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Rates of virological failure in patients treated in a home-based versus a facility-based HIV-care model in Jinja, southeast Uganda: a cluster-randomised equivalence trial

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Summary

Background—Identification of new ways to increase access to antiretroviral therapy in Africa is an urgent priority. We assessed whether home-based HIV care was as effective as was facility-based care.

Methods—We undertook a cluster-randomised equivalence trial in Jinja, Uganda. 44 geographical areas in nine strata, defined according to ratio of urban and rural participants and distance from the clinic, were randomised to home-based or facility-based care by drawing sealed cards from a box. The trial was integrated into normal service delivery. All patients with WHO stage IV or late stage III disease or CD4-cell counts fewer than 200 cells per μL who started antiretroviral therapy between Feb 15, 2005, and Dec 19, 2006, were eligible, apart from those living on islands. Follow-up continued until Jan 31, 2009. The primary endpoint was virological failure, defined as RNA more than 500 copies per mL after 6 months of treatment. The margin of equivalence was 9% (equivalence limits 0·69–1·45). Analyses were by intention to treat and adjusted for baseline CD4-cell count and study stratum. This trial is registered at http://isrctn.org, number ISRCTN 17184129.

Findings—859 patients (22 clusters) were randomly assigned to home and 594 (22 clusters) to facility care. During the first year, 93 (11%) receiving home care and 66 (11%) receiving facility care died, 29 (3%) receiving home and 36 (6%) receiving facility care withdrew, and 8 (1%) receiving home and 9 (2%) receiving facility care were lost to follow-up. 117 of 729 (16%) in

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home care had virological failure versus 80 of 483 (17%) in facility care: rates per 100 person-years were 8·19 (95% CI 6·84–9·82) for home and 8·67 (6·96–10·79) for facility care (rate ratio [RR] 1·04, 0·78–1·40; equivalence shown). Two patients from each group were immediately lost to follow-up. Mortality rates were similar between groups (0·95 [0·71–1·28]). 97 of 857 (11%) patients in home and 75 of 592 (13%) in facility care were admitted at least once (0·91, 0·64–1·28).

Interpretation—This home-based HIV-care strategy is as effective as is a clinic-based strategy, and therefore could enable improved and equitable access to HIV treatment, especially in areas with poor infrastructure and access to clinic care.

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Introduction

Antiretroviral drug therapy has been scaled up rapidly in Africa, and is now given to more than 2 million people. A global commitment has been made to provide universal coverage, but another 5 million people, mostly living in rural and semiurban areas, are estimated to need such treatment. Achievement of high coverage in these populations will be a challenge. Two major barriers to increasing coverage exist—a severe shortage of clinically qualified staff, which has reached crisis point in most of Africa, and difficulty for patients in accessing clinics because of high costs and poor availability of transport and low-cash incomes.

WHO proposes decentralised antiretroviral therapy delivery, and so far services for such therapy have been provided through nurse-led centres with simplified protocols in several settings, including in Malawi, Zambia, Mozambique, Botswana, and South Africa. Good patient outcomes have been reported from short-term assessments done in some sites, but interpretation of this evidence is difficult because of poor retention rates. Furthermore, nursing staff as well as doctors are in very short supply and care needs to be delegated to non-clinical workers, although evidence for use of non-clinical workers in HIV care is scarce. In Tororo, Uganda, a home-based programme with lay workers has achieved good outcomes, but it consisted of home visits made every week with good access to clinical staff when needed—a model that would be difficult to scale up. No direct comparisons of hospital-based HIV care versus any form of decentralised HIV care have been done in Africa. We assessed home-based HIV care, with lay workers delivering antiretroviral therapy and monitoring patients, versus facility-based HIV care.

Methods

Study setting and patients

We undertook a trial based at the AIDS Support Organisation (TASO) clinic in Jinja district, southeast Uganda. TASO is a large non-governmental organisation with 11 centres in the country, offering counselling and social and clinical services to people with HIV. The Jinja district and surrounding area is poor, with inhabitants on low-cash incomes. TASO clinic serves a predominantly rural and semiurban population from a radius of about 100 km. Most TASO clients are subsistence farmers, and very few work in the formal sector earning wages.

