-election environment in Kenya, instability in Sudan, and their potential effects on Kakuma, amounted to a threat that the field period would coincide with a political development that could severely delay or render the work altogether unfeasible. This risk put additional pressure on fulfilling a rigorous, defensible study in Malaysia as the thesis centrepiece and more time was taken in Malaysia in response to this risk. After Malaysia, an effort was made to delay the Kenya sub-study until doctoral requirements were fulfilled; however, this was not acceptable due to the consultancy agreement that had previously been negotiated. UNHCR can use a "nil consultancy agreement" with a PhD student in which the consultant (PhD student) receives expenses but no fee, but these are not allowed by UNHCR rules with non-students. This agreement was initially negotiated over six months through a Memorandum of Understanding (a copy may be found in Registry or upon request from the candidate). With the nil-consultancy, the contract would have required an open bidding process which would have added cost and amounted to a substantial change to the structure of the project. Fortunately, in the end, all were very satisfied with the project outputs.

Second, there were considerable delays in receiving all the approvals needed for the research; approximately four months in Kenya, and in excess of 8 months in Malaysia. The difference in clearance times between the two countries was large due to refugee politics. The ethics clearance in Malaysia was delayed as a result of concerns linked to uncertain and contested domestic refugee policy. Malaysia has not signed the Refugee Convention, yet the Government actively cooperates with UNHCR to manage refugee issues. Moreover, governmental Ministries and Units including the Ministry of Health and branches of law enforcement, defer to Home Ministry authority on issues of immigration or refugee policy. This dynamic engenders some bureaucratic gray areas where jurisdictions overlap. An ambiguous ethical approval was issued by the national Ethics Committee, which stated "From the ethical aspects of the study design, the MREC [National Ethics Committee] has no objection to the conduct of the study. However there are sensitive issues pertaining to this study in relation to refugees status and its association with national security issues; the concern on the interpretation of the study and its findings especially future presentation, utilization, and dissemination of the findings." After months of delay, an agreement was reached to sanction a final, unambiguous ethical clearance, where an official in the Ministry of Health agreed to act as the liaison between the Home Ministry, the Ministry of Health, UNHCR, and the Study.

Third, there were distinct challenges pertaining to study implementation in each field setting. In Malaysia, it was decided to recruit refugees on the day of their normal clinic appointments which occurred only once per week, and, similarly, to restrict host community recruitment to a second day per week (nationals have three days per week available for appointments). This

decision was taken with consideration for the wide variety of languages spoken, the costs of assembling a full team to cover a range of languages each day with the possibility of low turnout by a single language group on any particular day, and the desire to balance the time to full recruitment between groups. In hindsight, the work could have been accelerated by actively recruiting refugees and interviewing them on multiple days per week (and doing the same for the host community). However, slowing down the work in the early stages allowed us to debrief as a team thoroughly at the end of each interview day and to make appropriate adjustments to any aspects of the protocol that were not functioning efficiently. Later in the study, we adopted an active recruitment protocol to accelerate the work in the face of pressing deadlines. In doing so, it became clear that using the normal clinic appointments was in fact the safest way to approach refugees and to ensure they were eligible. Inviting ineligible refugees on days where they did not have a scheduled appointment was asking them to sacrifice potential wages and placed them at increased risk of arrest while in transit to the clinic. In Kenya, the challenges were of a different sort, and largely more physical in nature. The environment is harsh in Kakuma, and research interviews took place in UNHCR-issued tents equipped with chairs and fans. Temperatures in the tents were typically very high and when the winds picked up the tents were coated inside and out with grit. Refreshments were provided to participants during interviews but the conditions in relation to heat and comfort were not ideal. Incentivising home-based care workers allowed us to effectively track and recruit both refugees and the host community, who sometimes lived as far away as Lodwar (40 kms from Kakuma). It is typical for the Turkana to walk great distances, and our Turkana home-based care colleagues would often walk ("foot" in their terms) considerable distances in an evening after a regular day of work in order to contact prospectively study-eligible clients or to discreetly enquire about their whereabouts.

Lastly, the thesis took a mixed methods approach, which brought accompanying challenges. Mixed methods are rewarding but complicated to undertake with a large research team in relatively short periods of time. In this particular study, I do not think the mixed methods approach compromised depth of either method as significant time was spent collecting and analysing both the quantitative and qualitative components; however, this approach added time to the study overall. It seemed that one method would have been limiting. On the one hand, a survey-only study would have precluded more intimate contacts with clients who were able to provide important insights into the barriers and facilitators of adherence that they faced. An exclusively qualitative study would have made it impossible to measure treatment outcomes, a key objective of the study. The learning curve for each method, both for the candidate and for the local staff, however, did cost additional time in preparation and training both before and during fieldwork due to inexperience methods and a decision taken to conduct qualitative

interviews outside of the clinic in Malaysia in order to create a more casual interview environment (this option was not practical in Kenya).

CONCLUSION

Refugees have a right to equal access to HIV treatment based on the principles of fairness and human rights, and this access will help confer both individual and population-based public health benefit. Given limited resources for expanding treatment, questions have been raised as to whether this group would achieve sufficient levels of adherence and viral suppression to justify sustaining and expanding their access. Equitable and acceptable treatment outcomes had previously been found in a range of settings serving forcibly displaced clients. However, most of the studies that had been performed were among populations who were conflict-affected, internally-displaced, or among refugees based in high income countries. The present study added to the evidence by showing that refugees residing in asylum were capable of treatment success, and when problems achieving and sustaining viral suppression occurred, they were not due to previous forced displacement or to refugee status itself. To remedy or prevent occurrences of virological failure where refugees access treatment, interventions ought to be implemented for both refugee and host communities wherever necessary. Evidence from Malaysia suggested that men, clients with documented sub-optimal adherence to pharmacy prescription refills, shorter time from diagnosis to HAART start, clients who had temporarily migrated for $\geq$1 consecutive month in the past year, and those who spend $\geq$1 hour in transit to the clinic had increased odds of having an unsuppressed viral load and should be targeted for intervention. Meanwhile, in Kakuma, smaller household sizes were associated with lack of virological suppression. The weak evidence for an association of this outcome with self-reported underdosing by clients was also suggestive of intervention opportunities. Since HIV-positive individuals on HAART with good adherence will rarely transmit HIV to their sexual partners [12], it is in the enlightened self-interest of host country governments to support HIV programs that serve HIV-positive refugees and host clients equally. There is a clear public health and humanitarian interest in guaranteeing access to ART, promoting optimal adherence and sustaining viral suppression in these vulnerable groups.

References

1. Garang PG, Odoi RA, Kalyango JN (2009) Adherence to antiretroviral therapy in conflict areas: a study among patients receiving treatment from Lacor Hospital, Uganda. AIDS Patient Care STDS 23: 743-747.

2. Bisson GP, Rowh A, Weinstein R, Gaolathe T, Frank I, et al. (2008) Antiretroviral failure despite high levels of adherence: discordant adherence-response relationship in Botswana. J Acquir Immune Defic Syndr 49: 107-110.

3. Trotta MP, Pierro P, Marconi P, Sette P, Zaccarelli M, et al. (2011) With current ARV treatments virological failure mostly occurs in the context of optimal self-reported adherence. Infection 39: S27-S28.

4. Tesoriero J, French T, Weiss L, Waters M, Finkelstein R, et al. (2003) Stability of adherence to highly active antiretroviral therapy over time among clients enrolled in the treatment adherence demonstration project. J Acquir Immune Defic Syndr 33: 484-493.

5. Sax PE, Baden LR (2009) When to start antiretroviral therapy -- Ready when you are? N Engl J Med 360.

6. Kitahata MM, Gange SJ, Abraham AG, Merriman B, Saag MS, et al. (2009) Effect of early versus deferred antiretroviral therapy for HIV on survival. N Engl J Med 360: 1815-1826.

7. NIAID (2012) Strategic Timing of Antiretroviral Treatment. Retrieved on 10 September 2012 http://www.niaid.nih.gov/volunteer/hivandinfectious/hivstudies/Pages/STARTStudy.aspx

8. Leaning J (2001) Ethics of research in refugee populations. Lancet 357: 1432-1433.

9. Emanuel EJ, Currie XE, Herman A (2005) Undue inducement in clinical research in developing countries: is it a worry? Lancet 366: 336-340.

10. Emanuel EJ (2004) Ending concerns about undue inducement. J Law Med Ethics 32: 100-105.

11. Ford N, Mills EJ, Zachariah R, Upshur R (2009) Ethics of conducting research in conflict settings. Confl Health 3:7.

12. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, et al. (2011) Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med 365: 493-505.

APPENDICES

APPENDIX A

MALAYSIA DATA COLLECTION FORMS AND TOPIC GUIDES

Eligibility and Registration Form: Adherence to HAART in Refugee and Host Communities (Sections 1-6)

INSTRUCTIONS:

1. Engage warmly with the client in front of you.
2. Ask questions as they are written on the page. "Be sure to read all the additional prompts in quotation marks."
3. [Follow all **bold** instructions in square brackets. Do not read them out loud.]
4. Where "Other" is specified, remember to specify.
5. After asking a question, be sure to prompt with response options unless it is indicated **[do not prompt]**. Circle any response given unless it is indicated **[circle only one]**.
6. Where applicable, circle or write in boxes, or write in the right-hand margin: 77=Not applicable; 88=Declined to answer; 99=Do not know . Never prompt with these options.

01.00	**[Administration only]** Client Code: 1B-YYYY = 1☐-☐☐☐	
	Refugee B=1 Participant =000-499 Host B=2 Non-participant =500-999	
SECTION 1: Identification		
01.01	Interviewer **[Enter your researcher code]**	☐☐
01.02	Today's date	(dd/mm/yyyy) ☐☐/☐☐/20☐☐
	[Skip to Q 02.01]	
01.03	Data entry 1 **[Enter your researcher code]**	☐☐
01.04	Date of data entry 1	(dd/mm/yyyy) ☐☐/☐☐/20☐☐
01.05	Data entry 2 **[Enter your researcher code]**	☐☐
01.06	Date of data entry 2	(dd/mm/yyyy) ☐☐/☐☐/20☐☐

SECTION 2: Language

02.01	What is your mother tongue? **[circle only one and do not prompt]**	English	01	Shan	11
		Bahasa Malaysia	02	Burmese	12
		Tamil	03	Hakka/Lai	13
		Mandarin	04	Cantonese	14
		Kachin	05	Tedim	15
		Karenni	06	Mizo	16
		Poe Karen	07	Falam	17
		Sagaw Karen	08	Hokkien	18
		Mon	09	Other (Specify:_____)	50
		Arakan	10		

02.02	Are you able to understand and to express yourself in one of Bahasa Malaysia, Tamil, Mandarin, Burmese, or English?	No	0
		Yes	1
02.03	**[Researcher only]** Will an interpreter be required? **[If YES, ask client to wait and see Coordinator – Interview will be rescheduled]**	No	0
		Yes	1

02.04	**[Researcher only]** Interview to be conducted in: **[circle only one and do not prompt]**	English	01	Shan	11
		Bahasa Malaysia	02	Burmese	12
		Tamil	03	Hakka/Lai	13
		Mandarin	04	Cantonese	14
		Kachin	05	Tedim	15
		Karenni	06	Mizo	16
		Poe Karen	07	Falam	17
		Sagaw Karen	08	Hokkien	18
		Mon	09	Other (Specify:_____)	50
		Arakan	10		

SECTION 3: Information Sheet

[Give the client a copy of the information form. Read the information form out loud. Offer the client a drink.] "Do you have any questions?"

03.01	**[Researcher only]** Has the client read/heard the information sheet?	No	0
		Yes	1
03.02	Are you willing to participate? **[If YES, go to Section Q 04.01. If NO, end]** "Thank-you."	No **[Skip to Q 06.01]**	0
		Yes	1

SECTION 4: Eligibility

04.01	**[Researcher only]** Gender	Male	1
		Female	2
		Transgender/transexual	3

[77=Not applicable; 88=Declined to answer; 99=Do not know]

04.02	Date of birth	(dd/mm/yyyy) ☐☐/☐☐/☐☐☐☐
04.03	Age **[Calculate from Q 04.02 and verify with client IC or UNHCR card]**	☐☐ years
04.04	**[Researcher only]** Respondent >=18 years of age? **[If NO, explain why they cannot be included in the study and end the interview]** "Thank-you."	No **[End]** 0 Yes 1
04.05	What day, month and year did you start on HAART?	(dd/mm/yyyy) ☐☐/☐☐/☐☐☐☐
04.06	**[Researcher only]** Was HAART initiated >=30 days before today? **[If NO, explain why they cannot be included in this study and end the interview]** "Thank-you."	No **[End]** 0 Yes 1
04.07	Do you normally pick-up your HAART from this clinic and/or the Standard Pharmacy in Kuala Lumpur?	No 0 Yes 1
04.08a	Have you ever picked up your HAART from someplace else?	No **[Skip to Q 04.09]** 0 Yes 1
04.08b	Specify last date of pick-up from other pharmacy: (dd/mm/yyyy) ☐☐/☐☐/☐☐☐☐ Specify pharmacy/clinic:_____ Specify city:_____	
04.09	What is your current nationality/country of citizenship? If you have neither please list your country of origin.	Malaysian 01 Burmese 02 Indonesian 03 No citizenship 15 Other (Specify:_____) 16
04.10	Does the client have Malaysian citizenship? **[Check with Identify Card]**	No 0 Yes **[Skip to Q 05.01]** 1
04.11	Do you currently have refugee status in Malaysia? **[Check with UNHCR Card]**	No 0 Yes 1
[If YES to either Q 04.10 or Q 04.11, candidate is eligible to participate. Go to next section, Q 05.01. If NO to both questions, explain why they cannot be included in the study and end the interview.] "Thank-you"		

[77=Not applicable; 88=Declined to answer; 99=Do not know]

SECTION 5: Informed Consent

[Give the client a copy of the consent form. Read the consent form out loud.] "Do you have any questions?"

05.01	**[Researcher only]** Has client heard/read the consent form?	No	0
		Yes	1
05.02	**[Researcher only]** Did the client agree to participate by signing the consent form?	No	0
		Yes	1

[If YES to Q 05.02, go to MAIN Questionnaire, Q 07.01] "Thank-you. Let's start the main questionnaire."

[If NO to Q 05.02, go to Q 06.01] "Before you go, may I ask you just a few quick questions?"

SECTION 6: Reasons for Non-Participation

06.01	**[If NO to Q 05.02]** Why did you decide not to participate? This is important for us to know so we can improve future studies. **[Do not prompt and circle all that apply]**	Not interested in the study	1
		Did not have time	2
		Did not understand information about the study	3
		Not comfortable, but do not know why	4
		Other (Specify:_____)	5
		Declined to answer	88
06.02	**[Researcher only]** If the client was unable or incapable of giving informed consent or answering the questionnaire, why?	Disability	1
		Language difficulties	2
		Other (Specify:_____)	3
		Do not know	99

END.

[77=Not applicable; 88=Declined to answer; 99=Do not know]

Follow-up Form: Adherence to HAART in Refugee and Host Communities

Contact details		
00.xx	Client code [Transcribe from Form 1]:	1☐-☐☐☐
00.01	IC/UNHCR No.	☐☐☐☐☐☐☐☐☐☐☐☐
00.02	Sungai Buloh No.	☐☐☐☐☐☐☐
00.03	Telephone No (Home):	
00.04	Telephone No (Mobile):	
00.05	Email:	
00.06	Street number:	
00.07	Street name:	
00.08	Flat or apartment number:	
00.09	City:	
00.10	Post code:	

***Make sure to list 2 contact telephone numbers (e.g. mobile + friend's mobile or mobile + home etc.)**

Main Form: Adherence to HAART in Refugee and Host Communities (Sections 7-12)

INSTRUCTIONS:

1. Engage warmly with the client in front of you.
2. Ask questions as they are written on the page. "Be sure to read all the additional prompts in quotation marks."
3. [Follow all **bold** instructions in square brackets. Do not read them out loud.]
4. Where "Other" is specified, remember to specify.
5. After asking a question, be sure to prompt with response options unless it is indicated **[do not prompt]**. Circle any response given unless it is indicted **[circle only one]**.
6. Where applicable, circle or write in boxes, or write in the right-hand margin: 77=Not applicable; 88=Declined to answer; 99=Do not know. Never prompt with these options.

SECTION 7: Identification		
07.xx	Client code **[Transcribe from Form 1]**	1☐-☐☐☐
07.01	Interviewer **[Enter your researcher code]**	☐☐
07.02	Date of interview	(dd/mm/yyyy) ☐☐/☐☐/20☐☐
	[Skip to Q 08.01]	
07.03	Data entry 1 **[Enter your researcher code]**	☐☐
07.04	Date of data entry 1	(dd/mm/yyyy) ☐☐/☐☐/20☐☐
07.05	Data entry 2 **[Enter your researcher code]**	☐☐
07.06	Date of data entry 2	(dd/mm/yyyy) ☐☐/☐☐/20☐☐

SECTION 8: Socio-Demographic and Background Information

"Many thanks for participating in this study. Before we get started, would you like something to drink? We will then begin by asking you some basic questions about yourself."