In accordance with guidelines from the Ugandan Ministry of Health, people with HIV were eligible to start antiretroviral therapy if they were assessed to be at WHO stage IV or late stage III disease, or if they had a CD4-cell count of fewer than 200 cells per μL. Eligible patients were prepared for therapy by TASO staff during three visits to clinic, which were usually spread over 4 weeks. Information and counselling were provided both in groups and

in one-to-one sessions. Participants were given drugs for 28 days of treatment and issued with a pill box. A buffer supply for 2 days was provided. Patients were also strongly encouraged to identify a so-called medicine companion to provide support and reminders. Medicine companions were given information by TASO about the basic principles of antiretroviral therapy and adherence.

All TASO patients older than 18 years who were starting on antiretroviral therapy for the first time were invited to join the trial, apart from those living on islands, which were about 100 km away and where provision of home-based care was not possible. All patients provided written informed consent. The trial protocol was approved by the Ugandan National Council of Science and Technology and the Institutional Review Boards of the Uganda Virus Research Institute, Centers for Disease Control and Prevention, and London School of Hygiene and Tropical Medicine. Patients were informed about their rights to refuse to join the trial or withdraw subsequently. Those who did were offered facility-based HIV care (including antiretroviral therapy) from TASO Jinja.

Study design

Recruitment began Feb 15, 2005, and ended Dec 19, 2006, and follow-up continued until Jan 31, 2009. Numbers of patients eligible for antiretroviral therapy were not known in advance—participants were identified after they were tested for CD4-cell counts and clinically assessed. The catchment area was divided into nine strata according to ratio of urban and rural participants and approximate distance from a central point to the TASO Jinja clinic. In every stratum, an even number of clusters (geographical areas) were defined for randomisation along subdistrict boundaries, or, in the case of a few large subdistricts, by known barriers within the subdistrict. Clusters in every stratum had a similar estimated number of people with HIV who were registered at TASO Jinja. Distribution of strata and clusters was as follows: (1) four clusters in urban areas or near the TASO Jinja facility; (2) eight in periurban intermediate distance; (3) eight in rural and far; (4) four in Kamuli district; (5) four in Mukono district near; (6) six in Mukono district far; (7) six in Mayuge district; (8) two in Iganga district near; and (9) two in Iganga district far. Strata and clusters were devised by two people with knowledge of the area (one TASO staff member and one researcher) and cross-checked independently by two other people on two separate occasions.

For all patients, antiretroviral therapy was started at the TASO Jinja clinic, and thereafter patients received care according to the treatment to which their residential area had been assigned. After giving consent, patients were enrolled into the study by research staff, and their addresses were confirmed from TASO records. At every clinic visit, research staff interviewed participants in privacy in a separate building soon after their arrival and before they saw TASO staff.

Randomisation

Clusters in each strata were allocated to either home-based or facility-based care by drawing cards from a concealed box. The cards were sealed in advance and labelled with the stratum number by the trial coordinator and TASO senior medical officer who organised the allocation event and placed the cards into the box for each stratum. Cards were drawn by two patient representatives, a TASO medical officer, TASO counsellor, and TASO field officer, each taking turns. This process was done in the presence of senior TASO staff, researchers, and local public health representatives.

Models of care

The trial was done in conditions similar to those of actual health services, with TASO staff responsible for service delivery. Numbers of counsellors, nurses, and laboratory and

pharmacy staff in Jinja were similar to those at other TASO centres. The clinic had five medical officers but the number present usually varied between two and four, with some support from local part-time physicians during the trial. Most medical officers were newly qualified. Clinical staff were trained on antiretroviral therapy and supported by a senior medical officer.

For the home-based group, trained field officers travelling on motorcycles visited patients at home every month to deliver drugs, monitor participants with a checklist that included signs and symptoms of drug toxicity or disease progression, and provide adherence support. Most field officers had degree qualifications or college diplomas and underwent 4 weeks of intensive training at the start of the study and yearly refresher courses thereafter about the principles of antiretroviral therapy and adherence support. They were supported at the TASO clinic by counsellors and medical officers.

Field officers referred patients to a physician or counsellor at the TASO clinic when they judged referral to be necessary. They had mobile phones and could contact physicians when unsure about referral. At the end of every day, a medical officer reviewed the notes made by field officers and, when needed, asked officers to return to the patient's home to refer them. Patients who were not at home for their monthly appointment were visited again—usually the next day. If they were absent again, fieldworkers left a message for them to come to the clinic. All patients were invited to the clinic for routine reviews by a medical officer and a counsellor at 2 and 6 months after starting therapy and every 6 months thereafter. Drugs were not dispensed during clinic visits for those allocated to home-based case. Before antiretroviral therapy started, TASO offered free voluntary counselling and testing in the home to household members of participants. This offer was repeated during home visits for drug delivery for those who were absent previously.

In the facility-based group, patients obtained drugs every month from the clinic and had routine reviews with a medical officer and counsellor that were scheduled at 2 and 3 months after start of treatment and every 3 months thereafter. Apart from scheduled reviews, patients were assessed during clinic visits by a nurse and referred to a doctor when necessary. When an appointment was missed, patients were followed up at home by a field officer (if patients had given permission for home visits), usually after 2–3 days, and reminded to attend clinic. Participants were also given vouchers for their household for free voluntary counselling and testing at TASO Jinja. Patients in both groups were asked to come to the clinic any time that they felt unwell. They were also given a telephone number to call for advice. In exceptional cases, and when TASO resources allowed, home care was provided by a team, including a physician, to patients who were bedridden. No financial or other incentives were provided to patients or staff and TASO clinical management procedures were identical for trial and non-trial participants.

Procedures

Independent research staff assessed adherence. Patients in both groups were interviewed during routine clinical and counselling visits at 2 months and 6 months after starting therapy and then every 6 months. Questionnaires were translated into the local language, Luganda, and then back into English by an independent person, and cross-checked by another researcher who was not involved with the trial.

Clinical data were transcribed from patient notes. A change to a second-line regimen was decided by a TASO case conference, consisting of physicians and counsellors, and was made when a patient had one of the following criteria: (1) new or recurrent WHO clinical stage IV or advanced stage III disease; (2) clinical deterioration (eg, weight loss) and two or more consecutive CD4-cell counts less than baseline, or a fall to 50% less than peak CD4-

cell count attained after the start of antiretroviral therapy; or (3) CD4-cell counts persistently fewer than 100 cells per μL. Survival status was established through home follow-ups or hospital records, dependent on where deaths took place. We established the status of participants who withdrew from TASO records.

CD4-cell counts were monitored by TASO staff every 6 months for all patients as part of their clinical care. CD4-positive cells were measured with TriTEST reagents (Becton-Dickenson, Franklin Lakes, NJ, USA), according to an inhouse dual-platform protocol and MultiSET and Attractors software (version 2.2) with a FACScan flow cytometer (Becton-Dickinson, Franklin Lakes, NJ, USA). Additional blood was taken to measure plasma viral load, but this testing was for research reasons and done in batches later. Plasma was separated within 2 h and stored immediately at −80°C. HIV-1 RNA was tested with the VERSANT RNA 3.0 (Bayer, Bayer HealthCare, NY, USA) assay (with a lower limit of detection of 50 copies per mL) for baseline samples, and the Amplicor MONITOR 1.5 (Roche, Roche Molecular Systems, NJ, USA) for other samples (400 per copies per mL). After we established close correlation between results of the two assays, the Amplicor assay was used to keep costs to a minimum.