08.01	In which country were you born? **[circle only one]**	Burma	01
		Malaysia	02
		Indonesia	03
		Other (Specify:_____)	15
08.02	What is your religion? **[circle only one]**	Catholic	01
		Other Christian	02
		Muslim	03
		Hindu	04
		Buddhist	05
		Other (Specify:_____)	11
08.03	What is your current marital and/or relationship status? **[circle only one]**	Currently married or living as married, 1 spouse	01
		Currently married or living as married, >1 spouse	02
		Not married, currently in a relationship with 1 person	03
		Current ly married, living as married, and/or in a relationship with >1 person	04
		Divorced/separated from marriage and currently single	05
		Widowed and currently single	06
		Single	07
08.04	What type of accommodation do you currently live in? **[circle only one]**	Private house or apartment	01
		Dormitory	02
		Tent	03
		Guest house/hotel	04
		None	05
		Other (Specify:_____)	06
08.05	How many people live with you in your current household? By household, I mean one person or a group of persons who usually live and eat together.		☐☐☐
08.06	What are your average weekly household earnings (include any salary, subsidy, allowance, or grant)?	Malaysian Ringgits:	☐☐☐☐.☐☐
08.07	Do you currently work for pay outside or inside the home? **[circle only one]**	No	0
		Yes	1
08.08	Do you currently have children? **[circle only one]**	No **[Skip to Q 08.10]**	0
		Yes	1
08.09	If you have children, how many currently live with you in the same household?	Record number:	☐☐

[77=Not applicable; 88=Declined to answer; 99=Do not know]

08.10	How would you rate your current standard of living? **[circle only one]**			Very poor Poor Average Good Very good	1 2 3 4 5
[If client is NOT currently a refugee - refer to Q 04.11 - SKIP to Q 08.14]					
08.11	What month/year did you enter this country?			(mm/yyyy) ☐☐/☐☐☐☐	
08.12	What month/year did you gain refugee status?			(mm/yyyy) ☐☐/☐☐☐☐	
08.13	How would you rate your standard of living prior to leaving your home country? **[circle only one]**			Very poor Poor Average Good Very good	1 2 3 4 5
08.14	In the last 12 months have you been away from the city where you currently live for one continuous month or more? **[circle only one]**			No **[Skip to Q 08.16]** Yes	0 1
08.15	If yes, what was the main reason why you were away from this city for one month or more? **[Do not prompt and circle only one]**	Employment Trade Family-related Political reasons Conflict-related Education-related	01 02 03 04 05 06	Prison or detention in country Health-related Religion-related Holiday Deportation Other (Specify: _____)	07 08 09 10 11 12
08.16	What is the highest level of education you have completed? **[circle only one]**			Have never attended school Did not complete primary education Completed primary Some secondary but did not complete it Completed secondary Some college or university but did not complete it Completed college or university	01 02 03 04 05 06 07
08.17	How often have you visited this clinic (Sungai Buloh Hospital) for any reason within the past 3 months? **[circle only one]**			10 times or more 7-9 times 4-6 times 1-3 times Never	1 2 3 4 5
08.18	How often do you collect your HAART medication from this clinic (Sungai Buloh Hospital)? **[circle only one]**			Always Most of the time Some of the time Never	1 2 3 4

08.19	When were you diagnosed as having HIV?	(mm/yyyy) ☐☐/☐☐☐☐	
08.20	In which country were you diagnosed as having HIV? **[circle only one]**	Your home country	1
		This host country	2
		Other (Specify:_____)	3
08.21	Is HIV a virus that lives inside your body? **[circle only one]**	No	0
		Yes	1
		Do not know	99
08.22	Does the HIV virus cause AIDS? **[circle only one]**	No	0
		Yes	1
		Do not know	99
08.23	Why did you originally seek an HIV test? **[Do not prompt]**	Voluntary test as general precaution	01
		Voluntary test recommended by a health care provider	02
		Mandatory test	03
		Fear of exposure to HIV	04
		Symptoms such as fatigue weight loss, etc.	05
		Other (Specify: _____)	06

REFERENCE FOR RESEARCHER ONLY: STANDARD HAART PRESCRIBED

#	Trade name	Generic name	Typical regimen
01	Combivir	lamivudine/zidovudine	One tablet (150 mg lamivudine + 300 mg zidovudine) twice a day. May be be taken with or without food.
02	SLN 30	stavudine/lamivudine/ nevirapine	One tablet (30 mg stavudine + 150 mg lamivudine + 200 mg nevirapine) twice a day. May be taken with or without food.
03	Nevipan	nevirapine	One 200 mg tablet daily for the first 14 days, followed by one 200 mg tablet twice a day. May be taken with or without food.
04	Stocrin	efavirenz	One 600 mg tablet once a day before bedtime. May be taken with or without food.
05	Crixivan	indinavir	Two 400 mg capsules, three times a day. Taken 1 hour before or 2 hours after meal. (At least 2 liters of liquid should be consumed every 24 hours.)
06	Norvir	ritonavir	If taken in combination with Crixivan: Crixivian two 400 mg capsules twice a day and Norvir 1 capsule twice a day. May be taken with or without food.
07	Kaletra	lopinavir/ritonavir	Three (133.3 mg lopinavir + 33.3 mg ritonavir) capsules twice a day. Take with food.
08	Videx EC 250 mg	didanosine (enteric-coated)	One 250 mg capsule, once a day for patients <=60kg. To be taken on empty stomach.
09	Videx EC 400 mg	didanosine (enteric-coated)	One 250 mg capsule, once a day for patients >=60kg. To be taken on empty stomach.
10	Retrovir	zidovudine (AZT)	Three 100 mg capsules, twice a day. May be taken with or without food.
11	Virostav	Stavudine (d4T)	One 30 mg capsule, twice a day. May be taken with or without food.
12	3TC	Lamivudine (3TC)	One 150 mg tablet, twice a day. May be taken with or without food.
13	ddI Tablet (Videx)	Didanosine (ddI)	Three 100 mg tablets, once a day for patients <=60kg. Four 100 mg tablets once a day for patients >=60kg or two 100 mg tablets twice a day. To be taken on empty stomach.

SECTION 9: HAART Medications, Adherence, and Side-Effects

[Complete this worksheet with the client. If possible, identify regimen in advance. Otherwise, compare with record such as medical records, medication card, or physical medication. Reconcile any differences with the client.]

09.01 Please help us to identify the HAART medications you are currently taking, doses, pills per dose, and doses per day.
[All future questions relating to medication are in relation to THESE medications. Complete Steps 1-5 below for each HAART medication currently used by the client.]

Step 1 HAART trade name [Circle number only and all that apply]	Step 2 Dose (mg) (per tablet)	Step 3 No. times per day (doses per day)	Step 4 No. pills each time	Step 5 Confirmed with records? (0=No; 1=Yes)
Combivir 01	☐☐☐	☐	☐	☐
SLN 30 02	☐☐☐	☐	☐	☐
Nevipan 03	☐☐☐	☐	☐	☐
Stocrin 04	☐☐☐	☐	☐	☐
Crixivan 05	☐☐☐	☐	☐	☐
Norvir 06	☐☐☐	☐	☐	☐
Kaletra 07	☐☐☐	☐	☐	☐
Videx EC(250mg) 08	☐☐☐	☐	☐	☐
Videx EC(400mg) 09	☐☐☐	☐	☐	☐
Retrovir 10	☐☐☐	☐	☐	☐
Virostav 11	☐☐☐	☐	☐	☐
3TC 12	☐☐☐	☐	☐	☐
Ddl Tablet 13	☐☐☐	☐	☐	☐
Other1 14	☐☐☐	☐	☐	☐
Other2 15	☐☐☐	☐	☐	☐
Other1 (Specify):				
Other2 (Specify):				

09.02 **[Researcher only]** Was the client able to list ALL of their HAART medications without assistance?

No 0
Yes 1
Not applicable (records unavailable) 77

[77=Not applicable; 88=Declined to answer; 99=Do not know]

"Most people with HIV have many pills to take at different times during the day. Many people find it hard to always remember their pills. Some people get busy and forget to carry their pills with them; some people find it hard to take their pills according to all the instructions such as "with meals" or "on an empty stomach", "every 8 hours", "with plenty of fluids"; some people decide to skip pills to avoid side effects or for other reasons. We need to understand how people with HIV are really doing with taking their HAART pills. Please tell us what you are actually doing. Do not worry about telling us that you do not take your pills. We need to know what is really happening, not what you think we "want to hear." This information will not be reported to anyone and is strictly confidential. This section of the questionnaire asks about the medications that you may have missed taking over last four days prior to today. If you took only a portion of a dose (for example, you missed taking one pill in the morning) please report that dose(s) as being missed."

09.03 **[Complete the table below with the client, using one line for each HAART medication the client is supposed to be taking, and using the names/codes from Q 09.01. If client did not miss any doses, write a zero (0). Note that the table asks about DOSES, NOT PILLS. If client responds that they took only a portion of a dose on one or more of these days, please report the dose(s) as being missed. Prompt in reverse time order.]**

Step 1 [List trade name and numeric code from Q 09.01] "The HAART medicines you take are..."	**Step 2** Doses missed yesterday (1 day ago):	**Step 3** Doses missed the day before yesterday (2 days ago):	**Step 4** Doses missed 3 days ago:	**Step 5** Doses missed 4 days ago:
i. _____ ☐☐	☐☐ doses	☐☐ doses	☐☐ doses	☐☐ doses
ii. _____ ☐☐	☐☐ doses	☐☐ doses	☐☐ doses	☐☐ doses
iii. _____ ☐☐	☐☐ doses	☐☐ doses	☐☐ doses	☐☐ doses
iv. _____ ☐☐	☐☐ doses	☐☐ doses	☐☐ doses	☐☐ doses

09.04	During the past 4 days, on how many days have you missed taking all your doses? **[circle only one]**	None	1
		One day	2
		Two days	3
		Three days	4
		Four days	5
09.05	Most HAART medications need to be taken on a schedule, such as '2 times a day' or '3 times a day' or 'every 8 hours.' How closely did you follow your specific schedule over the last four days? **[circle only one]**	Never	1
		Some of the time	2
		About half of the time	3
		Most of the time	4
		All of the time	5
09.06	Do any of your study medications have special instructions, such as "take with food" or "on an empty stomach" or "with plenty of fluids"? **[circle only one]**	No **[Skip to Q 09.08]**	0
		Yes	1
		Do not know	99

[77=Not applicable; 88=Declined to answer; 99=Do not know]

09.07	If yes, how often did you follow those special instructions over the last four days? **[circle only one]**	Never	1
		Some of the time	2
		About half of the time	3
		Most of the time	4
		All of the time	5
09.08	On special days when people do not work, such as days off work or weekend days, some people find that they forget to take their pills. Did you miss any of your HAART pills during your last weekend/day off? **[circle only one]**	No	0
		Yes	1
09.09	When was the last time you missed any of your medications? **[circle only one]**	Within the past week	01
		1 – less than 2 weeks ago	02
		2 – less than 4 weeks ago	03
		1 – less than 3 months ago	04
		3 months or more ago	05
		Never skip medications	06
09.10	Have you experienced any ill health since starting HAART? **[circle only one]**	No **[Skip to Q 09.33]**	0
		Yes	1

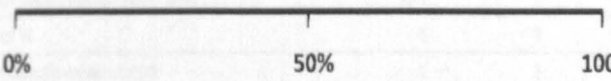
If yes, what symptoms have you experienced in the last 4 weeks?		**I have not had this symptom during the past 4 weeks**	**I have had this symptom during the past 4 weeks**
09.11	Fatigue or loss of energy?	0	1
09.12	Fevers, chills or sweats?	0	1
09.13	Feeling dizzy or lightheaded?	0	1
09.14	Pain, numbness or tingling in the hands or feet?	0	1
09.15	Trouble remembering things?	0	1
09.16	Nausea or vomiting?	0	1
09.17	Felt sad, down, or depressed?	0	1
09.18	Felt nervous or anxious?	0	1
09.19	Difficulty falling or staying asleep?	0	1
09.20	Skin problems, such as rash, dryness or itching?	0	1
09.21	Cough or trouble breathing?	0	1
09.22	Headache?	0	1
09.23	Loss of appetite or a change in the taste of food?	0	1
09.24	Bloating, pain or gas in your abdomen?	0	1
09.25	Muscle aches or joint pain?	0	1
09.26	Problems with having sex, such as loss of interest or lack of satisfaction?	0	1
09.27	Changes in the way your body looks, such as fat deposits or weight gain?	0	1
09.28	Problems with weight loss or wasting?	0	1

[77=Not applicable; 88=Declined to answer; 99=Do not know]

09.29	Hair loss or changes in the way your hair looks?	0	1
09.30	Mouth ulcers or difficulty swallowing?	0	1
09.31	Other	0	1
09.32	Specify Other: _____		

09.33 **[Remind client that the information they provide will not be reported to anyone. Remind client of the medications they listed in Q 09.01. Turn the page around to face the client.]**

"Put a cross **(X)** on the line below at the point showing your best guess about how much HAART medication you have taken in the last month, e.g. 0% means you have taken no medication; 50% means you have taken half your medication; 100% means you have taken every single dose of medication. We would be surprised if this was 100% for most people."



SECTION 10: Reasons and Barriers

"Thank-you. Let's continue. How much do you believe that..."		[circle only one] Not at all	A little bit	Very	Extremely
10.01	You are able to take all or most of your medication as directed?	1	2	3	4
10.02	The medication will have a positive effect on your health?	1	2	3	4
10.03	If you do not take your medication exactly as instructed, the HIV virus in your body will become resistant to HIV medications?	1	2	3	4

10.04	In general, how satisfied are you with the support you get from your friends and family members? **[circle only one]**	Extremely satisfied	1
		Satisfied	2
		Dissatisfied	3
		Very dissatisfied	4
10.05	To what extent do your friends and/or family members help you remember to take your medication? **[circle only one]**	Not at all	1
		A little	2
		Somewhat	3
		A lot	4

"People may miss taking their medications for various reasons. What are the main reasons why you ever miss taking your HAART?"		[circle only one] Never	Rarely	Sometimes	Often
10.06	Away from home	1	2	3	4
10.07	Busy with other things (e.g. at home or at work)	1	2	3	4
10.08	Simply forgot	1	2	3	4
10.09	Have too many pills to take	1	2	3	4
10.10	Want to avoid side effects	1	2	3	4
10.11	Not want others to notice you taking medication	1	2	3	4
10.12	Have a change in daily routine	1	2	3	4
10.13	Feel like the drug was toxic/harmful	1	2	3	4
10.14	Fall asleep/slept through dose time	1	2	3	4
10.15	Feel sick or ill	1	2	3	4
10.16	Feel depressed/overwhelmed	1	2	3	4
10.17	Have problem taking pills at specified times (e.g. with meals, on empty stomach, etc.)	1	2	3	4
10.18	Run out of pills	1	2	3	4
10.19	Detained or incarcerated by the authorities	1	2	3	4
10.20	Difficulty concentrating	1	2	3	4
10.21	Feeling irritable or having outbursts of anger	1	2	3	4
10.22	Less interest in daily activities	1	2	3	4
10.23	Feeling that you have less skills than you had before	1	2	3	4
10.24	Having difficulty dealing with new situations	1	2	3	4
10.25	Feeling unable to make daily plans	1	2	3	4
10.26	Worrying too much about things	1	2	3	4
10.27	Feeling hopeless about the future	1	2	3	4
10.28	Detention or prison without my HAART	1	2	3	4
10.29	Other "Can you think of any other reasons that were not mentioned?"				
	i._____	1	2	3	4
	ii._____	1	2	3	4
	iii._____	1	2	3	4

The following questions ask about your alcohol and drug use. Please be honest in your answers. We will not report what you say to anyone.

10.30	How often have you had a drink containing alcohol (e.g. beer, rice wine, liquor, samsu, tapai) in the last 30 days? **[Prompt with examples of local drinks and circle only one]**	Daily	01
		5 or 6 times per week	02
		3 or 4 times per week	03
		1 or 2 times per week	04
		2 or 3 times in the past month	05
		Once in the past month	06
		Never **[Skip to Q 10.32]**	07
10.31	During the past 30 days, how often have you had 5 or more drinks of alcohol in a row, that is, within a few hours (eg. 2-4 hours)? **[circle only one]**	Daily	01
		5 or 6 times per week	02
		3 or 4 times per week	03
		1 or 2 times per week	04
		2 or 3 times in the past month	05
		Once in the past month	06
		Never	07
10.32	Have you ever used an illegal drug or not illegal but potentially harmful or unprescribed drug (e.g. heroine, marijuana, valium, glue sniffing, etc)? **[Prompt with examples of commonly used drugs and circle only one]**	No **[Skip to Q 10.34]**	0
		Yes	1

			Rarely (<=1/week)	Often (>=2/week)
10.33	List the three illegal drugs or potentially harmful (but not illegal) drugs that you have used most often within the last 6 months. **[If none, leave blank]**	Drug i:_____	0	1
		Drug ii:_____	0	1
		Drug iii:_____	0	1

10.34	Have you visited a alternative/traditional/herbal medicine practicitioner in the past 6 months? **[circle only one]**	No	0
		Yes	1
10.35	Have you used alternative/traditional/herbal treatments or practices (herbs, teas, pills, spells etc.) within the past 6 months? **[circle only one]**	No **[Skip to Q 10.37]**	0
		Yes	1
10.36	Have you ever used alternative/traditional/herbal treatments instead of HAART to treat your HIV infection? **[circle only the most recent one]**	Never	1
		Yes, in the past 4 days	2
		Yes, in the past week	3
		Yes, in the past 4 weeks	4
		Yes, in the past 6 months	5

"To what extent are the following statements true?"		[circle only one] Not true	Sometimes true	Often true
10.37	I can't afford to eat properly.	1	2	3
10.38	I am often hungry but I don't eat because I can't afford enough food.	1	2	3
10.39	I eat less than I think I should because I don't have enough money for food.	1	2	3
10.40	**[Skip to Q 11.01 if client has no children]** I cannot give my child(ren) a balanced meal because I can't afford that.	1	2	3

SECTION 11: Patient-Provider Relationship, Clinic, and Social Trust

"Thinking about the doctor that prescribes your HAART medication, how much do you trust that..."		[circle only one] Strong disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
11.01	He/she offers the best medical care they can provide?	1	2	3	4	5
11.02	He /she wants to give you the best care possible?	1	2	3	4	5

11.03	Which of the following health care providers do you interact with most often? **[circle only one]**	HAART doctor **[Skip to Q 11.06]**	01
		Nurse	02
		HIV or HAART counsellor	03
		Outreach home-based care	04
		Shelter home-based care	05
		Health coordinator or worker from your community	06
		Other doctor	07
		Other (Specify:_____)	08
		Do not know	99

"Thinking about this person, how much do you trust that..."		[circle only one] Strong disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
11.04	He/she offers the best medical care they can provide?	1	2	3	4	5
11.05	He /she wants to give you the best care possible?	1	2	3	4	5

"The following questions ask about your experience with this clinic in the last month."

11.06	How long, on average, do you spend travelling from your home to this clinic? **[circle only one]**	Less than 30 minutes	1
		30 minutes – less than 1 hour	2
		1 hour – less than 1.5 hours	3
		1.5 hours – less than 2 hours	4
		2 hours or more	5
11.07	Do you incur costs related to taking HAART (e.g. transport to clinic, special diet etc.)? **[circle only one]**	No **[Skip to Q 11.09]**	0
		Yes	1

[77=Not applicable; 88=Declined to answer; 99=Do not know]

11.08	Thinking about the last week (including today), how much did you spend on unsubsidised HAART related-costs like transport to clinic/pharmacy, additional food to your regular diet, or lost wages?	Malaysian Ringgits:	□□□.□□
11.09	In the last three months, have you left the clinic before a scheduled appointment due to the waiting time? **[circle only one]**	No Yes	0 1
11.10	In the last three months, were you ever unable to refill your HAART medication prescription at the pharmacy even if you wanted to? **[circle only one]**	No **[Skip to Q 11.12]** Yes	0 1
11.11	What was the main reason why you were unable to refill your HAART medication? **[Do not prompt]**	It costs too much to go to pharmacy I cannot leave my children alone I cannot miss work or I will be fired I am not motivated I waited too long at the pharmacy The staff at the pharmacy did not understand me The staff at the pharmacy turned me away Fear of being stopped by police if I travel Other (Specify:_____)	01 02 03 04 05 06 07 08 09
The following questions ask you about the people around you...			
11.12	Do you think that most people would try to take advantage of you if they got the chance, or would they try to be fair? **[circle only one]**	Take advantage of you Try to be fair	1 2
11.13	Generally speaking, would you say that most people can be trusted or that you can't be too careful in dealing with people? **[circle only one]**	Most people can be trusted Can't be too careful in dealing with people	1 2
11.14	Have you disclosed your HIV status to your current spouse or sexual partner? **[circle only one]**	No Yes Not applicable	0 1 77
11.15	Have you disclosed your HIV status to other members of your family and/or closest friends? **[circle only one]**	No Yes	0 1
11.16	Have you disclosed your HIV status to others in your community? **[circle only one]**	No Yes	0 1

SECTION 12: Supplementary Adherence Measures

"To finish, I would like to ask you some final questions about your HAART medication. The medications you said that you take are ..." **[Remind client of medications they listed in Q 09.01 and to think about doses e.g. all pills taken at one time. Remind them that all the information they provide will be completely confidential.]**

12.01	In the last month, how often did you take your HAART medications? **[circle only one]**	None of the time	01
		A little of the time	02
		Some of the time	03
		A good bit of the time	04
		Most of the time	05
		All of the time	06
12.02	Please rate your ability to take all your medications as prescribed over the last month. **[circle only one]**	Very poor	01
		Poor	02
		Fair	03
		Good	04
		Very good	05
		Excellent	06
12.03	If you ever interrupted your HAART in the past month for any reason, for how many consecutive days did the longest interruption last? **[circle only one]**	1 day	01
		2 days	02
		3 days	03
		4 days	04
		>4 days	05
		Never interrupted	06
12.04	Were you previously taking a different HAART regimen than the one you are currently taking (including in another place such as another city, province, or another country where you lived in the past)? **[circle only one]**	No **[End]**	0
		Yes	1
		Do not know	99

12.05	If YES to Q 12.03, can you remember the names of those medications that you took previously? **[Prompt client to remember each previous HAART regimen. List one regimen on each line (each pill by trade name or describe pill by shape and colour e.g. Combivir/Stocrin or blue/circular) starting from the most recent regimen prior to current regimen and going backwards in time.]**	Specify:	i. _____
			ii. _____
			iii. _____
			iv. _____

"Thank-you for your participation. Now we will go to the place where you normally give a blood sample."