Our economic analysis took a societal perspective and included recurrent and capital costs incurred by the provider, transport and other related costs, and income lost by patients while accessing care. We reported all costs in 2008 US$; the mean exchange rate from 2005 to 2008 was 1732 Ugandan shillings to $1. Cost data and all data for care provided by TASO were obtained from TASO accounts. We used three steps to allocate costs. First, we established the proportion of all TASO clients who were receiving antiretroviral therapy. Second, we calculated the percentage of TASO clients on therapy who entered the trial. Both percentages changed over time, rising initially as numbers of patients who were put on therapy increased, and then falling when recruitment stopped. To capture this dynamic situation, we gathered and aggregated monthly cost data every 6 months, and converted data to US$ with the prevailing exchange rate, with adjustment for inflation.

Third, we allocated costs to facility and home groups. When possible, we used actual service data—eg, information about numbers of doctor visits was used to allocate staff time. We assigned antiretroviral therapy costs proportionally by patient numbers in both groups for that period. Drug prices included purchase cost, insurance, and freight to Uganda and were adjusted to account for substantial price reductions that occurred early in the project. We established costs incurred by patients through a questionnaire.

Health-services costs consisted of: staff costs (doctors, field officers, cousellors, and other staff), transport (motorcycle and vehicle costs of fuel and maintenance, and other transport costs); all drugs; laboratory and clinical expenses (radiograph, ultrasound, and laboratory and CD4 tests); sensitisation (AIDS education via radio, other media, and drama); training, teambuilding, and workshops; utilities (electricity, telephone, postage, and security), supervision and overheads (stationery, repairs, overheads, and supervision costs), and capital costs (buildings, furniture, vehicles, equipment, and inventory). Buildings depreciated over 50 years and other elements 5 years (eg, The AIDS Support Organisation practice). Patient costs consisted of: cost of transport (including transport of medicine companion), childcare, and lunches, if applicable, median weighted by proportion ($2·88 for women and $3·46 for men); and lost work time, estimated 1 day for clinic visits and 0·5 days for home visits, valued at Uganda mean per head gross domestic product from 2005–08 (World Bank data) for 300 working days per year.

The primary endpoint was rate of virological failure, defined as time (starting from 6 months) to a plasma RNA viral load of more than 500 copies per mL. The secondary

outcome measures were time to either detectable plasma viral load of more than 500 copies per mL at any visit from 12 months onwards in patients with viral loads of fewer than 500 copies per mL at 6 months, or an increase of 1000 copies per mL between two consecutive tests in those not achieving a viral load of fewer than 500 copies per mL at 6 months. Other secondary outcomes were all-cause mortality; virological failure as defined in the primary outcome or death; time to first admission; death, admission, or change to second-line antiretroviral therapy; outpatient attendance; adherence during the previous 28 days (measured with a standardised questionnaire); and costs incurred by the health service and patients.

Statistical analysis

We designed the study as an equivalence trial. Virological failure time was taken as halfway between the last measure of RNA of 500 copies per mL or fewer and the first of more than 500 copies per mL. Testing was repeated in patients who had viral loads between 500 and 1000 copies per mL to exclude the possibility of small transient increases. We assumed that in one group the rate of virological failure during follow-up would be about 20%, and that the other group could be regarded as equivalent if the rate of virological failure did not exceed 20% by more than 9%—ie, 29% or less. Thus, the upper limit of our equivalence interval was 29/20 or 1·45, and by symmetry the lower limit was 20/29 or 0·69. A sample size of 20 clusters per group with a total of 1200 participants gave more than 95% power to show equivalence, on the assumption of a between-cluster coefficient of variation of 0·2.

Analysis was by intention to treat, in which all participants were regarded as randomly assigned to the group corresponding to the cluster in which they lived. Analyses were done for the individual by fitting generalised linear mixed models with a log-link and poisson distribution, with every patient contributing an outcome of 1 if they had virological failure and 0 if they did not. The model had fixed terms for study regions, baseline CD4-cell counts (categorised as a four-level factor with counts of 0–49, 50–99, 100–149, and 150 or more cells per μL), and study groups, with the log of exposure time included as an offset variable, and a random term for study cluster. The model was fitted with the assumption that the random cluster effects followed a γ distribution. For the primary endpoint, exposure time was calculated from the 6-month visit to midway between the last date on which the patient did not have virological failure and the date of virological failure. For other endpoints, exposure time was calculated from enrolment. Those who withdrew or were lost to follow-up before 12 months were excluded from the primary endpoint analysis, and for other endpoints they were censored on the last date seen.

Role of the funding source

Sponsor staff had a role in the study design, data collection, data analysis, data interpretation, and writing of the report. The corresponding author had full access to the data and had final responsibility for the decision to submit for publication.

Results

Figure 1 shows the trial profile. The two groups were well balanced according to baseline characteristics apart from CD4-cell count, which was lower in the home-based than in the facility-based group (table 1). The median cluster size for home-based care was 36 people (range 6–84) and for facility-based care was 25 (2–65). Overall, 1403 patients (97%) were taking co-trimoxazole prophylaxis and 101 (7%) were being treated for tuberculosis. 119 patients withdrew during the course of the trial. Their status at the end of the trial was: three (3%, one from the facility and two from the home group) had died, 98 (82%, 48 facility and 50 home) were receiving antiretroviral therapy, one (<1%, facility) was alive and not

receiving antiretroviral therapy, and 17 (15%, eight home and nine facility) were no longer in contact with TASO. The median follow-up of survivors on home-based care was 28 months (IQR 18–35) and on facility-based care was 27 months (13–34).

Table 2 shows rates of virological failure, death, and hospital admission by group. Figure 2 shows HIV-RNA virological suppression and survival over time by study group. Rates of detection of plasma viral loads of more than 500 copies per mL after a 6-month visit were much the same in both groups. Also similar were the composite rates of either plasma RNA viral loads of more than 500 copies per mL after a 6-month visit in those who had undetectable viral loads at 6 months, or an increase in plasma RNA viral load of 1000 copies per mL between two consecutive tests in those who had detectable viral loads at 6 months. 184 (24%) patients having home and 145 (27%) facility care either had virological failure, were lost to follow-up, or withdrew from the trial (adjusted rate ratio [RR] 0·88, 95% CI 0·70–1·10).

Mortality rates were much the same in the two groups during the study (figure 2). Combined mortality rates per 100 person-years were 16·47 (95% CI 13·69–19·82) during the first 5 months after treatment started, 6·69 (4·94–9·05) for 6–11 months, 2·71 (1·92–3·84) for 12–23 months, and 0·97 (0·54–1·76) for 24 months and after. By the end of the study, 566 (66%) participants in the home group and 377 (63%) in the facility group were alive, receiving follow-up, and had undetectable plasma viral loads.

Admission diagnoses were similar in both groups (table 3). 20 (13%) patients who were admitted died (15 on home and five on facility care) and eight (5%) worsened and requested discharge (six on home and two on facility care)—seven died subsequently. Table 4 shows frequency of outpatient attendance at clinic, number of presentations in which a new diagnosis was made, and new diagnoses by number and type. Distribution of diagnoses was similar between groups and more than half were infectious and parasitic disease.

CD4-cell counts increased rapidly in both groups (figure 3). 748 (87%) participants in home care and 521 (88%) in facility care were tested for CD4-cell count at least once after starting treatment, with median intervals between baseline and final tests of 32 months (IQR 25–39) for home and 29 months (23–35) for facility. 608 (81%) in home and 419 (80%) in facility had CD4-cell counts of greater than 200 cells per μL at the final visit. Counts at this visit were lower than baseline in 32 (4%) of those in home compared with 29 (6%) in facility care. At routine clinical and counselling reviews, home participants reported complete adherence to therapy in the past 28 days in 3698 of 3951 (94%) visits compared with 2527 of 2768 (91%) visits made by facility participants (figure 4). Patients were too sick to be interviewed in a further 78 (2%) home-group and 39 (1%) facility-group visits. Only two patients, both in home-based care, refused to answer adherence questions—saying they were in a hurry to return home.