POST-INTERVIEW INSTRUCTIONS:

1. Check through the questionnaire to make sure nothing was missed or unclear.
2. Make sure you have double-checked their HAART medications with their medication card or medical record.
3. Make sure that the Client Follow-up Form (Form 2) is completed.
4. Place all Forms in a document envelope and make sure the Client Code is written on the front cover.

For use with Q 10.06 – 10.29

NEVER	RARELY	SOMETIMES	OFTEN

[77=Not applicable; 88=Declined to answer; 99=Do not know]

Year	AGE
2010	0
2009	1
2008	2
2007	3
2006	4
2005	5
2004	6
2003	7
2002	8
2001	9
2000	10
1999	11
1998	12
1997	13
1996	14
1995	15
1994	16
1993	17
1992	18
1991	19
1990	20
1989	21
1988	22
1987	23
1986	24
1985	25
1984	26
1983	27
1982	28
1981	29
1980	30
1979	31
1978	32
1977	33
1976	34
1975	35
1974	36
1973	37
1972	38
1971	39
1970	40
1969	41
1968	42
1967	43
1966	44
1965	45
1964	46
1963	47
1962	48
1961	49
1960	50
1959	51
1958	52
1957	53
1956	54
1955	55

Year	AGE
1954	56
1953	57
1952	58
1951	59
1950	60
1949	61
1948	62
1947	63
1946	64
1945	65
1944	66
1943	67
1942	68
1941	69
1940	70
1939	71
1938	72
1937	73
1936	74
1935	75
1934	76
1933	77
1932	78
1931	79
1930	80
1929	81
1928	82
1927	83
1926	84
1925	85
1924	86
1923	87
1922	88
1921	89
1920	90
1919	91
1918	92
1917	93
1916	94
1915	95
1914	96
1913	97
1912	98
1911	99
1910	100
1909	101
1908	102
1907	103
1906	104
1905	105
1904	106
1903	107
1902	108
1901	109
1900	110

[77=Not applicable; 88=Declined to answer; 99=Do not know]

Post-Interview Form: Adherence to HAART in Refugee and Host Communities

INSTRUCTIONS: Where applicable, circle or write 77=Not applicable

SECTION 13: Medical records

13.xx Client code: 1☐-☐☐☐ Sungai Buloh No: ☐☐☐☐☐☐☐

13.01a Date of birth: dd/mm/yyyy ☐☐/☐☐/☐☐☐☐ | 13.01b Age: ☐☐

13.02a Ethnicity: Malay 1, Tamil 2, Chinese 3, Burmese 4, Other 5, Specify: _____ | 13.02b Marital status: Married 1, Single 2, Divorced 3, Other 4, Specify _____

13.03 Date of HAART start from records (if available): (dd/mm/yyyy) ☐☐/☐☐/☐☐☐☐

		PRE-HAART (A)	HAART START (B)	6 MO. FROM MOST RECENT (C)	MOST RECENT (D)
13.04	Weight (kg)	☐☐☐ dd/mm/yyyy:	☐☐☐ dd/mm/yyyy:	☐☐☐ dd/mm/yyyy:	☐☐☐ dd/mm/yyyy:
13.05	CD4 (cells/ uL)	☐☐☐☐ dd/mm/yyyy:	☐☐☐☐ dd/mm/yyyy:	☐☐☐☐ dd/mm/yyyy:	☐☐☐☐ dd/mm/yyyy:
13.06	Viral load (copies/ mL)	☐☐☐☐☐☐☐ dd/mm/yyyy:	☐☐☐☐☐☐☐ dd/mm/yyyy:	☐☐☐☐☐☐☐ dd/mm/yyyy:	☐☐☐☐☐☐☐ dd/mm/yyyy:

Viral Load History [Previous 24 months from present in reverse chronological order]

13.07 First (1) viral load since most recent: copies/mL: ☐☐☐☐☐☐☐ Date: (dd/mm/yyyy) ☐☐/☐☐/☐☐☐☐

13.08 Second (2) viral load since most recent: copies/mL: ☐☐☐☐☐☐☐ Date: (dd/mm/yyyy) ☐☐/☐☐/☐☐☐☐

13.09 Third (3) viral load since most recent: copies/mL: ☐☐☐☐☐☐☐ Date: (dd/mm/yyyy) ☐☐/☐☐/☐☐☐☐

13.10 Fourth (4) viral load since most recent: copies/mL: ☐☐☐☐☐☐☐ Date: (dd/mm/yyyy) ☐☐/☐☐/☐☐☐☐

13.11 Fifth (5) viral load since most recent: copies/mL: ☐☐☐☐☐☐☐ Date: (dd/mm/yyyy) ☐☐/☐☐/☐☐☐☐

13.12	Seventh (6) viral load since most recent: copies/mL: ☐☐☐☐☐☐☐	Date: (dd/mm/yyyy) ☐☐/☐☐/☐☐☐☐
13.13	Seventh (7) viral load since most recent: copies/mL: ☐☐☐☐☐☐☐	Date: (dd/mm/yyyy) ☐☐/☐☐/☐☐☐☐
13.14	Regimen change since HAART start? **[circle only one]**	No 0 / Yes 1
13.15	Current TB status (from Rx)	No 0 / Yes 1
13.16	Was client HAART ever stopped by doctor in the last 30 days from the date of interview (for background study, from date of last physician visit)?	No 0 / Yes 1

HAART History [List in reverse from current, one regimen per box; 24 months from interview or last visit] Drug: 01 AZT 02 D4T 03 3TC 04 EFV 05 NVP 06 IDV 07 DDI 08 RTV 09 LPV 10 ABC 11 TDF		Regimen: Drug [List every drug included for each regimen]	Regimen: mg/pill	Regimen: pills/day	Regimen: pills/each time (dose)	Regimen start and finish (dd/mm/yyyy)	Default status [>=3 mo. consecutive missed Rx) from date of interview or last scheduled clinic visit N=0; Y=1]	Lost to follow up [>=6 mo. Consecutive missed Rx from date of interview or last scheduled visit N=0; Y=1]	Indications for change, if any 01 Viral load (incl failure) 02 CD4 03 Tolerability/ side-effects 04 Adherence 05 WHO stage 06 Other
	13.17 Current					Start: Finish:	0 1	0 1	NA
	13.18					Start: Finish:	0 1	0 1	☐☐ Other:
	13.19					Start: Finish:	0 1	0 1	☐☐ Other:
	13.20					Start: Finish:	0 1	0 1	☐☐ Other:
	13.21					Start: Finish:	0 1	0 1	☐☐ Other:
	13.22					Start: Finish:	0 1	0 1	☐☐ Other:

Post-Interview Form: Adherence to HAART in Refugee and Host Communities

INSTRUCTIONS:
1. Where applicable, circle or write 77=Not applicable, 99=Do not know in margin
2. Use this date to complete Form 5, 14.viii Claim Period End Date

SECTION 13: Medical records

13.xx	Client code:	1 ☐-☐☐☐	13.yy Hospital No:	☐☐☐☐☐☐☐☐
13.i - a	Research Date	☐☐/☐☐/2010	13.ii Researcher Code [Enter researcher code]	☐☐
13.i - b	Interview Date	☐☐/☐☐/☐☐☐☐	[Use least recent of: study end (29/07/2010) OR death]	
13.iii	Data Entry 1 [Enter researcher code]	☐☐	13.iv Date of Data Entry 1	☐☐/☐☐/2010
13.v	Data Entry 2 [Enter researcher code]	☐☐	13.vi Date of Data Entry 2	☐☐/☐☐/2010
13.01a	Date of birth: [dd/mm/yyyy]	☐☐/☐☐/☐☐☐☐	13.01b Age:	☐☐
13.01c	Gender	Male 1 Female 2 Other (e.g. transgender) 3		
13.02a	Ethnicity	Malay 1 Burmese 4 Tamil 2 Other 5 Chinese 3 Specify:	13.02b Marital status:	Married 1 Single 2 Divorced 3 Other 4 Specify:_____

13.03 Date of HAART start from records (if available): (dd/mm/yyyy) ☐☐/☐☐/☐☐☐☐

		PRE-HAART (A)	HAART START (B)	6 MO. FROM MOST RECENT (C)	MOST RECENT (D)
13.04	Weight (kg)	☐☐☐ dd/mm/yyyy:	☐☐☐ dd/mm/yyyy:	☐☐☐ dd/mm/yyyy:	☐☐☐ dd/mm/yyyy:
13.05	CD4 (cells/ uL)	☐☐☐☐ dd/mm/yyyy:	☐☐☐☐ dd/mm/yyyy:	☐☐☐☐ dd/mm/yyyy:	☐☐☐☐ dd/mm/yyyy:
13.06	Viral load (copies/ mL)	☐☐☐☐☐☐ dd/mm/yyyy:	☐☐☐☐☐☐ dd/mm/yyyy:	☐☐☐☐☐☐ dd/mm/yyyy:	☐☐☐☐☐☐ dd/mm/yyyy:

Viral Load History [Previous 24 months from present in reverse chronological order]				
13.07	First (1) viral load since most recent: copies/mL: ☐☐☐☐☐☐☐		Date: (dd/mm/yyyy ☐☐/☐☐/☐☐☐☐	
13.08	Second (2) viral load since most recent: copies/mL: ☐☐☐☐☐☐☐		Date: (dd/mm/yyyy) ☐☐/☐☐/☐☐☐☐	
13.09	Third (3) viral load since most recent: copies/mL: ☐☐☐☐☐☐☐		Date: (dd/mm/yyyy) ☐☐/☐☐/☐☐☐☐	
13.10	Fourth (4) viral load since most recent: copies/mL: ☐☐☐☐☐☐☐		Date: (dd/mm/yyyy) ☐☐/☐☐/☐☐☐☐	
13.11	Fifth (5) viral load since most recent: copies/mL: ☐☐☐☐☐☐☐		Date: (dd/mm/yyyy) ☐☐/☐☐/☐☐☐☐	
13.12	Seventh (6) viral load since most recent: copies/mL: ☐☐☐☐☐☐☐		Date: (dd/mm/yyyy) ☐☐/☐☐/☐☐☐☐	
13.13	Seventh (7) viral load since most recent: copies/mL: ☐☐☐☐☐☐☐		Date: (dd/mm/yyyy) ☐☐/☐☐/☐☐☐☐	
13.14	Regimen change since HAART start? **[circle only one]**			No 0 Yes 1
13.15	Current TB status (from Rx)? **[circle only one]**			No 0 Yes 1
13.16a	Was client HAART ever stopped by a doctor in the last 30 days from the date of interview? **[circle only one]**			No 0 Yes 1
13.16b-i	In 24 months since Research Date, according to records has client ever pick up HAART from a pharmacy other than Sungai Buloh Hospital Pharmacy?			No 0 Yes 1
13.16b-ii	If yes, indicate pharmacy and dates for each place of alternative collection indicated in records:	Alt Pharmacy1:	Date started (dd/mm/yyyy): Date ended (dd/mm/yyyy):	☐☐/☐☐/☐☐☐☐ ☐☐/☐☐/☐☐☐☐
		Alt Pharmacy2:	Date started (dd/mm/yyyy): Date ended (dd/mm/yyyy):	☐☐/☐☐/☐☐☐☐ ☐☐/☐☐/☐☐☐☐
		Alt Pharmacy3:	Date started (dd/mm/yyyy): Date ended (dd/mm/yyyy):	☐☐/☐☐/☐☐☐☐ ☐☐/☐☐/☐☐☐☐

HAART History [List in reverse from current, one regimen per box; 24 months from interview or last visit. Circle fixed dose regimens] Drug: 01 AZT 02 D4T 03 3TC 04 EFV 05 NVP 06 IDV 07 DDI 08 RTV 09 LPV 10 ABC 11 TDF/EMB		Regimen: Drug [List every drug included for each regimen]	Regimen: mg/pill	Regimen: pills/day	Regimen: pills/each time (dose)	Regimen start and finish (dd/mm/yyyy)	Default status [>=3 mo. consecutive missed Rx) from interview date N=0; Y=1]	Lost to follow up [>=6 mo. Consecutive missed Rx from interview date N=0; Y=1]	Indications for change, if any 01 Viral load (incl failure) 02 CD4 03 Tolerability/ side-effects 04 Adherence 05 WHO stage 06 Other
	13.17 Current					Start: Finish:	0 1	0 1	NA
	13.18					Start: Finish:	0 1	0 1	☐☐ Other:
	13.19					Start: Finish:	0 1	0 1	☐☐ Other:
	13.20					Start: Finish:	0 1	0 1	☐☐ Other:
	13.21					Start: Finish:	0 1	0 1	☐☐ Other:
	13.22					Start: Finish:	0 1	0 1	☐☐ Other:

13.23a	Is client defaulting or not taking HAART at date of interview?	No 0 Yes 1
13.23b	If defaulting / not taking HAART at date of interview, was client HAART stopped by doctor?	No 0 Yes 1
13.23c	If yes, indicate date of last stoppage [dd/mm/yyyy]	☐☐/☐☐/☐☐☐☐
13.23d	Indicate reason for last doctor stoppage [Circle all that apply]	Viral load (incl failure) 01 CD4 02 Tolerability/ side-effects 03 Adherence 04 WHO stage 05 Other (Specify: _____) 06

List appointment history for 24 months from interview date:				
13.24a	Appt 1 [dd/mm/yyyy]	□□/□□/□□□□	13.24b	Routine ID doctor follow-up 01 Routine ID blood 02 Counseling 03 Emergency 04 ID inpatient admission 05 Step down (PKKN) visit 06 Unscheduled 07 Other (Specify:_____) 08
13.25a	Appt 2 [dd/mm/yyyy]	□□/□□/□□□□	13.25b	Routine ID doctor follow-up 01 Routine ID blood 02 Counseling 03 Emergency 04 ID inpatient admission 05 Step down (PKKN) visit 06 Unscheduled 07 Other (Specify:_____) 08
13.26a	Appt 3 [dd/mm/yyyy]	□□/□□/□□□□	13.26b	Routine ID doctor follow-up 01 Routine ID blood 02 Counseling 03 Emergency 04 ID inpatient admission 05 Step down (PKKN) visit 06 Unscheduled 07 Other (Specify:_____) 08
13.27a	Appt 4 [dd/mm/yyyy]	□□/□□/□□□□	13.27b	Routine ID doctor follow-up 01 Routine ID blood 02 Counseling 03 Emergency 04 ID inpatient admission 05 Step down (PKKN) visit 06 Unscheduled 07 Other (Specify:_____) 08
13.28a	Appt 5 [dd/mm/yyyy]	□□/□□/□□□□	13.28b	Routine ID doctor follow-up 01 Routine ID blood 02 Counseling 03 Emergency 04 ID inpatient admission 05 Step down (PKKN) visit 06 Unscheduled 07 Other (Specify:_____) 08
13.29a	Appt 6 [dd/mm/yyyy]	□□/□□/□□□□	13.29b	Routine ID doctor follow-up 01 Routine ID blood 02 Counseling 03 Emergency 04 ID inpatient admission 05 Step down (PKKN) visit 06 Unscheduled 07 Other (Specify:_____) 08

13.30a	Appt 7 [dd/mm/yyyy]	☐☐/☐☐/☐☐☐☐	13.30b	Routine ID doctor follow-up 01 Routine ID blood 02 Counseling 03 Emergency 04 ID inpatient admission 05 Step down (PKKN) visit 06 Unscheduled 07 Other (Specify:_____) 08
13.31a	Appt 8 [dd/mm/yyyy]	☐☐/☐☐/☐☐☐☐	13.31b	Routine ID doctor follow-up 01 Routine ID blood 02 Counseling 03 Emergency 04 ID inpatient admission 05 Step down (PKKN) visit 06 Unscheduled 07 Other (Specify:_____) 08
13.32a	Appt 9 [dd/mm/yyyy]	☐☐/☐☐/☐☐☐☐	13.32b	Routine ID doctor follow-up 01 Routine ID blood 02 Counseling 03 Emergency 04 ID inpatient admission 05 Step down (PKKN) visit 06 Unscheduled 07 Other (Specify:_____) 08
13.33a	Appt 10 [dd/mm/yyyy]	☐☐/☐☐/☐☐☐☐	13.33b	Routine ID doctor follow-up 01 Routine ID blood 02 Counseling 03 Emergency 04 ID inpatient admission 05 Step down (PKKN) visit 06 Unscheduled 07 Other (Specify:_____) 08
13.34a	Appt 11 [dd/mm/yyyy]	☐☐/☐☐/☐☐☐☐	13.34b	Routine ID doctor follow-up 01 Routine ID blood 02 Counseling 03 Emergency 04 ID inpatient admission 05 Step down (PKKN) visit 06 Unscheduled 07 Other (Specify:_____) 08
13.35a	Appt 12 [dd/mm/yyyy]	☐☐/☐☐/☐☐☐☐	13.35b	Routine ID doctor follow-up 01 Routine ID blood 02 Counseling 03 Emergency 04 ID inpatient admission 05 Step down (PKKN) visit 06 Unscheduled 07 Other (Specify:_____) 08

13.36a	Appt 13 [dd/mm/yyyy] ☐☐/☐☐/☐☐☐☐	13.36b	Routine ID doctor follow-up 01 Routine ID blood 02 Counseling 03 Emergency 04 ID inpatient admission 05 Step down (PKKN) visit 06 Unscheduled 07 Other (Specify:_____) 08
13.37a	Appt 14 [dd/mm/yyyy] ☐☐/☐☐/☐☐☐☐	13.37b	Routine ID doctor follow-up 01 Routine ID blood 02 Counseling 03 Emergency 04 ID inpatient admission 05 Step down (PKKN) visit 06 Unscheduled 07 Other (Specify:_____) 08
13.38a	Appt 15 [dd/mm/yyyy] ☐☐/☐☐/☐☐☐☐	13.38b	Routine ID doctor follow-up 01 Routine ID blood 02 Counseling 03 Emergency 04 ID inpatient admission 05 Step down (PKKN) visit 06 Unscheduled 07 Other (Specify:_____) 08
13.39a	Appt 16 [dd/mm/yyyy] ☐☐/☐☐/☐☐☐☐	13.39b	Routine ID doctor follow-up 01 Routine ID blood 02 Counseling 03 Emergency 04 ID inpatient admission 05 Step down (PKKN) visit 06 Unscheduled 07 Other (Specify:_____) 08
13.40a	Appt 17 [dd/mm/yyyy] ☐☐/☐☐/☐☐☐☐	13.40b	Routine ID doctor follow-up 01 Routine ID blood 02 Counseling 03 Emergency 04 ID inpatient admission 05 Step down (PKKN) visit 06 Unscheduled 07 Other (Specify:_____) 08
13.41a	Appt 18 [dd/mm/yyyy] ☐☐/☐☐/☐☐☐☐	13.41b	Routine ID doctor follow-up 01 Routine ID blood 02 Counseling 03 Emergency 04 ID inpatient admission 05 Step down (PKKN) visit 06 Unscheduled 07 Other (Specify:_____) 08

Attach more sheets if required.

Pharmacy Claim Form: Adherence to HAART in Refugee and Host Communities

INSTRUCTIONS:

1. **Begin with *Claim Period End Date*.** For each claim, in reverse **chronological order**, indicate the next *Dispense Date*. Based on the *Total Tablets Prescribed per Day*, calculate the *Total Expected Claim (TEC)*. Enter all tablets collected on the *Dispense Date* as *Total Actual Claim (TAC)*. (Note: *Claim Accuracy* and *Claim Status* will be evaluated by the Study). Enter all dates as **dd/mm/yyyy**.
2. Where it is indicated ADMIN ONLY, this information is provided by the STUDY.
3. For Claim Status, if $3 \geq CA \geq -3$ of the TEC, circle 1 (Yes). If $3 < CA < -3$ of TEC, circle 0 (No).
4. Pharmacy claim adherence = Total complete claims, divided by total claims over the total claim period x100.

SECTION 14: Pharmacy claim [Admin only, except for Researcher Code, Claim Period Start Date]

14.xx	**Client Code:**	1☐-☐☐☐	**Hospital No.:**	☐☐☐☐☐☐☐☐☐☐
14.i	**Research Date**	☐☐/☐☐/2010	14.ii **Researcher Code** [Enter researcher code]	☐☐
14.iii	**Data Entry 1** [Enter researcher code]	☐☐	14.iv **Date of Data Entry 1**	☐☐/☐☐/2010
14.v	**Data Entry 2** [Enter researcher code]	☐☐	14.vi **Date of Data Entry 2**	☐☐/☐☐/2010
14.vii	**Claim Period Start Date** [Delete all but one: HAART start date **OR** max. 24 months from Claim Period End Date **OR** start of pharmacy electronic records. **PROVIDED BY PHARMACY**			☐☐/☐☐/20☐☐
14.viii	**Claim Period End Date** [Delete all but one: Date of structured interview **OR** last physician visit **OR** date of appt. default (missed=3) **OR** death. **ADMIN ONLY - PROVIDED BY STUDY**			☐☐/☐☐/20☐☐

Claim #	Regimen [Input new regimen where applicable. Use trade name(s) e.g. Combivir]	Dispense Date (DD) [For Claim 00, use Claim Period Start Date; enter dates as dd/mm/yyyy]	Days Between Dispense Dates [Range: day after previous claim until day of next claim]	Total Tablets Prescribed per Day (TTD)	Total Expected Claim (TEC) [Total tablets required since previous claim]	Total Actual Claim (TAC) [Total tablets collected on DD]	Claim Accuracy (CA) [TEC – TAC / TTD] ADMIN ONLY	Claim Status [Circle, 0=N; 1=Y] ADMIN ONLY
00	Current regimen	☐☐/☐☐/20☐☐						
01		☐☐/☐☐/20☐☐	☐☐☐	☐☐	☐☐☐	☐☐☐	☐☐☐	0 1
02		☐☐/☐☐/20☐☐	☐☐☐	☐☐	☐☐☐	☐☐☐	☐☐☐	0 1
03		☐☐/☐☐/20☐☐	☐☐☐	☐☐	☐☐☐	☐☐☐	☐☐☐	0 1
04		☐☐/☐☐/20☐☐	☐☐☐	☐☐	☐☐☐	☐☐☐	☐☐☐	0 1
05		☐☐/☐☐/20☐☐	☐☐☐	☐☐	☐☐☐	☐☐☐	☐☐☐	0 1
06		☐☐/☐☐/20☐☐	☐☐☐	☐☐	☐☐☐	☐☐☐	☐☐☐	0 1

FORM 5

Claim #	Regimen [Input new regimen where applicable. Use trade name(s) e.g. Combivir]	Dispense Date (DD) [For Claim 00, use Claim Period Start Date; enter dates as dd/mm/yyyy]	Days Between Dispense Dates [Range: day after previous claim until day of next claim]	Total Tablets Prescribed per Day (TTD)	Total Expected Claim (TEC) [Total tablets required since previous claim]	Total Actual Claim (TAC) [Total tablets collected on DD]	Claim Accuracy (CA) [TEC – TAC / TTD] ADMIN ONLY	Claim Status [Circle, 0=N; 1=Y] ADMIN ONLY
07		□□/□□/20□□	□□□	□□	□□□	□□□	□□□	0 1
08		□□/□□/20□□	□□□	□□	□□□	□□□	□□□	0 1
09		□□/□□/20□□	□□□	□□	□□□	□□□	□□□	0 1
10		□□/□□/20□□	□□□	□□	□□□	□□□	□□□	0 1
11		□□/□□/20□□	□□□	□□	□□□	□□□	□□□	0 1
12		□□/□□/20□□	□□□	□□	□□□	□□□	□□□	0 1
13		□□/□□/20□□	□□□	□□	□□□	□□□	□□□	0 1
14		□□/□□/20□□	□□□	□□	□□□	□□□	□□□	0 1
15		□□/□□/20□□	□□□	□□	□□□	□□□	□□□	0 1
16		□□/□□/20□□	□□□	□□	□□□	□□□	□□□	0 1
17		□□/□□/20□□	□□□	□□	□□□	□□□	□□□	0 1
18		□□/□□/20□□	□□□	□□	□□□	□□□	□□□	0 1
19		□□/□□/20□□	□□□	□□	□□□	□□□	□□□	0 1
20		□□/□□/20□□	□□□	□□	□□□	□□□	□□□	0 1
21		□□/□□/20□□	□□□	□□	□□□	□□□	□□□	0 1
22		□□/□□/20□□	□□□	□□	□□□	□□□	□□□	0 1
23		□□/□□/20□□	□□□	□□	□□□	□□□	□□□	0 1

Summary [ADMIN ONLY]

14.24	14.25	14.26
Total claims over claim period [Claim Period Start Date – Claim Period End Date]	Total pharmacy claims submitted	Raw adherence score (Column 14.24 ÷ Column 14.25x100)
□□□	□□□	□□.□□

In-depth interview Topic Guide for Clients: Adherence to HAART in Refugee and Host Communities

INSTRUCTIONS:

1. Ensure you have all necessary materials (recorder, 2 pens, notebook, drinks, topic guide, and client reimbursement
2. Greet client in front of premises and ensure interview space is confidential.
3. Read information form. Ensure it is understood and answer client's questions. Sign consent form.
4. Remember: keep questions open, do not lead client, and use probing techniques.
5. At end of interview, reimburse client for transport and meal (obtain signature). Assist client in finding their way out of premises and finding taxi or public transport, if required.

1. Background Information

Client Code	1☐-☐☐☐	Hospital No.	☐☐☐☐☐☐☐☐☐☐
Research Date	☐☐/☐☐/2010	Researcher Name/Code	_____ ☐☐
Interview Start Time	☐☐:☐☐ am/pm	Interview End Time	☐☐:☐☐ am/pm
Language(s) [List all languages used in order of most use]		Client Gender [circle]	1 Male 2 Female 3 Other
Audio Location	Recorder # [See back of recorder]:	Folder:	File #:

2. Information & Consent Form

Read information form [check box]	☐
Researcher/client sign consent form [check box]	☐

3. Interview

See Topic Guide, Next page (p.2).

4. Reimbursement Signature

Client Reimbursement Signature [Transport=30 MYR or receipts, whichever is greater; Meal=10MYR]	X

Referrals for counselling

In the event of a medical emergency, call line **999**. Then, CALL SUPERVISOR **014 638 6187 (Josh)** or **017 308 9030 (Mai Mai)**.

In the event of a distressed client (emergency), CALL SUPERVISOR **014 638 6187 (Josh)** or **017 308 9030 (Mai Mai)**. If Supervisor is unavailable, call Janet (ACTS) **016 383 0393**. Stay with the client until informed otherwise.

In the event of a distressed client (non-emergency), Ask client if they wish to receive counselling. If they consent, CALL SUPERVISOR **014 638 6187 (Josh)** or **017 308 9030 (Mai Mai)** and provide Hospital No. and Client Contact Tel. No.

	Topic Guide for Clients	Notes [Use to assist with probing]
1.	**Introduction and client history** • Discuss current living situation, work, relationship status, and day-to-day life. [E.g. "Where do you live in Malaysia/Kuala Lumpur…"] • Identify home country and region. Describe (briefly) the client's migration sequence from home country to present country of asylum. • Where/when was HIV diagnosed? When was HAART first prescribed and taken?	**[~15 min]**
2.	**Highly Active Antiretroviral Therapy (HAART)** • Discuss current HAART regimen and day-to-day life in relation to HAART. [E.g. "Tell me about your HAART medication"] [E.g. "How has your life changed ever since you take HAART?"]	**[~10 min]**
3.	**Everyday experiences with adhering to HAART** • Discuss the client's understanding of what adherence to HAART means to them? [E.g. "What does it mean to you to 'adhere' to HAART"?] • Discuss present strategies used to remember HAART [E.g. "I am interested to know about the strategies you use to remember your HAART… "] • Discuss present challenges in relation to adhering to HAART. [E.g. Can you tell me about anything that has prevented you from taking your HAART medication as prescribed?	**[~20 min]**

4.	**Adherence timeline**
	• Develop a HAART adherence timeline with the client.
	[E.g."You mentioned that you first started taking HAART on (date) in (country). I would like to know more about your experiences with HAART over time. Tell me about your first week of taking HAART…."]
	• As you discuss the timeline, ask about:
	  • Major successes and failures on HAART from start to present.
	  • Regimen switches and reasons for switches.
	  • Critical moments when adherence was difficult, threatened, or not achieved and turning points when adherence challenges were overcome.
	  • Memorable missed doses and/or periods of time when adherence to HAART was challenged.
	  • If adherence is excellent, ask client to explain why. What helps make it so?
		[~30 min]
		CONTINUE ON on NEXT PAGE

5.	**Summary and lessons learned** • Ask the client to summarise the most important factors affecting their adherence (both helping and challenging their adherence) in the last 1 month, 6 months, and since starting HAART. [E.g. "Tell me about the most important factor(s) that have affected your adherence in the last month. Howabout since starting HAART? [E.g. "What is the most important lesson you have learned about taking HAART effectively?"] • Discuss the client's future expectations of life with HAART. [E.g. "How do you plan the future and fit in HAART in the plan?"	**[~15 min]**

Post-Interview Notes [Attach pages if necessary]

Main Summary of Interview [Make a point form list of all main points that emerged from the interview in relation to the research objectives]

Extended Summary of Interview [Write an extended summary of the interview using the main topics as a guide]

Selected quotations [Select quotations (2 or more) and write them here. Listen to the recording, and write them both in the language of the interview, and in English]	
Language of interview	English
Interviewer Reflections [Write about your own experience of the interview and your thoughts on this client and their adherence to HAART. Discuss any challenges they have faced and any obstacles they have overcome]	

Interviewer Self-Evaluation [List 3 things that went well about the interview and 3 things that you wish to improve about your own technique for the next interview]

APPENDIX B

KENYA DATA COLLECTION FORMS AND TOPIC GUIDES

Eligibility and Registration Form: Adherence to HAART in Refugee and Host Communities (Sections 1-6)

INSTRUCTIONS:

1. Engage warmly with the client.
2. Ask questions exactly as they are written on the page. Be sure to read all the additional prompts in "quotation marks."
3. [Follow all **bold** instructions in square brackets, but do **NOT** read them out loud.]
4. Where you answer "Other", remember to specify.
5. After asking a question, **be sure to prompt with response options** unless it is indicated **[do not prompt]**. Circle any response given unless it you are instructed **[circle only one]**.
6. Where applicable, circle or write in boxes, or write in the right-hand margin: Serial 7s (eg. 7, 77, 777, etc)=Not applicable; Serial 8s=Declined to answer; Serial 9s=Do not know . Never prompt with these options.

01.00	[Admin only]	Client Code: 2☐-☐☐☐		
SECTION 1: Identification				
01.01	Interviewer **[Enter your researcher code]**	☐☐		
01.02	Today's date **[dd/mm/yyyy]**	☐☐/☐☐/20☐☐		
	[Interviewer Skip to Q 01.07]			
01.03	Data entry 1 **[Enter your researcher code]**	☐☐	01.04 Date of data entry 1 **[dd/mm/yyyy]**	☐☐/☐☐/20☐☐
01.05	Data entry 2 **[Enter your researcher code]**	☐☐	01.06 Date of data entry 2 **[dd/mm/yyyy]**	(dd/mm/yyyy) ☐☐/☐☐/20☐☐

[Tell client the following:]

"Today, we are interviewing people for a study about HIV treatment. We would like to assess whether or not you are eligible. "If I can continue, this will take just a few seconds. Afterwards, you will be given a choice about your participation."

01.07	Why have you come to the clinic today? **[circle only one]**	Routine doctor appointment	01
		Counseling appointment	02
		Routine medication pick-up	03
		Accompanying friend, relative, or spouse	04
		Contacted by study team and invited for scheduled interview	05
		Heard about study and have come for interview/more information	06
		Other (Specify:_____)	07

SECTION 2: Language

02.01	What is your mother tongue? **[circle only one]**	English	01	Amharic	32
		Kiswahili	30	Somali	33
		Juba Arabic	31	Nga'turkana	34
				Other (Specify:_____)	50
02.02	Are you able to understand and to express yourself in one of English, Kiswahili, Nga'turkana, Amharic, Juba Arabic, Somali, or French?			No	0
				Yes	1
02.03	**[Researcher only]** Will an interpreter be required? **[If YES, and Reseacher can act as an interpreter, continue. If not, see the Coordinator]**			No	0
				Yes	1
02.04	Interview conducted in: **[If multiple languages used, circle the primary language used]**	English	01	Amharic	32
		Kiswahili	30	Somali	33
		Juba Arabic	31	Nga'turkana	34
				Other (Specify:_____)	50

SECTION 3: Information Sheet

[Give the client a copy of the information form. Read the information sheet out loud.] "Do you have any questions?"

03.01	**[Researcher only]** Has the client read/heard the information sheet?	No	0
		Yes	1

SECTION 4: Screening

04.01	**[Researcher only]** Gender	Male	1
		Female	2
		Other (e.g. transgender/transsexual)	3

04.02	a. Date of birth – client reported **[dd/mm/yyyy]** ☐☐/☐☐/☐☐☐☐	04.03 Age ☐☐ years **[Calculate from Q04.02a.]**
	b. Date of birth – recorded on UNHCR card or identity card **[dd/mm/yyyy]** ☐☐/☐☐/☐☐☐☐	

04.04	**[Researcher only]** Respondent >=18 years of age?	No **[End]**	0
	[If NO, explain why they cannot be included in the study and end the interview] "Thank-you."	Yes	1

04.05a	Date of HAART start? **[dd/mm/yyyy]** ☐☐/☐☐/☐☐☐☐ **[Please ensure mm/yyyy is complete. Prompt client by asking if start was at beginning of year, mid-year, or end year]**	04.05b Country of HAART start:	Kenya	04
			Sudan	05
			Somalia	06
			Ethiopia	07
			Democratic Republic of Congo	08
			Rwanda	09
			Other (Specify:_____)	15

[77=Not applicable; 88=Declined to answer; 99=Do not know]

04.06	**[Researcher only]** Was HAART initiated >=30 days before today? **[Client eligible if HAART started and taken for >=30 days before today, whatever their current HAART status. If NO, explain why they cannot be included in this study and end the interview]** "Thank-you."	No **[End]** Yes	0 1
04.07	Do you normally pick-up your HAART from the Comprehensive Care Clinic (CCC) in Kakuma Refugee Camp?	No Yes	0 1
04.08a	Have you ever picked up your HAART from someplace else?	No **[Skip to Q 04.09]** Yes	0 1
04.08b	Specify last date of pick-up from other pharmacy: **[dd/mm/yyyy]** ☐☐/☐☐/☐☐☐☐ Specify pharmacy/clinic:_____ Specify city:_____		
04.09	What is your current nationality/country of citizenship? If you have neither please tell me your country of origin. **[circle only one]**	Kenyan 04 Somali 05 Sudanese 06 Ethiopian 07 Congolese 08 Rwandan 09 Burundian 10 Eritrean 11 Other 16 (Specify:_____)	
04.10	What is your current status? **[circle only one]**	Citizen of Kenya Refugee Asylum seeker Other migrant	01 02 03 04
[Q 04.11- 04.14b: women only]			
04.11	Are you currently pregnant? **[circle only one]**	No **[Skip to Q 04.13]** Yes	0 1
04.12a	Are you currently taking HAART during your pregnancy? **[circle only one]**	No Yes	0 1
04.12b	Were you taking HAART before your current pregnancy? **[circle only one]**	No Yes	0 1
04.13	Have you ever been pregnant? **[circle only one]**	No **[Skip to Q 05.01]** Yes	0 1
04.14a	**[Not including current pregnancy, if any]** Have you ever taken HAART during any previous pregnancy? **[circle only one]**	No Yes	0 1
04.14b	**[Not including current pregnancy, if any]** Have you ever taken HAART before or after any previous pregnancy? **[circle only one]**	No Yes	0 1

SECTION 5: Informed Consent

[Give the client a copy of the consent form. Read the consent form out loud.] "Do you have any questions?"

05.01	**[Researcher only]** Has client heard/read the consent form?	No	0
		Yes	1
05.02	**[Researcher only]** Did the client agree to participate by signing the consent form?	No	0
		Yes	1

[If YES to Q 05.02, go to FORM 2] "Thank-you. I would now like to start asking you the main study questions."

[If NO to Q 05.02, go to Q 06.01] "Before you go, may I ask you just a few quick questions?"