138 (16%) of patients in home care had a drug substitution at a median 9 months (IQR 2–24) versus 123 (21%) in facility care at 8 months (3–22) after treatment started. Most substitutions were because of adverse reactions to antiretroviral therapy (table 5). Only one person in home-based and two in facility-based care had their first-line treatment changed to second-line.

Table 6 shows mean yearly health services cost per patient calculated during 4 years, (including capital and recurrent expenses, and those of the starting phase and subsequent years). A large proportion of the costs were for drugs and staff salaries. The main cause of excess expenditure for the facility-based group was the increased number of contacts with health staff—especially with nurses and medical officers. These costs outweighed those of transport for field officers in the home-based group. Patient costs (transport of patient and

companion, lunches, child care, and time lost from work) were much higher for the facility-based than for the home-based group (table 6).

During the first year, when many visits were needed to start antiretroviral therapy, median yearly costs incurred by every patient were higher in facility than in home (table 6). Much of this expense was for transport. After the first year, patient costs for the home-based group were fairly low but remained high for the facility-based group, showing the economic burden of monthly clinic visits. Overall, the median cost of a clinic visit was $2·30—about 13% of reported monthly cash incomes for men and 20% for women.

Discussion

We have shown that a home-based HIV-care strategy with trained lay workers supporting drug delivery and monitoring patients was as effective as was a nurse-led and doctor-led clinic-based strategy for prevention of virological failure, mortality, and other adverse outcomes. For our primary endpoint of virological failure, the adjusted RR was contained between the pre-specified equivalence limits of 0·69 to 1·45. Results were similar for other endpoints. The home-based strategy did not result in higher costs for the health service. Moreover, home-based care was slightly cheaper than facility-based care by about $45 per patient per year, or 6% of the total cost. Costs incurred by patients to access care were much less for those in the home group than for those receiving facility-based care.

We have identified a strategy to provide effective HIV care in the many settings in Africa in which clinical staff are scarce and patient access to clinics is difficult. Our findings were achieved in a standard resource-constrained health-service setting. Mortality rates in our facility-based group of about six deaths per 100 person-years and virological failure rates of nine per 100 person-years were better than or at least as good as were those reported from most other settings. Other researchers have reported mortality rates ranging from six to more than 15 deaths per 100 person-years and virological failure rates from 15% to more than 40% for 12–24 months. Thus, findings from our home-based care strategy were compared with a well functioning facility-based model and identified to be equivalent. Mortality rates in developed countries are about two deaths per 100 person-years and most of the increased mortality in Africa takes place during the first year of follow-up, as we identified. This mortality rate could be reduced through starting of antiretroviral therapy earlier than it is at present, but how people with HIV infection who need treatment can be identified early and encouraged to seek care is less clear, and needs to be investigated. Our study shows that community-based approaches would be important.

We transferred care from the clinic to trained lay workers visiting homes of patients. The costs of the home visits were offset by the savings from reduced attendence at clinic—thus, 75% fewer clinic visits were made by patients in the home-based group, and 50% fewer consultations with a doctor took place when a new clinical disorder was recorded. We recorded no negative effect on survival, plasma viral load, or other outcomes. Patients had regular counselling and adherence support, especially in the home group in which support was personalised and often provided by the same individual. This support could have had a major positive effect on outcomes. Such an approach should be achievable throughout Africa since counsellors and other support staff are more easily available and rapidly trained than are clinical staff and incur much less expense for health services. A large randomised trial at two sites in Uganda and one in Zimbabwe recorded health-service costs of $846 (2008 exchange rate) for a model of laboratory and clinical monitoring at a health facility, which is similar to $793 in our home group and $838 in our facility group.