SECTION 6: Reasons for Non-Participation

06.01	**[If NO to Q 05.02]** "May I ask you why you decided not to participate? This is important for us to know so we can improve future studies. **[Do not prompt and circle all that apply]**	Not interested in the study	1
		Did not have time	2
		Did not understand information about the study	3
		Other (Specify:_____)	4
		Declined to answer	88
06.02	**[Researcher only]** If the client was incapable of giving informed consent or answering the questionnaire, why?	Disability	1
		Language difficulties	2
		Other (Specify:_____)	3

[7=Not applicable; 88=Declined to answer; 99=Do not know]

Follow-up Form: Adherence to HAART in Refugee and Host Communities

Contact details		
00.xx	Client code [Transcribe from Form 1]:	2□-□□□
00.01	IC/UNHCR No.	□□□□□□□□□□
00.02	Hospital/clinic Identification No.	□□□□
00.03	Telephone No (Home):	
00.04	Telephone No (Mobile):	
00.05	Email:	
00.06	Cluster name & number/Village name:	
00.07a	Zone number (in camp):	
00.07b	Block number (in camp):	
00.08	Postal number:	
00.09	City / town:	
00.10	Post code:	

***Please list 2 contact telephone numbers (e.g. mobile + friend's mobile or mobile or home)**

Main Form: Adherence to HAART in Refugee and Host Communities (Sections 7-12)

SECTION 7: Identification

07.xx	Client code [Transcribe from Form 1]	2☐-☐☐☐	
07.01	Interviewer [Enter your researcher code] ☐☐	07.02	Date of interview [dd/mm/yyyy] ☐☐/☐☐/20☐☐
[Interviewer, Skip to Q08.01]			
07.03	Data entry 1 [Enter your researcher code] ☐☐	07.04	Date of data entry 1 [dd/mm/yyyy] ☐☐/☐☐/20☐☐
07.03	Data entry 1 [Enter your researcher code] ☐☐	07.04	Date of data entry 1 [dd/mm/yyyy] ☐☐/☐☐/20☐☐

SECTION 8: Socio-Demographic and Background Information

"Many thanks for participating in this study. Before we get started, would you like something to drink? We will then begin by asking you some general questions about yourself."

08.01	In which country were you born? [circle only one]	Kenya	04
		Sudan	05
		Somalia	06
		Ethiopia	07
		Democratic Republic of the Congo (DRC)	08
		Rwanda	09
		Other (Specify:_____)	15
08.02	What is your religion? [circle only one]	Christian - Catholic	01
		Christian - Protestant (Specify:_____)	02
		Muslim	03
		No religion	06
		Traditionalist	10
		Other (Specify:_____)	11
08.03	What is your current marital status? [circle only one]	Currently married or living as married, 1 spouse	01
		Currently married or living as married, >1 spouse	02
		Not married, currently in a relationship with 1 person	03
		Current ly married, living as married, and/or in a relationship with >1 person	04
		Divorced/separated from marriage and currently single	05
		Widowed and currently single	06
		Single	07

08.04	What type of accommodation do you currently live in? **[circle only one]**	Private house or apartment 01 Dormitory 02 Temporary home/Tent 03 Guest house/hotel 04	None 05 Other (Specify:_____) 06
08.05	How many people live with you in your current household? By household, I mean one person or a group of persons who usually live and eat together.		☐☐☐
08.06a	What are your average weekly personal earnings (include any salary, subsidy, allowance or grant received by yourself)?	Kenyan Shillings:	☐☐☐☐.☐☐
08.06b	What are the average weekly earnings of your household (include any salary, subsidy, allowance or grant received by any member of your household)?	Kenyan Shillings:	☐☐☐☐.☐☐
08.07	Do you currently work for pay outside or inside the home? **[circle only one]**	No 0 Yes 1	
08.08	Do you currently have children? **[circle only one]**	No **[Skip to Q 08.10]** 0 Yes 1	
08.09	If you have children, how many currently live with you in the same household?	Record number:	☐☐
08.10	How would you rate your current standard of living? **[circle only one]**	Very poor 1 Poor 2 Average 3 Good 4 Very good 5	
[If client is NOT currently a refugee or asylum seeker - SKIP to Q 08.14]			
08.11	What month/year did you enter this country?	(mm/yyyy)	☐☐/☐☐☐☐
08.12	What month/year were you registered with UNHCR?	(mm/yyyy)	☐☐/☐☐☐☐
08.13	How would you rate your standard of living prior to leaving your home country? **[circle only one]**	Very poor 1 Poor 2 Average 3 Good 4 Very good 5	
08.14a	In the last **12 months** have you been away from the community where you currently live for one continuous month or more? **[circle only one]**	No **[Skip to Q 08.16]** 0 Yes 1	
08.14b	How many times have you been away from the community for one continuous month or more (in the past 12 months)?		☐☐

08.15	What was the **main** reason why you were away from this place for one month or more (the most recent time)? **[Do not prompt and circle only one]**	Employment	01	Prison or detention in country	07
		Trade	02	Health-related	08
		Family-related	03	Religion-related	09
		Political reasons	04	Holiday	10
		Violent conflict	05	Involuntary deportation	11
		Education-related	06	Other (Specify: _____)	12
				Started living here <12 months ago	13
				Voluntary return to home country	14
				Nomadic/Pastoralist	15
08.16	What is the highest level of education you have completed? **[circle only one]**			Have never attended school	01
				Attended but did not complete primary education	02
				Completed primary but did not attend secondary	03
				Some secondary but did not complete it	04
				Completed secondary but did not go on to college/university	05
				Some college or university but did not complete it	06
				Completed college or university	07
				Language School only (Enter no. of years completed: ____	08
08.17	How often have you visited this clinic (Comprehensive Care Clinic) for any reason within the past **3 months**?			☐☐	
08.18	Do you usually collect your HAART medication from this clinic (Comprehensive Care Clinic) in Kakuma? **[circle only one]**			Always	1
				Most of the time	2
				Some of the time	3
				Never	4
08.19	When were you diagnosed as having HIV?			(mm/yyyy) ☐☐/☐☐☐☐	
08.20	In which country were you diagnosed as having HIV? **[circle only one]**			Your home country	1
				Kenya	2
				Other (Specify:_____)	3
08.21	Is HIV a virus that lives inside your body? **[circle only one]**			No	0
				Yes	1
				Do not know	9
08.22	Can the HIV virus cause AIDS? **[circle only one]**			No	0
				Yes	1
				Do not know	9
08.23	Why did you originally seek an HIV test (main reason)? **[Do not prompt. Circle only one]**			Voluntary test as general precaution	01
				Voluntary test recommended by a health care provider	02
				Mandatory test (e.g. in prison)	03
				Fear that I had been exposed to HIV and wanted to know for sure	04
				Had symptoms such as fatigue, weight loss, etc.	05
				Other (Specify: _____)	06

[77=Not applicable; 88=Declined to answer; 99=Do not know]

SECTION 9: HAART Medications, Adherence, and Side-Effects

[Complete this worksheet with the client and compare with records. Reconcile any differences with the client.]

09.01 Please help us to identify the HAART medications you are currently taking, doses, pills per dose, and doses per day. **[Complete Steps 1-5 below for each HAART medication currently used by the client. Use posters and/or pill books to assist. For Step 5, verification must come from medical record. Mark 0 if different; 1 if same; 9 if not known. Where the brand name is different than the one provided, please write the brand name in CAPITAL LETTERS in the left-hand margin. If the client names a medication that is not listed, please write the brand name in "Other"]**

Step 1 HAART trade name [Circle number only and all that apply]	**Step 2** Dose (total mg) (per tablet)	**Step 3** No. times per day (doses per day)	**Step 4** No. pills each time	**Step 5** Confirmed with records
AZT+3TC 01	☐☐☐	☐	☐	☐
3TC+d4T+NVP 02	☐☐☐	☐	☐	☐
Nevirapine (NVP) 03	☐☐☐	☐	☐	☐
Efcure (EFV) 04	☐☐☐	☐	☐	☐
Aluvia (LPV/r) 07	☐☐☐	☐	☐	☐
Zidovudine (AZT) 10	☐☐☐	☐	☐	☐
Stavudine (d4T) 11	☐☐☐	☐	☐	☐
Lamivudine (3TC) 12	☐☐☐	☐	☐	☐
Abacavir (ABC) 16	☐☐☐	☐	☐	☐
Viread (TDF) 17	☐☐☐	☐	☐	☐
Viracept (NFV) 18	☐☐☐	☐	☐	☐
AZT+3TC+NVP 19	☐☐☐	☐	☐	☐
D4T+3TC 20	☐☐☐	☐	☐	☐
Other 1 21 Specify:_____	☐☐☐	☐	☐	☐
Other 2 22 Specify:_____	☐☐☐	☐	☐	☐

09.02 **[Researcher only]** Was the client able to list ALL of their HAART medications without assistance? **[Enter "Yes" if client can name their medications, or identify them from a poster, pill book, or their own medication bottle]** No 0 Yes 1

[77=Not applicable; 88=Declined to answer; 99=Do not know]

"Most people with HIV have many pills to take at different times during the day. Many people find it hard to always remember their pills. Some people get busy and forget to carry their pills with them; some people find it hard to take their pills according to all the instructions such as "with meals" or "on an empty stomach", "every 8 hours", "with plenty of fluids"; some people decide to skip pills to avoid side effects or for other reasons. We need to understand how people with HIV are really doing with taking their pills. Please tell us what you are actually doing. Do not worry about telling us if you do not take your pills. We need to know what is really happening, not what you think we "want to hear." This information will not be reported to anyone and is strictly confidential. This section of the questionnaire asks about the medications that you may have taken or missed taking over the last four days prior to today. If you took only a portion of a dose (for example, you missed taking one pill in the morning) please report that dose(s) as being missed."

09.03 **[Complete the table below with the client, using one line for each HAART medication the client is supposed to be taking, and using the abbreviations from Q 09.01. If client did not miss any doses, write a zero (0). If the client missed two doses, write two (2), if they missed three doses (3) etc. Note that the table asks about FULL DOSES MISSED, NOT PILLS MISSED. If client responds that they took only a portion of a dose on one or more of these days (e.g. 1 out of 2 pills), please report the dose(s) as being missed. Late doses do not count as missed.]**

Step 1 [List trade name and numeric code from Q 09.01] "The HAART medicines you take are..."	**Step 2** Doses missed yesterday (1 day ago):	**Step 3** Doses missed the day before yesterday (2 days ago):	**Step 4** Doses missed 3 days ago:	**Step 5** Doses missed 4 days ago:
i. _____ ☐☐	☐ doses	☐ doses	☐ doses	☐ doses
ii. _____ ☐☐	☐ doses	☐ doses	☐ doses	☐ doses
iii. _____ ☐☐	☐ doses	☐ doses	☐ doses	☐ doses
iv. _____ ☐☐	☐ doses	☐ doses	☐ doses	☐ doses

09.04	During the past **four days**, on how many days have you missed taking all your doses? **[circle only one]**	None	1
		One day	2
		Two days	3
		Three days	4
		Four days	5
09.05	Most HAART medications need to be taken on a schedule, such as '2 times a day' or '3 times a day' or 'every 8 hours.' How closely did you follow your specific schedule over the last four days? **[circle only one]**	Never	1
		Some of the time	2
		About half of the time	3
		Most of the time	4
		All of the time	5
09.06	Do any of your HAART medications have special instructions, such as "take with food" or "on an empty stomach" or "with plenty of fluids"? **[circle only one]**	No **[Skip to Q 09.08]**	0
		Yes	1
		Do not know	9
09.07	If yes, how often did you follow those special instructions over the last **four days**? **[circle only one]**	Never	1
		Some of the time	2
		About half of the time	3
		Most of the time	4
		All of the time	5

[7=Not applicable; 88=Declined to answer; 99=Do not know]

09.08	On special days when people do not work, such as weekend days, holidays, or other days when they do not work, some people find that they forget to take their pills. Did you miss any of your HAARTpills **during your last day off work, weekend day, or holiday**? **[circle only one]**	No Yes	0 1
09.09	When was the last time you missed any of your medications? **[circle only one]**	Within the past week 1 – less than 2 weeks ago 2 – less than 4 weeks ago 1 – less than 3 months ago 3 months or more ago Never skip medications	01 02 03 04 05 06
09.10a	Have you experienced any ill health since starting HAART? **[circle only one]**	No Yes	0 1
09.10b	Have you experienced any ill health in the last **4 weeks**? **[circle only one]**	No **[Skip to Q 09.33]** Yes	0 1

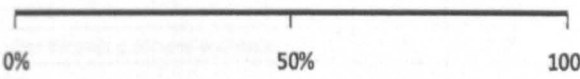
"If yes, what symptoms have you experienced in the last **4 weeks**?"		**I HAVE NOT had this symptom during the past 4 weeks**	**I HAVE had this symptom during the past 4 weeks**
09.11	Fatigue or loss of energy?	0	1
09.12	Fevers, chills or sweats?	0	1
09.13	Feeling dizzy or lightheaded?	0	1
09.14	Pain, numbness or tingling in the hands or feet?	0	1
09.15	Trouble remembering things?	0	1
09.16	Nausea or vomiting?	0	1
09.17	Felt sad, down, or depressed?	0	1
09.18	Felt nervous or anxious?	0	1
09.19	Difficulty falling or staying asleep?	0	1
09.20	Skin problems, such as rash, dryness or itching?	0	1
09.21	Cough or trouble breathing?	0	1
09.22	Headache?	0	1
09.23	Loss of appetite or a change in the taste of food?	0	1
09.24	Bloating, pain or gas in your abdomen?	0	1
09.25	Muscle aches or joint pain?	0	1
09.26	Problems with having sex, such as loss of interest or lack of satisfaction?	0	1
09.27	Changes in the way your body looks, such as fat deposits or weight gain?	0	1
09.28	Problems with weight loss or wasting?	0	1
09.29	Hair loss or changes in the way your hair looks?	0	1
09.30	Mouth ulcers or difficulty swallowing?	0	1
09.31	Other (Specify:_____)	0	1

[77=Not applicable; 88=Declined to answer; 99=Do not know]

09.32	Other (Specify:_____)	0	1

09.33 **[Remind client that the information they provide will not be reported to anyone. Remind client of the medications they listed in Q 09.01. Turn the page around to face the client, hand pen to client. Client must mark X themselves]**

"Put a cross **(X)** on the line below at the point showing your best guess about what proportion of your HAART medication you have taken in the last month, e.g. 0% means you have taken no medication; 50% means you have taken half your medication; 100% means you have taken every single dose of medication. We would be surprised if this was 100% for most people."



"Some people with HIV are also asked to take another drug called cotrimoxazole (also called "Septrin" or "Bactrim") every day which prevents various infections that are more common in people with HIV. Here are some cotrimoxazole tablets" **[Show the cotrimoxazole tablets that are most widely available locally]**

9.34	Since you were diagnosed with HIV, have you ever been prescribed cotrimoxazole to take daily?	No **[Skip to Q 10.01]**	0
		Yes	1
9.35	If yes, have you ever taken the cotrimoxazole?	No	0
		Yes	1
9.36	Are you currently on (being prescribed) cotrimoxazole?	No	0
		Yes	1
9.37	Did you take it yesterday?	No	0
		Yes	1

SECTION 10: Reasons and Barriers

	"Thank-you. Let's continue. How confident are you that..."	[circle only one] Not confident at all	A little bit confident	Very confident	Extremely confident
10.01	You are able to take all or most of your medication as directed?	1	2	3	4
10.02	The medication will have a positive effect on your health?	1	2	3	4
10.03	If you do not take your medication exactly as instructed, the HIV virus in your body will become resistant to HIV medications?	1	2	3	4

10.04	In general, how satisfied are you with the support you get from your friends and family members? **[circle only one]**	Very dissatisfied	1
		Dissatisfied	2
		Satisfied	3
		Extremely satisfied	4

10.05	To what extent do your friends and/or family members help you remember to take your medication? **[circle only one]**	Not at all A little Somewhat A lot	1 2 3 4

"People may MISS taking their medications for various reasons. What are the main reasons why you have ever missed taking your HAART?" **[Prompt for each]**		**[circle only one]**			
		Never	**Rarely**	**Sometimes**	**Often**
10.06	Away from home	1	2	3	4
10.07	Busy with other things (e.g. at home or at work)	1	2	3	4
10.08	Simply forgot	1	2	3	4
10.09	Have too many pills to take	1	2	3	4
10.10	Want to avoid side effects	1	2	3	4
10.11	Not want others to notice you taking medication	1	2	3	4
10.12	Have a change in daily routine	1	2	3	4
10.13	Feel like the drug was toxic/harmful	1	2	3	4
10.14	Fall asleep/slept through dose time	1	2	3	4
10.15	Feel sick or ill	1	2	3	4
10.16	Feel depressed/overwhelmed	1	2	3	4
10.17	Have problem taking pills at specified times	1	2	3	4
10.18	Run out of pills	1	2	3	4
10.19	Detained or incarcerated by the authorities	1	2	3	4
10.20	Difficulty concentrating	1	2	3	4
10.21	Feeling irritable or having outbursts of anger	1	2	3	4
10.22	Less interest in daily activities	1	2	3	4
10.23	Feeling that you have less skills than you had before	1	2	3	4
10.24	Having difficulty dealing with new situations	1	2	3	4
10.25	Feeling unable to make daily plans	1	2	3	4
10.26	Worrying too much about things	1	2	3	4
10.27	Feeling hopeless about the future	1	2	3	4
10.SUPa	Detention or prison without my HAART	1	2	3	4
10.SUPb	Suspicious of treatment	1	2	3	4
10.SUPc	Want to be free of medicines	1	2	3	4
10.SUPd	Financial constraints	1	2	3	4
10.SUPe	Other illnesses	1	2	3	4
10.SUPf	Felt fine/healthy	1	2	3	4
10.SUPg	Decreased quality of life	1	2	3	4
10.SUPh	Uncertainty	1	2	3	4
10.SUPi	Disruptions/chaotic routine	1	2	3	4

[77=Not applicable; 88=Declined to answer; 99=Do not know]

		[circle only one]			
		Never	**Rarely**	**Sometimes**	**Often**
10.29	Other "Can you think of any other reasons that were not mentioned?"				
	i._____	1	2	3	4
	ii._____	1	2	3	4
	iii._____	1	2	3	4

"The following questions ask about your alcohol and drug use. Please be honest in your answers. We will not report what you say to anyone"

10.30	How often have you had a drink containing alcohol (e.g. beer, chang'a, busaa, kaada) in the last 30 days? **[Prompt with examples of local drinks and circle only one]**	Daily	01
		5 or 6 times per week	02
		3 or 4 times per week	03
		1 or 2 times per week	04
		2 or 3 times in the past month	05
		Once in the past month	06
		Never **[Skip to Q 10.32]**	07
10.31	During the past 30 days, how often have you had 5 or more drinks of alcohol in a row, that is, within a few hours (eg. 2-4 hours)? **[circle only one]**	Daily	01
		5 or 6 times per week	02
		3 or 4 times per week	03
		1 or 2 times per week	04
		2 or 3 times in the past month	05
		Once in the past month	06
		Never	07
10.32	Have you ever used an illegal drug or not illegal but potentially harmful or unprescribed drug, such as mirra, marijuana, valium, tobacco, kienyeji, muganga, cocaine etc)? **[Prompt with examples of commonly used drugs and circle only one]**	No **[Skip to Q 10.34]**	0
		Yes	1

			Rarely (<=1/week)	Often (>=2/week)
10.33	List the three illicit drugs you have used most often within the last 6 months, starting with the one you have used most often. Did you use each rarely (1 time or less per week) or often (2 or more times per week) **[If none, leave blank]**	Drug i:_____	0	1
		Drug ii:_____	0	1
		Drug iii:_____	0	1

10.34	Have you visited a alternative/traditional/herbal medicine practicitioner in the past 6 months? **[circle only one]**	No	0
		Yes	1
10.35	Have you used alternative/traditional/herbal treatments or practices (herbs, teas, pills, spells etc.) within the past 6 months? **[circle only one]**	No	0
		Yes	1

[77=Not applicable; 88=Declined to answer; 99=Do not know]

10.36	Have you ever used alternative/traditional/herbal treatments instead of HAART to treat your HIV infection? **[circle only one, most recent]**	Never	01
		Yes, in the past 4 days	02
		Yes, in the past week	03
		Yes, in the past 4 weeks	04
		Yes, in the past 6 months	05
		Yes, more than 6 months ago	06

"To what extent are the following statements true?"		[circle only one] Not true	Sometimes true	Often true
10.37	I can't afford to eat properly.	1	2	3
10.38	I am often hungry but I don't eat because I can't afford enough food.	1	2	3
10.39	I eat less than I think I should because I don't have enough money for food.	1	2	3
10.40	**[Skip to Q 10.41 if client has no children / dependents]** I cannot give my child(ren) / dependents a balanced meal because I can't afford that.	1	2	3

"People may be VERY GOOD at taking their medications for various reasons. What are the main reasons that have helped you not to miss taking your HAART?"		[circle only one] Never	Rarely	Sometimes	Often
10.41	Meds take priority over substance or alcohol abuse	1	2	3	4
10.42	I have accepted my HIV status and learned to manage it	1	2	3	4
10.43	My HAART gives me good results	1	2	3	4
10.44	I understand why I must adhere to HAART	1	2	3	4
10.45	I believe that HAART works	1	2	3	4
10.46	My HAART regimen is simple	1	2	3	4
10.47	My routine is fixed	1	2	3	4
10.48	I use reminders like my phone alarm	1	2	3	4
10.49	I live for someone (child, spouse, etc.)	1	2	3	4
10.50	I was part of the decision to start HAART	1	2	3	4
10.51	My family and/or friends remind me to take HAART	1	2	3	4
10.52	My family and/or friends support me emotionally	1	2	3	4
10.53	My family and/or friends support me financially	1	2	3	4
10.54	I respect my doctor and listen to their advice	1	2	3	4
10.55	People know I am HIV+ so I have nothing to lose	1	2	3	4
10.56	I trust in my ability to take my HAART	1	2	3	4
10.57	I have a bright future ahead	1	2	3	4
10.58	Other "Can you think of any other reasons that were not mentioned?"				
	i._____	1	2	3	4
	ii._____	1	2	3	4

[77=Not applicable; 88=Declined to answer; 99=Do not know]

SECTION 11: Patient-Provider Relationship, Clinic, and Social Trust

"Thinking about the doctor that prescribes your HAART medication, how much do you trust that..."		[circle only one] Not at all	A little	Quite a bit	Extremely
11.01	He/she offers the best medical care they can provide?	1	2	3	4
11.02	He /she puts your health above everything else?	1	2	3	4
11.03	Which of the following health care providers do you interact with most often? **[circle only one]**	Doctor **[Skip to Q 11.06]**			01
		Nurse			02
		HIV or HAART counsellor			03
		Outreach home-based care			04
		Health coordinator or worker from your community			05
		Other (Specify:_____)			06
		Do not know			99
"Thinking about this person, how much do you trust that..."		[circle only one] **Not at all**	**A little**	**Quite a bit**	**Extremely**
11.04	He/she offers the best medical care they can provide?	1	2	3	4
11.05	He /she puts your health above everything else?	1	2	3	4
"The following questions ask about your experience with this clinic."					
11.06	How long, on average, do you spend travelling from your home to this clinic? **[circle only one]**	Less than 30 minutes			1
		30 minutes – less than 1 hour			2
		1 hour – less than 1.5 hours			3
		1.5 hours – less than 2 hours			4
		2 hours or more			5
11.07	Do you incur costs related to taking HAART (e.g. transport to clinic, special diet etc.)? **[circle only one]**	No **[Skip to Q 11.09]**			0
		Yes			1
11.08	Thinking about the last week (including today), how much (in local currency) did you spend on any HAART related-costs like transport to clinic or pharmacy?	Kenyan Shillings: ☐☐☐☐.☐☐			
11.09	In the last three months, have you left the clinic before a scheduled appointment due to the waiting time being too long? **[circle only one]**	No			0
		Yes			1
		Not Applicable (e.g. I never attended)			7
11.10	In the last three months, were you ever unable to refill your HAART medication prescription even if you wanted to? **[circle only one]**	No **[Skip to Q 11.SUPa]**			0
		Yes			1
		Not applicable (e.g. I never refilled)			7

11.11	Why were you unable to refill your HAART medication? **[Do not prompt and circle any that apply]**	It costs too much to go to pharmacy	01
		I cannot leave my children alone	02
		I cannot miss work or I will be fired	03
		I am not motivated	04
		I waited too long at the pharmacy	05
		The staff at the pharmacy did not understand me	06
		The staff at the pharmacy turned me away	07
		Fear of being stopped by the police if I travel	08
		Other (Specify:_____)	09

"Please tell us how much you feel about the following statements" **[circle only one]**		Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
11.SUPa	I am treated justly and with respect during my visits to the clinic	1	2	3	4	5
11.SUPb	When I go for medical care, they are careful to check everything when treating and examining me	1	2	3	4	5
11.SUPc	Sometimes I wonder if the provider's tests and treatments are correct	1	2	3	4	5
11.SUPd	I was given a choice concerning the type of treatment that was prescribed to me	1	2	3	4	5

"The following questions ask you about the people around you..."

11.12	Do you think that most people would try to take advantage of you if they got the chance, or would they try to be fair? **[circle only one]**	Take advantage of you	1
		Try to be fair	2
11.13	Generally speaking, would you say that most people can be trusted or would you say that you must be very careful in dealing with people? **[circle only one]**	Most people can be trusted	1
		Must be very careful in dealing with people	2
11.14	Have you disclosed your HIV status to your current spouse or sexual partner? **[circle only one]**	No	0
		Yes	1
		Not applicable	7
11.15	Have you disclosed your HIV status to other members of your family and/or closest friends? **[circle only one]**	No	0
		Yes	1
11.16	Have you disclosed your HIV status to others in your community? **[circle only one]**	No	0
		Yes	1

SECTION 12: Supplementary Adherence Measures

"To finish, I would like to ask you some final questions about your HAART medication. The medications you said that you take are..." **[Remind client of medications listed in Q 09.01 and to think about doses e.g. all pills taken at one time. Remind them that all the information they provide will be completely confidential.]**

12.01	In the last month, how often did you take your HAART medications? **[circle only one]**	None of the time	01
		A little of the time	02
		Some of the time	03
		A good bit of the time	04
		Most of the time	05
		All of the time	06
12.02	Please rate your ability to take all your medications as prescribed over the last month. **[circle only one]**	Very poor	01
		Poor	02
		Fair	03
		Good	04
		Very good	05
		Excellent	06
12.03a	If you ever stopped taking your HAART in the past month for any reason, for how many consecutive days did the longest interruption last? **[circle only one]**	1 day	01
		2 days	02
		3 days	03
		4 days	04
		>4 days	05
		Never interrupted	06

12.03b	How many HAART interruptions of 2 days or more while taking your HAART medication have you had in the last: **[If no interruption, write 00]**	i. 1 month (from today)?	No. ☐☐
		ii. 3 months (from today)?	No. ☐☐
		iii. 6 months (from today)?	No. ☐☐
12.03c	What is the longest HAART interruption (in consecutive days) that you have experienced in the last: **[If no interruption, write 00]**	i. 1 month (from today)?	days ☐☐
		ii. 3 months (from today)?	days ☐☐
		iii. 6 months (from today)?	days ☐☐

12.03d	The last time you stopped taking HAART for 2 days or more, was it...: **[circle only one]**	(mm/yyyy) ☐☐/☐☐☐☐	Your own decision **[Skip to Q 12.03e]** 0
			Your doctor's decision **[Skip to Q 12.03f]** 1
			Not applicable **[Skip to Q 12.04]** 7

[77=Not applicable; 88=Declined to answer; 99=Do not know]

12.03e	If you stopped your HAART by yourself, was it because...	I felt well	01
		I was having side effects from medications	02
		I was travelling and could not refill medications	03
		I took herbal medications instead of HAART	04
		I am afraid to be seen taking my medications	05
		Other (Specify:_____)	06
12.03f	If your HAART was stopped by your doctor, was it because...	I was taking HAART from another clinic and was not prescribed HAART at this clinic	01
		My doctor found me using alcohol or drugs	02
		My doctor said I was healthy	03
		I was not taking my HAART so my doctor stopped giving it to me	04
		My doctor switched my medications and I waited to receive the new one	05
		Other (Specify:_____)	06
12.04	Were you previously taking a different HAART regimen than the one you are currently taking (for example, in another place such as another city, province, or another country where you lived in the past)? **[circle only one]**	No **[End]**	0
		Yes	1
		Do not know	9

12.05 If YES to Q 12.04, can you remember the names of those medications that you took previously, before the HAART pills you are presently taking?

[Prompt client to remember each previous HAART pill taken. List each according to which pills were taken together, at one time, separated by \ (e.g. Set 1: Combivir\Efcure). Start from the current regimen. If client cannot remember the name of their pills, ask them to describe each HAART pill they previously took by shape and colour]

Current	_____	Start: ☐☐/☐☐☐☐	City:
		Finish: ☐☐/☐☐☐☐	Country:
SET 2	_____	Start: ☐☐/☐☐☐☐	City:
		Finish: ☐☐/☐☐☐☐	Country:
SET 3	_____	Start: ☐☐/☐☐☐☐	City:
		Finish: ☐☐/☐☐☐☐	Country:
SET 4	_____	Start: ☐☐/☐☐☐☐	City:
		Finish: ☐☐/☐☐☐☐	Country:

"Thank-you for your participation. We have now finished the main part of the questionnaire but I will now take a blood sample."

POST-INTERVIEW INSTRUCTIONS:

1. Take client for blood sample. Ensure that all identifying information (Client ID, Clinic #) are correctly transferred to the Sample label - the Technician will fill out the information.
2. Do not leave the client until the sample has been taken.
3. Remind the client that once the sample is given, the interview is completed.

In-depth interview Topic Guide for Clients: Adherence to HAART in Refugee and Host Communities

INSTRUCTIONS:

1. Ensure you have all necessary materials (recorder, 2 pens, notebook, drinks, topic guide, and client reimbursement
2. Greet client in front of premises and ensure interview space is confidential.
3. Read information sheet. Ensure it is understood and you have answered client's questions. Sign consent form.
4. Remember: keep questions open, do not lead client, and use probing techniques.
5. At end of interview, reimburse client for transport and meal (obtain signature). Assist client in finding their way out of premises and finding taxi or public transport, if required.

1. Background Information

Client Code	2☐-☐☐☐	Hospital No.	☐☐☐☐☐☐☐☐☐☐
Research Date	☐☐/☐☐/2010	Researcher Name/Code	_____ ☐☐
Interview Start Time	☐☐:☐☐ am/pm	Interview End Time	☐☐:☐☐ am/pm
Language(s) [List all languages used in order of most use]		Client Gender [circle]	1 Male 2 Female 3 Other
Audio Location	Recorder # [See back of recorder]:	Folder:	File #:

2. Information & Consent Form

Read information form [check box]	☐	Researcher/client sign consent form [check box]	☐

3. Interview

See Topic Guide, Next page (p.2).

4. Adherence self-report

Client completed Visual Analog Scale

4. Reimbursement Signature

Client Reimbursement Signature [200 KES]	X

Referrals for counselling

In the event of a distressed client, CALL SUPERVISOR 0718 489 997 (Josh)

	Topic Guide for Clients	Notes [Use to assist with probing]
1.	**Introduction and client history** • Discuss current living situation, work, relationship status, and day-to-day life. [E.g. "Where do you live in Kakuma..."] • Identify client's home country and region. Ask client to describe (briefly) his/her migration sequence from home country to present country of asylum. • Where/when was HIV diagnosed? When was HAART first prescribed and taken?	**[~15 min]**
2.	**Highly Active Antiretroviral Therapy (HAART)** • Discuss current HAART regimen and day-to-day life in relation to HAART. [E.g. "Tell me about your HAART medication"] [E.g. "How has your life changed ever since you take HAART?"]	**[~10 min]**
3.	**Everyday experiences with adhering to HAART** • Discuss the client's understanding of what adherence to HAART means to them? [E.g. "What does it mean to you to 'adhere' to HAART"?] • Discuss present strategies used to remember HAART [E.g. "I am interested to know about the strategies you use to remember your HAART..."] • Discuss present challenges in relation to adhering to HAART. [E.g. Can you tell me about anything that has prevented you from taking your HAART medication as prescribed?	**[~20 min]**

4.	**Adherence timeline**
	• Develop a HAART adherence timeline with the client.
	[E.g."You mentioned that you first started taking HAART on (date) in (country). I would like to know more about your experiences with HAART over time. Tell me about your first week of taking HAART..."]
	• As you discuss the timeline, ask about:
	  • Major successes and failures on HAART from start to present.
	  • Regimen switches and reasons for switches.
	  • Critical moments when adherence was difficult, threatened, or not achieved and turning points when adherence challenges were overcome.
	  • Memorable missed doses and/or periods of time when adherence to HAART was challenged.
	  • If adherence is excellent, ask client to explain why. What helps make it so?
		[~30 min]
		CONTINUE ON on NEXT PAGE

5.	**Summary and lessons learned** • Ask the client to summarise the most important factors affecting their adherence (both helping and challenging their adherence) in the last 1 month, 6 months, and since starting HAART. [E.g. "Tell me about the most important factor(s) that have affected your adherence in the last month. Howabout since starting HAART? [E.g. "What is the most important lesson you have learned about taking HAART effectively?"] • Discuss the client's future expectations of life with HAART. [E.g. "How do you plan the future and fit in HAART in the plan?"	**[~15 min]**

Post-Interview Notes [Attach pages if necessary]

Main Summary of Interview [Make a point form list of all main points that emerged from the interview in relation to the research objectives]

Extended Summary of Interview [Write an extended summary of the interview using the main topics as a guide]

Selected quotations [Select quotations (2 or more) and write them here. Listen to the recording, and write them both in the language of the interview, and in English]	
Language of interview	English
Interviewer Reflections [Write about your own experience of the interview and your thoughts on this client and their adherence to HAART. Discuss any challenges they have faced and any obstacles they have overcome]	

Interviewer Self-Evaluation [List 3 things that went well about the interview and 3 things that you wish to improve about your own technique for the next interview]

APPENDIX C

RESEARCH CLEARANCES, ETHICAL CLEARANCES, INFORMATION SHEETS, AND CONSENT FORMS

LONDON SCHOOL OF HYGIENE
& TROPICAL MEDICINE

ETHICS COMMITTEE

APPROVAL FORM
Application number: **5547**

Name of Principal Investigator	**Joshua Mendelsohn**
Department	**Epidemiology and Population Health**
Head of Department	**Professor Laura Rodrigues**

Title: **Assessing adherence to Highly Active Antiretroviral Therapy (HAART) in Refugee and Host Populations**

This application is approved by the Committee.

Chair of the Ethics Committee ..... T. W. Meade .....

Date ..... 29 July 2009 .....

Approval is dependent on local ethical approval having been received.

Any subsequent changes to the application must be submitted to the Committee via an E2 amendment form.

UNIT PERANCANG EKONOMI
Economic Planning Unit
JABATAN PERDANA MENTERI
Prime Minister's Department
BLOK B5 & B6
PUSAT PENTADBIRAN KERAJAAN PERSEKUTUAN
62502 PUTRAJAYA
MALAYSIA

EPU

Telefon : 603-8888 3333

Rujt. Tuan:
Your Ref.:

Rujt. Kami: UPE: 40/200/19/2487
Our Ref.:

Tarikh: 14 October 2009
Date:

Joshua Mendelsohn
14 Warbonnet Drive
Nepean
On, Canada
Email: joshua.mendelsohn@lshtm.ac.uk

APPLICATION TO CONDUCT RESEARCH IN MALAYSIA

With reference to your application dated **10 August 2009**, I am pleased to inform you that your application to conduct research in Malaysia has been *approved* by the **Research Promotion and Co-Ordination Committee, Economic Planning Unit, Prime Minister's Department.** The details of the approval are as follows:

Researcher's name	:	JOSHUA MENDELSOHN
Passport No. / I. C No:		LJ577483
Nationality	:	CANADA
Title of Research	:	"ASSESSING ADHERENCE TO HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART) IN REFUGEE AND HOST POPULATIONS"
Period of Research Approved:		SIX MONTHS
Name of Malaysian Counterpart:		DR SUSHEELA BALASUNDARAM

2. Please collect your Research Pass in person from the Economic Planning Unit, Prime Minister's Department, Parcel B, Level 1 Block B5, Federal Government Administrative Centre, 62502 Putrajaya, Malaysia and bring along two (2) passport size photographs, a copy of your passport and payment of **RM150** only. All payments must be made in bank draft (from any Malaysian bank) or money order/postal order (from any Malaysian post office) in favour of the Director General, Economic Planning Unit. Payment in **cash or personal cheque is not allowed**.

3. Please take note that the study should avoid sensitive issues pertaining to local values and norms as well as political elements while undertaking your research project in Malaysia. You have to adhere to the conditions stated by the code of conduct for foreign researchers. You are also required to comply with the rules and regulations stipulated from time to time by the agencies with which you have dealings in the conduct of your research.

4. You must always keep your local counterpart informed of activities and information or knowledge related to the research work.

5. I would like to draw your attention to the undertaking signed by you that you will submit without cost to the Economic Planning Unit the following documents:

a) A brief summary of your research findings on completion of your research and before you leave Malaysia; and

b) Three (3) copies of your final dissertation/publication.

6. Lastly, please submit a copy of your preliminary and final report directly to the State Government where you carried out your research. Thank you.

Yours sincerely,

(MUNIRAH BT. ABD MANAN)
For Director General,
Economic Planning Unit.
E-mail: munirah@epu.gov.my
Tel: 88725281/88725272
Fax: 88883961

ATTENTION

This letter is only to inform you the status of your application and **cannot be used as a research pass.**

Cc:

Dr Susheela Balasundaram
UNHCR Health Officer
UNHCR Malaysia,
No 570, Jalan Bukit Petaling,
P.O. Box 10185,
50706 Kuala Lumpur (Malaysian Counterpart)

HOSPITAL KUALA LUMPUR
PUSAT PENYELIDIKAN KLINIKAL
(CLINICAL RESEARCH CENTRE)
JALAN PAHANG
50586 KUALA LUMPUR

Tel : 603-26924249 / 603-26980310
Fax : 603-26911682
Email : contact@crc.gov.my
Website : www.crc.gov.my

Ref: MOH/CRC/CTA022/280509

Date: 28 May 2009

Joshua Mendelsohn
Infectious Diseases Epidemiology Unit
London School of Hygiene and Tropical Medicine
Keppel Street
London WC1E 7HT
UK
Tel: +44 (0)7725 987 777
Email: jmends@gmail.com

Dear Sir/Madam,

Re: Review of CTA, study budgets and related documents for Study (Protocol No.: 3275)

Research Title:
Assessing adherence to highly active antiretroviral therapy (HAART) in refugee and host populations

We are pleased to inform you that CRC has reviewed the following documents and our decisions and/or actions are indicated below as per the checked column. Please cite the above reference number, which is also printed in all documents reviewed, in all correspondence on the matter.

#	Documents	Decision and/or actions	Box checked where Applicable
1	Clinical Trial Agreement (CTA) (ad hoc/ pre-approved template)	• Document is valid; sponsor & investigator may proceed to sign off	☒ Yes ○ No
		• Amendment(s) to CTA require re-approval by PUU. Approved amendment(s) will be released to sponsor & investigator as soon as CRC has received them from PUU. This could take up to 3 months	○ Yes ☒ No
		• Sponsor and/or investigator must return a signed copy to CRC to be forwarded to PUU for record keeping	☒ To follow up
2	Study budget 1 payable to Investigators	• Document is valid; sponsor & investigator may proceed	☒ NA
3	Study budget 2 payable to Ministry of Health	• Document is valid; sponsor & investigator may proceed	☒ NA
		• A copy submitted to NIH MOH for record keeping & billing purpose	○ To follow up
4	Clinical Trial indemnification	• Document is valid; sponsor & investigator may proceed	☒ Yes
		• Indemnity insurance being secured: sponsor and investigator may proceed.	☒ Yes

HOSPITAL KUALA LUMPUR
PUSAT PENYELIDIKAN KLINIKAL
(CLINICAL RESEARCH CENTRE)
JALAN PAHANG
50586 KUALA LUMPUR

Tel : 603-26924249 / 603-26980310
Fax : 603-26911682
Email : contact@crc.gov.my
Website : www.crc.gov.my

Ref: MOH/CRC/CTA022/280509

5	Professional indemnification	• Document is valid; sponsor & investigator may proceed	☒ Yes
		• Indemnity insurance being secured; sponsor and investigator may proceed	☒ Yes
		• Professional indemnification not requested; please inform investigator accordingly.	☒ NA

We look forward to your continued support in conducting clinical trials in Malaysia. Thank you.

Yours sincerely,

Dr Lim Teck Onn
Director, Network of Clinical Research Centre
Ministry Of Health Malaysia

PEJABAT TIMBALAN KETUA PENGARAH KESIHATAN
OFFICE OF THE DEPUTY DIRECTOR-GENERAL OF HEALTH
(PENYELIDIKAN & SOKONGAN TEKNIKAL)
(RESEARCH & TECHNICAL SUPPORT)
KEMENTERIAN KESIHATAN MALAYSIA
MINISTRY OF HEALTH MALAYSIA
Aras 12, Blok E7, Parsel E, Presint 1
Level 12, Block E7, Parcel E, Precinct 1
Pusat Pentadbiran Kerajaan Persekutuan
Federal Government Administrative Centre
62590 PUTRAJAYA

Tel : 03 88832543
Faks : 03 88895184

JAWATANKUASA ETIKA & PENYELIDIKAN PERUBATAN
KEMENTERIAN KESIHATAN MALAYSIA
d/a Institut Pengurusan Kesihatan
Jalan Rumah Sakit, Bangsar
59000 Kuala Lumpur

Ruj. Kami : (6) dlm.KKM/NIHSEC/08/0804/P09-195

Tarikh : 21 Disember 2009

Joshua Mendelsohn
London School of Hygiene and Tropical Medicine

Dr Anuradha P Radhakrishnan
Jabatan Perubatan
Hospital Sungai Buluh
tel: 03-6145 4022

Tuan/Puan,

NMRR-09-239-3275
Assessing Adherence to Highly Active Antiretroviral Therapy (Haart) In Refugee And Host Populations

Dengan hormatnya perkara di atas adalah dirujuk.

2. Bersama dengan surat ini dilampirkan surat kelulusan saintifik dan etika bagi projek ini.

3. Adalah dimaklumkan bahawa Tuan perlu mengemukakan laporan tahunan, laporan tamat kajian dan juga laporan mengenai "*All adverse events, both serious and unexpected*" kepada Jawatankuasa Etika & Penyelidikan Perubatan, KKM.

Sekian terima kasih.

BERKHIDMAT UNTUK NEGARA

Saya yang menurut perintah,

(DATO' DR CHANG KIAN MENG)
Pengerusi
Jawatankuasa Etika & Penyelidikan Perubatan
Kementerian Kesihatan Malaysia

PEJABAT TIMBALAN KETUA PENGARAH KESIHATAN
OFFICE OF THE DEPUTY DIRECTOR-GENERAL OF HEALTH
(PENYELIDIKAN & SOKONGAN TEKNIKAL)
(RESEARCH & TECHNICAL SUPPORT)
KEMENTERIAN KESIHATAN MALAYSIA
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Faks : 03 88895184

MEDICAL RESEARCH & ETHICS COMMITTEE
MINISTRY OF HEALTH MALAYSIA
c/o Institute for Health Management
Jalan Rumah Sakit, Bangsar
59000 Kuala Lumpur

Ruj. Kami : (6)dlm.KKM/NIHSEC/08/0804/P09-285

Tarikh : 21 December 2009

Protocol Title :
Assessing Adherence to Highly Active Antiretroviral Therapy (Haart) In Refugee And Host Populations

Principal Investigator : Joshua Mendelsohn
London School of Hygiene and Tropical Medicine

Dr Anuradha P Radhakrishnan
Department of Medical
Hospital Sungai Buluh

Documents received and reviewed with reference to the above study:

1. Study Proposal, Dated 18 September 2009
2. Information Form for Client Questionnaire and Blood Sample – English & Malay
3. Letter of Indemnity, dated 8 April 2009
4. Clinical Trial Agreement, MOH/CRC/CTA022/280509
5. Curriculum Vitae of Investigators

The Medical Research & Ethics Committee, Ministry of Health Malaysia operates in accordance to the International Conference of Harmonization Good Clinical Practice Guidelines.

Comments (if any): ***From the ethical aspects of the study design, the MREC has no objection to the conduct of the study. However there are sensitive issues pertaining to this study ? refugee status and its association with national security issues; the concern on the interpretation of the study and its findings especially the future presentation, utilization and dissemination of the findings.***

Project Sites: Hospital Sungai Buluh

Decision by Medical Research & Ethics Committee:
(√) Approved
( ) Conditionally Approved
( ) Disapproved

Date of Decision : 29 September 2009

DATO' DR CHANG KIAN MENG
Chairman
Medical Research & Ethics Committee
Ministry of Health Malaysia

MEMBERS OF THE MEDICAL RESEARCH & ETHICS COMMITTEE WHO REVIEWED THE DOCUMENTS / PROTOCOL ON 25 AUGUST 2009

NAME	DESIGNATION	GENDER	TICK (√) IF PRESENT
MREC Chairman Dato' Dr Chang Kian Meng	Consultant Hematologist & Head, Department Of Hematology, Hospital Ampang	Male	X
Dato' Dr Zaki Morad Mohd Zaher	Lecturer in Medicine, International Medical University	Male	X
Professor Dr Victor Lim	Representative, Academy of Medicine Malaysia	Male	X
Dr Shahnaz Murad	Director, Institute For Medical Research	Female	√
Dr Yahya Baba	Director, Institute For Public Health	Female	√
Dr Lim Teck Onn	Director, Network Of Clinical Research Centre	Male	√
Dr Roslan Johari Mohd Ghazali	Director, Institute For Health Management	Female	√
Dr Azman Abu Bakar	Director, Institute For Health Systems Research	Male	√
Ms Siti Saadiah Hassan Nuddin	Director, Institute For Health Behavioural Research	Female	√
Dr Zakiah Ismail	Pathologist (Chemical Pathology)	Female	X
Dr Wan Nazaimoon Wan Mohamud	Senior Research Officer	Female	√
Dr Ho Tze Ming	Senior Research Officer	Male	√
Ms Rokiah Don	Nutritionist	Female	√
Dr Abdul Kahar Ghapar	Head, Department of Cardiology Hospital Serdang	Male	X
Mr Razif Abdul Aziz	Lawyer	Male	X
Mdm Wong Yoke Ying	Retiree	Female	√

Mr Razif Abdul Aziz & Mdm Wong Yoke Ying Are The Lay Persons In The Medical Research & Ethics Committee

NATIONAL INSTITUTES OF HEALTH APPROVAL FOR CONDUCTING RESEARCH IN THE MINISTRY OF HEALTH MALAYSIA

PENGESAHAN INSTITUSI PENYELIDIKAN NEGARA UNTUK MENJALANKAN PENYELIDIKAN DI KEMENTERIAN KESIHATAN

This is an auto computer - generated document.It is issued by one of the research institute under the National Institutes of Health (NIH). These are the Institute for Medical Research (IMR), Clinical Research Centre (CRC), Institute of Public Health (IPH), Institute for Health Management (IHM), Institute for Health Systems Research (IHSR), and Institute for Health Behavioural Research (IHBR)

Dokumen ini adalah cetakan berkomputer. Borang ini dikeluarkan oleh salah satu institusi dibawah National Institutes of Health (NIH) iaitu Institut Penyelidikan Perubatan (IMR), Pusat Penyelidikan Klinikal (CRC), Institut Kesihatan Umum (IKU), Institut Pengurusan Kesihatan (IPK), Institut Pergurusan Sistem Kesihatan (IPSK), Institut Penyelidikan Tingkahlaku Kesihatan (IPTK)

Unique NMRR Registration ID : [Nombor Pendaftaran]	NMRR-09-239-3275
Research Title : [Tajuk]	Assessing adherence to highly active antiretroviral therapy (HAART) in refugee and host populations
Protocol Number if available : [Nombor Protokol jika ada]	3275

#	Investigator Name [Name Penyelidik]	Institution Name [Nama Institusi]
1	Anuradha P Radhakrishnan	Sungai Buloh Hospital
2	Joshua Mendelsohn	United Nations High Commissioner for Refugees London School of Hygiene and Tropical Medicine

I have reviewed the above titled research, and approve of its design and conduct.

Saya telah menyemak kajian yang bertajuk seperti di atas dan meluluskan rekabentuk dan perlaksanaannya.

Name of Director : *[Nama Pengarah]*	Dr. Lim Teck Onn
NIH Institute (IMR, CRC, IPH, IHM, IHSR and IHBR) *[Nama Institusi di bawah NIH]*	Clinical Research Centre (CRC)
Signature & Official stamp : *[Tandatangan dan Cop Rasmi]*	This is computer generated document, therefore no signature is required.
Date : *[Tarikh]*	29-07-2009

(Note: This is a computer generated document. It may not carry any signature)

Information Sheet for Client Questionnaire and Blood sample *(You will be given a copy of this information sheet)*	
Title of Project:	**Assessing adherence to highly active antiretroviral therapy (HAART) in refugee and host populations**
Name, address, and contact details of investigator:	**Joshua Mendelsohn MSc, Dr Anuradha Radhakrishnan MBBS MRCP, Dr Susheela Balasundaram MBBS** **UNHCR Malaysia, No. 570, Jalan Bukit Petaling, P.O. Box 10185,** **50706 Kuala Lumpur, Malaysia** **Tel: 03-21411322 ext. 492**
This study has been approved by:	**Medical Research and Ethics Committee (MREC), Malaysia** **Clinical Research Centre (CRC), Malaysia** **London School of Hygiene and Tropical Medicine Ethics Committee**
Study sponsor:	**London School of Hygiene and Tropical Medicine**

We invite you to take part in this research project on how people take their antiretroviral medication. You should only take part if you want to. It is up to you to decide whether or not to take part. If you decide to take part you are still free to withdraw at any time and without giving a reason. If you choose not to participate or to withdraw it will involve no penalty or loss of benefits to which you are otherwise entitled. The standard of care you receive will be unaffected. This information sheet will now be read to you and you will be given an opportunity to ask questions and have answers provided. We would like you to consider taking part today, but if you wish, you may take this information sheet home for consideration. If you decide to take part you will be given this information sheet to keep and be asked to sign a form stating that you agree to take part in the study.

Aims of research: The purpose of the research is to understand how often people take their HIV medications (Highly Active Antiretroviral Therapy or "HAART"), and to understand factors that help people to take their medications or make it more difficult. Participants will include refugees and Malaysians who attend the same clinic.

Your role: Today you are being asked to participate in a client questionnaire and to provide a blood sample. If you choose to participate, you will be interviewed for approximately 1 hour here at Sungai Buloh Hospital and we will ask you to give a blood sample afterwards using the procedures normally used at the hospital. The interview will seek information about your adherence to HAART and challenges you may have faced while taking HAART. The blood sample will be used to test how much HIV virus is in your blood and may also be tested for resistance to your medication and other HIV or other infectious disease-related tests at a future time. Your blood sample will be stored for 5 years at Malaysian Liver Foundation Laboratories before being destroyed. We will also ask you to allow us to consult your medical records for up to three years in the past and for up to five years in the future.

Confidentiality: Interviews will be private and confidential. Your name will not be written on the interview questionnaire or on the blood sample specimen. Instead, a number will be used to protect your identity. All information obtained from interviews and the blood sample will be used in an anonymous way and may be used anonymously in future research. In the short term, the information you provide will be stored safely in Kuala Lumpur, Malaysia. In the longer term, it will also be stored safely in London, United Kingdom. If you choose to withdraw from the study blood samples and data you may have provided will be retained unless you wish otherwise.

Incentives: If you agree to participate you will be offered a snack or beverage during the interview and a maximum reimbursement of 30 Malaysian Ringgits for travel expenses incurred. You will not receive any financial incentive. We hope that this research will help the clinic to develop ways to make it easier for people like you to take their HIV treatment.

Risks: Some questions may ask for personal information which may cause discomfort. You may choose not to answer these questions. It is important that you communicate with the researcher in the event that you become very uncomfortable or anxious. Giving blood presents the possibility of bruising or swelling at the site and runs a minimal risk of infection. Discomfort tends to be brief and transient.

Follow-up: There is the potential we will invite you to participate in a follow-up interview at a different time. If so we will ask you at the end of this interview or be in touch within two weeks. In such instances, information will be provided and your consent will be sought again.

Thank-you for taking the time to consider participating in this study. Please contact the investigator named at the top of this sheet if you have any questions in the future related to your participation, rights or if you have any complaints.

Informed Consent Form for Client Questionnaire and Blood sample *(This form is to be completed by the participant after reading the Information Sheet and/or having listened to an explanation about the research)*

Title of Project:	**Assessing adherence to highly active antiretroviral therapy (HAART) in refugee and host populations**
Name, address, and contact details of investigator:	**Joshua Mendelsohn MSc, Dr Anuradha Radhakrishnan MBBS MRCP, Dr Susheela Balasundaram MBBS** **UNHCR Malaysia** **No. 570, Jalan Bukit Petaling, P.O. Box 10185,** **50706 Kuala Lumpur, Malaysia** **Tel: 03-21411322 ext. 492**
This study has been approved by:	**Medical Research and Ethics Committee (MREC), Malaysia** **Clinical Research Centre (CRC), Malaysia** **London School of Hygiene and Tropical Medicine Ethics Committee**
Study sponsor:	**London School of Hygiene and Tropical Medicine**

Participant's Statement

- I have read the information sheet concerning this study [and/or have understood the verbal explanation] and I understand what will be required of me and what will happen to me if I take part in it.
- My questions concerning this study have been answered by: **Name:** ..... **Position:** .....
- I understand that at any time I may withdraw from this study without giving a reason and without affecting my normal care and management.
- I consent to the use of my personal information for the purposes mentioned in the information sheet only and that it will not be used for any other purpose. I understand that such information will be treated as strictly confidential.
- I understand that confidentiality and anonymity will be maintained and it will not be possible to identify me from any publications.
- I understand that if I choose to withdraw from the study, blood samples and data that I may have provided will be retained unless I wish otherwise. If I do not withdraw, my blood samples will be destroyed after 5 years of storage at the Malaysian Liver Foundation Laboratories and all data provided by me will be maintained in strict confidence.
- I agree to be contacted in the future by researchers who would like to invite me to participate in follow-up studies.
- I agree to take part in this study.

Name (Printed):

Client code: 1□-□□□ **IC/UNHCR number:** □□□□□□□□□□□□

Signanture (or thumbprint):

Date (dd/mm/yyyy):

Investigator's Statement

I confirm that I have carefully explained the purpose of the study to the participant and outlined any reasonably foreseeable risks or benefits (where applicable).

Name (Printed):

Researcher code: □□ **IC/UNHCR number:** □□□□□□□□□□□□

Signanture:

Date (dd/mm/yyyy):

Information Form for In-depth Interviews with Clients (You will be given a copy of this information sheet)	
Title of Project:	**Assessing adherence to highly active antiretroviral therapy (HAART) in refugee and host populations**
Name, address, and contact details of investigator:	**Joshua Mendelsohn MSc, Dr Anuradha Radhakrishnan MBBS MRCP, Dr Susheela Balasundaram MBBS** **UNHCR Malaysia** **No. 570, Jalan Bukit Petaling, P.O. Box 10185,** **50706 Kuala Lumpur, Malaysia** **Tel: 03-21411322 ext. 492**
This study has been approved by:	**Medical Research and Ethics Committee (MREC), Malaysia** **Clinical Research Centre (CRC), Malaysia** **London School of Hygiene and Tropical Medicine Ethics Committee**
Study Sponsor	**London School of Hygiene and Tropical Medicine**

We invite you to take part in this research project on how people take their antiretroviral medication. You should only take part if you want to. It is up to you to decide whether or not to take part. If you decide to take part you are still free to withdraw at any time and without giving a reason. If you choose not to participate or to withdraw it will involve no penalty or loss of benefits to which you are otherwise entitled. The standard of care you receive will be unaffected. This information sheet will now be read to you and you will be given an opportunity to ask questions and have answers provided. We would like you to consider taking part today, but if you wish, you may take this information sheet home for consideration. If you decide to take part you will be given this information form to keep and be asked to sign a form stating that you agree to take part in the study.

Aims of research: The purpose of the research is to understand how often people take their HIV medications (Highly Active Antiretroviral Therapy or "HAART"), and to understand factors that help people to take their medications or make it more difficult. Participants will include refugees and Malaysians who attend the same clinic.

Your role: Today you are being asked to participate in an in-depth interview to take place at _____. If you choose to participate, you will be interviewed for no more than 2 hours. If you give us permission, we would like to tape record your interview. This recording will only be used for research purposes. The interview will seek information about your adherence to HAART and challenges you may have faced while taking HAART.

Confidentiality: Interviews will be kept strictly confidential. All information obtained from interviews will be used in an anonymous way and may be used anonymously in future research. In the short term, the information you provide will be stored safely in Kuala Lumpur, Malaysia. In the longer term, it will also be stored safely in London, United Kingdom. If you choose to withdraw from the study data you may have provided will be retained unless you wish otherwise.

Incentives: If you agree to participate in this study you will receive a maximum reimbursement of 30 Malaysian Ringgits for travel expenses, a lunch, and a beverage. You will not receive any financial incentive. We hope that this research will help the clinic to develop ways to make it easier for people like you to take their HIV treatment.

Risks: Some of the issues discussed may be sensitive and could cause some discomfort. It is important that you communicate with the researcher in the event that you become very uncomfortable or anxious.

Follow-up: We may invite you to participate in a follow-up interview at a later time. In such instances, further information will be provided and your consent will be sought again.

Thank-you for taking the time to consider participating in this study. Please contact the investigator named at the top of this sheet if you have any questions in the future related to your participation, rights or if you have any complaints.

Informed Consent Form for In-depth Interviews with Clients *(This form is to be completed by the participant after reading the Information Sheet and/or having listened to an explanation about the research)*

Title of Project	**Assessing adherence to highly active antiretroviral therapy (HAART) in refugee and host populations**
Name, address, and contact details of investigator:	**Joshua Mendelsohn MSc, Dr Anuradha Radhakrishnan MBBS MRCP, Dr Susheela Balasundaram MBBS** **UNHCR Malaysia** **No. 570, Jalan Bukit Petaling, P.O. Box 10185,** **50706 Kuala Lumpur, Malaysia** **Tel: 03-21411322 ext. 492**
This study has been approved by:	**Medical Research and Ethics Committee (MREC), Malaysia** **Clinical Research Centre (CRC), Malaysia** **London School of Hygiene and Tropical Medicine Ethics Committee**
Study Sponsor	**London School of Hygiene and Tropical Medicine**

Participant's Statement

- I have read the information sheet concerning this study [and/or have understood the verbal explanation] and I understand what will be required of me and what will happen to me if I take part in it.
- My questions concerning this study have been answered by: **Name:** ..... **Position:** .....
- I understand that at any time I may withdraw from this study without giving a reason and without affecting my normal care and management.
- I consent to the use of my personal information for the purposes mentioned in the information sheet only and that it will not be used for any other purpose. I understand that such information will be treated as strictly confidential.
- I understand that confidentiality and anonymity will be maintained and it will not be possible to identify me from any publications.
- I understand that if I withdraw from the study, data that I may have provided will be retained unless I wish otherwise. If I do not withdraw, all data provided by me will be maintained in strict confidence.
- I agree to be contacted in the future by researchers who would like to invite me to participate in follow-up studies.
- I agree to the interview being tape recorded (*Please tick yes or no*): **Yes**..... **No**.....
- I agree to be quoted anonymously in research reports and publications. I understand that it will not be possible to identify me from any of these quotations. (*Please tick yes or no*): **Yes**..... **No**.....
- I agree to take part in this study.

Name (Printed):

Client code: 1□-□□□ **IC/UNHCR number:** □□□□□□□□□□□□

Signature (or thumbprint):

Date (dd/mm/yyyy):

Investigator's Statement

I confirm that I have carefully explained the purpose of the study to the participant and outlined any reasonably foreseeable risks or benefits (where applicable).

Name (Printed):

Researcher code: □□ **IC/UNHCR number:** □□□□□□□□□□□□

Signature:

Date (dd/mm/yyyy):

REPUBLIC OF KENYA

NATIONAL COUNCIL FOR SCIENCE AND TECHNOLOGY

Telegrams: "SCIENCETECH", Nairobi
Telephone: 254-020-241349, 2213102
254-020-310571, 2213123.
Fax: 254-020-2213215, 318245, 318249
When replying please quote

P.O. Box 30623-00100
NAIROBI-KENYA
Website: www.ncst.go.ke

Our Ref: NCST/RRI/12/1/MED/213/5

Date: 30th November 2010

Dr. Joshua Mendelsohn
London School of Hygiene & Tropical Medicine
UNITED KINGDOM

RE: RESEARCH AUTHORIZATION

Following your application for authority to carry out research on ***"Adherence to HAART in refugees and surrounding host communities: Is displacement a barrier to adherence?"*** I am pleased to inform you that you and your co-researcher, Dr. John Wagacha Burton have been authorized to undertake research **in Turkana District** for a period ending ***31st October 2011.***

You and your co-researcher are advised to report to **the District Commissioner, the District Education Officer, the Medical Superintendent, Turkana District and the Commissioner, United Nations High Commissioner for Refugees** before embarking on the research project.

On completion of the research, you are expected to submit **one hard copy and one soft copy** of the research report/thesis to our office.

P. N. NYAKUNDI
FOR: SECRETARY/CEO

Copy to:

The District Commissioner
Turkana District

The District Education Officer

Turkana District

The Medical Superintendent
Turkana District

The Commissioner
United Nations High Commissioner for Refugees
NAIROBI

KENYA MEDICAL RESEARCH INSTITUTE

P.O. Box 54840 - 00200 NAIROBI, Kenya
Tel: (254) (020) 2722541, 2713349, 0722-205901, 0733-400003; Fax: (254) (020) 2720030
E-mail: director@kemri.org info@kemri.org Website:www.kemri.org

KEMRI/RES/7/3/1 October 27, 2010

TO: DR. JOSHUA MENDELSOHN
PRINCIPAL INVESTIGATOR

THRO': DR. JOHN VULULE,
THE DIRECTOR, CGHR
KISUMU

RE: **SSC 1884(*INITIAL SUBMISSION*): ADHERENCE TO HAART IN REFUGEES AND HOST COMMUNITIES – IS DISPLACEMENT A BARRIER TO ADHERENCE?**

This is to inform you that during the 183rd meeting of the KEMRI/ERC meeting held on 19th October 2010, the above study was reviewed.

The committee notes that the aim of the above referenced study is threefold:

1. To evaluate HAART adherence, retention and defaulting at Kakuma refugee camp
2. To investigate factors that are associated with enhanced or reduced adherence to HAART refugees
3. To undertake a preliminary quantitative analysis and more detailed qualitative account of differences in adherence to HAART between refuges and surrounding host client groups who access their medications from shared clinics

Kindly note that the in the case of a research participant that cannot read or write an impartial witness will be required to sit in throughout the consenting process to ascertain that they (study subject) has an understanding of what they are in for.

Due consideration has been given to ethical issues and the study is hereby granted **annual renewal** effective this **27th day of October 2010**, for a period of twelve (12) months.

Please note that authorization to conduct this study will automatically expire on **26th October 2011**. If you plan to continue with data collection or analysis beyond this date, please submit an application for continuing approval to the ERC Secretariat by **8th September 2011**.

Sincerely,

R. C. KITHINJI,
FOR: SECRETARY,
KEMRI/NATIONAL ETHICS REVIEW COMMITTEE

KENYA MEDICAL RESEARCH INSTITUTE

P.O. Box 54840 - 00200 NAIROBI, Kenya
Tel: (254) (020) 2722541, 2713349, 0722-205901, 0733-400003, Fax: (254) (020) 2720030
E-mail: kemri-hq@nairobi.mimcom.net, director@kemri.org, Website: www.kemri.org

KEMRI/RES/7/3/1 November 22, 2011

TO: JOSHUA MENDELSOHN
PRINCIPAL INVESTIGATOR

FORWARDED
DIRECTOR
CENTRE FOR GLOBAL HEALTH RESEARCH

THRO': DR. J. VULULE
THE DIRECTOR, CGHR
KISUMU

RE: SSC NO.1884 (*REQUEST FOR ANNUAL RENEWAL*): ADHERENCE OF HAART IN REFUGEES AND SURROUNDING HOST COMMUNITIES: IS DISPLACEMENT A BARRIER TO ADHERENCE?

This is to inform that during the 195th meeting of the KEMRI/ERC meeting held on the 22nd of November 2011, the Committee conducted the annual review and approved the above referenced application for another year. We note this is the final project year and that the request for continuation is to allow additional time for analysis and dissemination.

This approval is valid from today **November 22, 2011** through to **November 21, 2012**. Please note that authorization to conduct this study will automatically expire on **November 21, 2012**. If you plan to continue with data collection or analysis beyond this date please submit an application for continuing approval to the ERC secretariat by September **1, 2012.**

You are required to submit any amendments to this protocol and other information pertinent to human participation in this study to the SSC and ERC for review prior to initiation.

Yours sincerely,

Caroline Kithinji,
FOR: Secretary
KEMRI/ETHICS REVEIW COMMITTEE

In Search of Better Health

Information Form for Client Questionnaire and Blood sample

(You will be given a copy of this information sheet.

Title of Project:	**Assessing adherence to highly active antiretroviral therapy (HAART) in refugee and host communities**
Name, address, and contact details of investigator:	**Joshua Mendelsohn MSc** **UNHCR Kenya, P. O. Box 43801-00100** **Nairobi, Kenya**
This study has been approved by:	**Kenya Medical Research Institute Ethical Review Board** **London School of Hygiene and Tropical Medicine Ethics Committee**
Study sponsor:	**London School of Hygiene and Tropical Medicine**

We invite you to take part in this research project on how people take their antiretroviral medication. You should only take part if you want to. It is up to you to decide whether or not to take part. If you decide to take part you are still free to withdraw at any time and without giving a reason. If you choose not to participate or to withdraw it will involve no penalty or loss of benefits to which you are otherwise entitled. The standard of care you receive will be unaffected. This information sheet will now be read to you and you will be given an opportunity to ask questions and have answers provided. We would like you to consider taking part today, but if you wish, you may take this information sheet home for consideration. If you decide to take part you will be given this information form to keep and be asked to sign a form stating that you agree to take part in the study.

Aims of research: The purpose of the research is to understand how often people take their HIV medications (Highly Active Antiretroviral Therapy or "HAART"), and to understand factors that help people to take their medications or make it more difficult. Participants will include refugees and Kenyans who attend the same clinic.

Your role: Today you are being asked to participate in a client questionnaire and to provide a blood sample. If you choose to participate, you will be interviewed for approximately 1 hour here at the Comprehensive Care Clinic (Kakuma) and we will ask you to give a blood spot sample afterwards. We do this by pricking the skin of your finger(s) and/or heel(s) and collecting five small drops of blood onto paper. The interview will seek information about your adherence to HAART and challenges you may have faced while taking HAART. The blood sample will be used to test how much HIV virus is in your blood and may also be tested for resistance to your medication and other HIV or other infectious disease-related tests at a future time. Your blood sample will be stored for 5 years at the Kenya Medical Research Institute/ Centres for Disease Control Laboratories (Kisumu) before being destroyed. We will also ask you to allow us to consult your medical records for up to three years in the past and for up to five years in the future.

Confidentiality: Interviews will be private and confidential. Your name will not be written on the interview questionnaire or on the blood sample specimen. Instead, a number will be used to protect your identity. All information obtained from interviews and the blood sample will be used in an anonymous way and may be used anonymously in future research. In the short term, the information you provide will be stored safely in Nairobi and Kisumu, Kenya. In the longer term, it will also be stored safely in London, UK. If you choose to withdraw from the study, blood samples and data that you already provided will be retained unless you wish otherwise.

Incentives: If you agree to take part you will be offered a snack or beverage and snack during the interview and 200 KSH to help you with transport and for any missed meals during interviews. You will not receive any financial incentive. We hope that this research will help the clinic to develop ways to make it easier for people like you to take their HIV treatment.

Risks: Some questions may ask for personal information which may cause discomfort. You may choose not to answer these questions. It is important that you communicate with the researcher in the event that you become very uncomfortable or anxious. Giving dried blood spot samples presents a minimal risk of infection. Discomfort tends to be brief and transient.

Follow-up: There is the potential we will invite you to participate in a follow-up interview at a different time. If so we will ask you at the end of this interview or be in touch within two weeks. In such instances, information will be provided and your consent will be sought again.

Thank-you for taking the time to consider participating in this study. Please contact the investigator named at the top of this sheet if you have any questions in the future related to your participation, rights or if you have any complaints.

Informed Consent Form for Client Questionnaire and Blood sample

(This form is to be completed by the participant after reading the Information Sheet and/or having listened to an explanation about the research.)

Title of Project:	**Assessing adherence to highly active antiretroviral therapy (HAART) in refugee and host communities**
Name, address, and contact details of investigator:	**Joshua Mendelsohn MSc** **UNHCR Kenya, P. O. Box 43801-00100** **Nairobi, Kenya**
This study has been approved by:	**Kenya Medical Research Institute Ethical Review Board** **London School of Hygiene and Tropical Medicine Ethics Committee**
Study sponsor:	**London School of Hygiene and Tropical Medicine**

Participant's Statement

- I have read the information sheet concerning this study [and/or have understood the verbal explanation] and I understand what will be required of me and what will happen to me if I take part in it.
- My questions concerning this study have been answered by: **Name:** ..... **Position:** .....
- I understand that at any time I may withdraw from this study without giving a reason and without affecting my normal care and management.
- I consent to the use of my personal information for the purposes mentioned in the information sheet only and I understand that it will not be used for any other purpose. I understand that such information will be treated as strictly confidential.
- I understand that confidentiality and anonymity will be maintained and it will not be possible to identify me from any publications.
- I understand that if I choose to withdraw from the study, blood samples and data that I may have provided will be retained unless I wish otherwise. If I do not withdraw, my blood samples will be destroyed after 5 years of storage at the Kenya Medical Research Institute / Centres for Disease Control Laboratories (Kisumu) and all data provided by me will be maintained in strict confidence.
- I agree to be contacted in the future by researchers who would like to invite me to participate in follow-up studies.
- I agree to take part in this study.

Name (Printed):

Client code: 2□-□□□ **Identity number:** □□□□□□□□□□□□

Signature (or thumbprint):

If thumbprint, signature of impartial witness:

Date (dd/mm/yyyy):

Investigator's Statement

I confirm that I have carefully explained the purpose of the study to the participant and outlined any reasonably foreseeable risks or benefits (where applicable).

Name (Printed):

Researcher code: □□ **Identity number:** □□□□□□□□□□□□

Signature:

Date (dd/mm/yyyy):

Information Form for In-depth Interviews with Clients

(You will be given a copy of this information sheet.

Title of Project:	**Assessing adherence to highly active antiretroviral therapy (HAART) in refugee and host communities**
Name, address, and contact details of investigator:	**Joshua Mendelsohn MSc** **UNHCR Kenya, P. O. Box 43801-00100** **Nairobi, Kenya**
This study has been approved by:	**Kenya Medical Research Institute Ethical Review Board** **London School of Hygiene and Tropical Medicine Ethics Committee**
Study Sponsor	**London School of Hygiene and Tropical Medicine**

We invite you to take part in this research project on how people take their antiretroviral medication. You should only take part if you want to. It is up to you to decide whether or not to take part. If you decide to take part you are still free to withdraw at any time and without giving a reason. If you choose not to participate or to withdraw it will involve no penalty or loss of benefits to which you are otherwise entitled. The standard of care you receive will be unaffected. This information sheet will now be read to you and you will be given an opportunity to ask questions and have answers provided. We would like you to consider taking part today, but if you wish, you may take this information sheet home for consideration. If you decide to take part you will be given this information form to keep and be asked to sign a form stating that you agree to take part in the study.

Aims of research: The purpose of the research is to understand how often people take their HIV medications (Highly Active Antiretroviral Therapy or "HAART"), and to understand factors that help people to take their medications or make it more difficult. Participants will include refugees and Kenyans who attend the same clinic.

Your role: Today you are being asked to participate in an in-depth interview to take place at the Comprehensive Care Clinic, Kakuma. If you choose to participate, you will be interviewed for no more than 2 hours. If you give us permission, we would like to tape record your interview. This recording will only be used for research purposes. The interview will seek information about your adherence to HAART and challenges you may have faced while taking HAART.

Confidentiality: Interviews will be kept strictly confidential. All information obtained from interviews will be used in an anonymous way and may be used anonymously in future research. In the short term, the information you provide will be stored safely in Nairobi, Kenya. In the longer term, it will also be stored safely in London, UK. If you choose to withdraw from the study, data that you already provided will be retained unless you wish otherwise.

Incentives: If you agree to take part in this study, you will be offered a snack and beverage during the interview and 200 KSH to help you with transport and for any missed meals during interviews. You will not receive any financial incentive. We hope that this research will help the clinic to develop ways to make it easier for people like you to take their HIV treatment.

Risks: Some of the issues discussed may be sensitive and could cause some discomfort. It is important that you communicate with the researcher in the event that you become very uncomfortable or anxious.

Follow-up: We may invite you to participate in a follow-up interview at a later time. In such instances, further information will be provided and your consent will be sought again.

Thank-you for taking the time to consider participating in this study. Please contact the investigator named at the top of this sheet if you have any questions in the future related to your participation, rights or if you have any complaints.

Informed Consent Form for In-depth Interviews with Clients

(This form is to be completed by the participant after reading the Information Sheet and/or having listened to an explanation about the research.)

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This study has been approved by:	**Kenya Medical Research Institute Ethical Review Board** **London School of Hygiene and Tropical Medicine Ethics Committee**
Study Sponsor	**London School of Hygiene and Tropical Medicine**

Participant's Statement

- I have read the information sheet concerning this study [and/or have understood the verbal explanation] and I understand what will be required of me and what will happen to me if I take part in it.
- My questions concerning this study have been answered by: **Name:** ..... **Position:** .....
- I understand that at any time I may withdraw from this study without giving a reason and without affecting my normal care and management.
- I consent to the use of my personal information for the purposes mentioned in the information sheet only and I understand that it will not be used for any other purpose. I understand that such information will be treated as strictly confidential.
- I understand that confidentiality and anonymity will be maintained and it will not be possible to identify me from any publications.
- I understand that if I withdraw from the study, data that I may have provided will be retained unless I wish otherwise.
- I agree to be contacted in the future by researchers who would like to invite me to participate in follow-up studies.
- I agree to the interview being tape recorded (*Please tick yes or no*): **Yes**..... **No**.....
- I agree to be quoted anonymously in research reports and publications. I understand that it will not be possible to identify me from any of these quotations. (*Please tick yes or no*): **Yes**..... **No**.....
- I agree to take part in this study.

Name (Printed):

Signature (or thumbprint):

If thumbprint, signature of impartial witness:

Date (dd/mm/yyyy):

Client code: 2☐-☐☐☐

Identify number: ☐☐☐☐☐☐☐☐☐☐☐☐

Investigator's Statement

I confirm that I have carefully explained the purpose of the study to the participant and outlined any reasonably foreseeable risks or benefits (where applicable).

Name (Printed):

Signature:

Date (dd/mm/yyyy):

Researcher code: ☐☐

Identity number: ☐☐☐☐☐☐☐☐☐☐☐☐