Costs of access to care are a major burden for most African people, especially for those living in rural areas, because cash incomes are very low. In our study, one clinic visit was

15–20% of monthly earnings for most people. In Africa, high travel costs relative to income are major determinants of poor access to care, late presentation, poor adherence, and low retention of people in antiretroviral-therapy programmes. Our study shows that home-based care could substantially reduce costs for patients and this outcome might have a major beneficial effect on their long-term adherence and retention.

In our study, TASO changed treatment to second-line therapy for three people only, which was substantially fewer than those who had falls in CD4-cell counts to less than their baseline or virological failure, showing the major differences in the diagnostic accuracy of clinical and laboratory assessments. When to change HIV treatment is a dilemma in many settings in Africa because of poor availability and high costs of second-line regimens and the absence of information about resistance to antiretroviral therapy—a situation that is unlikely to greatly change in the near future. We should, therefore, identify means to achieve the best possible adherence to extend the life of existing drugs. Our results suggest that community-based support of patients receiving antiretroviral therapy could lead to high adherence.

Very few studies have been done in which models of care are randomly assigned because of strong preferences of some individuals for a specific method of care and the role of stigma, which might result from HIV status disclosure—eg, if a field worker from a known AIDS support organisation visits a patient in the community. We overcame these difficulties by developing a partnership with the service provider, the community, and with patients from the beginning when the research question was defined, and then held regular meetings with stakeholders to discuss difficulties and provide information. No monetary incentives were provided to either the service provider or patients. Only 41 (3%) of participants refused to join the trial or later withdrew and cited stigma as a reason. All received antiretrovirals from TASO or other providers. The importance and effects of stigma in the long term when patients have sustained improved health and, for example, resumed normal relationships, is unclear. However, we have shown that community-based HIV care is feasible and that stigma is probably not an impediment to increasing coverage in settings in which trust and good relations between service providers and the community are present.

Our study could have been affected by selection bias, but numbers of refusals and withdrawals were low and almost identical in both groups. Most people who withdrew were alive at the end of the study—survival status was unknown for just 51 (4%) of participants. More were recruited in the home group than in the facility group but many more in the home group were screened, suggesting that this imbalance arose by chance. Median baseline CD4-cell count was also lower in the home group than in the facility group, but again this finding was probably attributable to chance (and was adjusted for in the analysis). These imbalances show the weakness of cluster-randomised trials in achievement of balance through randomisation, even in trials such as ours in which a large number of clusters were randomised.

We have shown that home-based HIV care with antiretroviral therapy is an effective strategy, which relies less on clinical staff and hospital services than does facility-based care and provides large savings for patients. Such community-based strategies could enable improved and equitable access to HIV treatment—especially in areas in which clinical infrastructure is scarce and patient access to clinic-based care is poor.

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Acknowledgments

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Acknowledgments

SJ, HG, AC, JM, and RB were the principal investigators, wrote the protocol, and supervised implementation of the study. SJ was the main author. SF wrote the protocols for the costs component and with RK analysed these data. JL analysed data for the primary and secondary endpoints. BA, GN, JB, and CN were responsible for coordination of field and clinical activities and data collection. NN was responsible for the virology testing and contributed to interpretation of laboratory data. AO and JWT gave input into study implementation and interpretation of findings. All authors contributed to writing of the report and have seen and approved the final version of the report.

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Data and safety monitoring board members are indicated by an asterisk. *Medical Research Council and Uganda Virus Research Institute Research Unit on AIDS (Entebbe, Uganda)* T Eliatu, P Kaleebu, E Tugumisirize, B Wolff, P Munderi*, S Muyingo*, J Todd*; *The AIDS Support Organisation (Kampala, Uganda)* B Etukoit, S Khanakhwa, J Luzze, E Mugalanzi; *Ministry of Health AIDS control programme (Kampala, Uganda*) E Madraa; *Jinja District Hospital (Uganda)* E Habyara; *Makerere University, Kampala (Uganda)* J Freers*.

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We declare that we have no conflicts of interest.

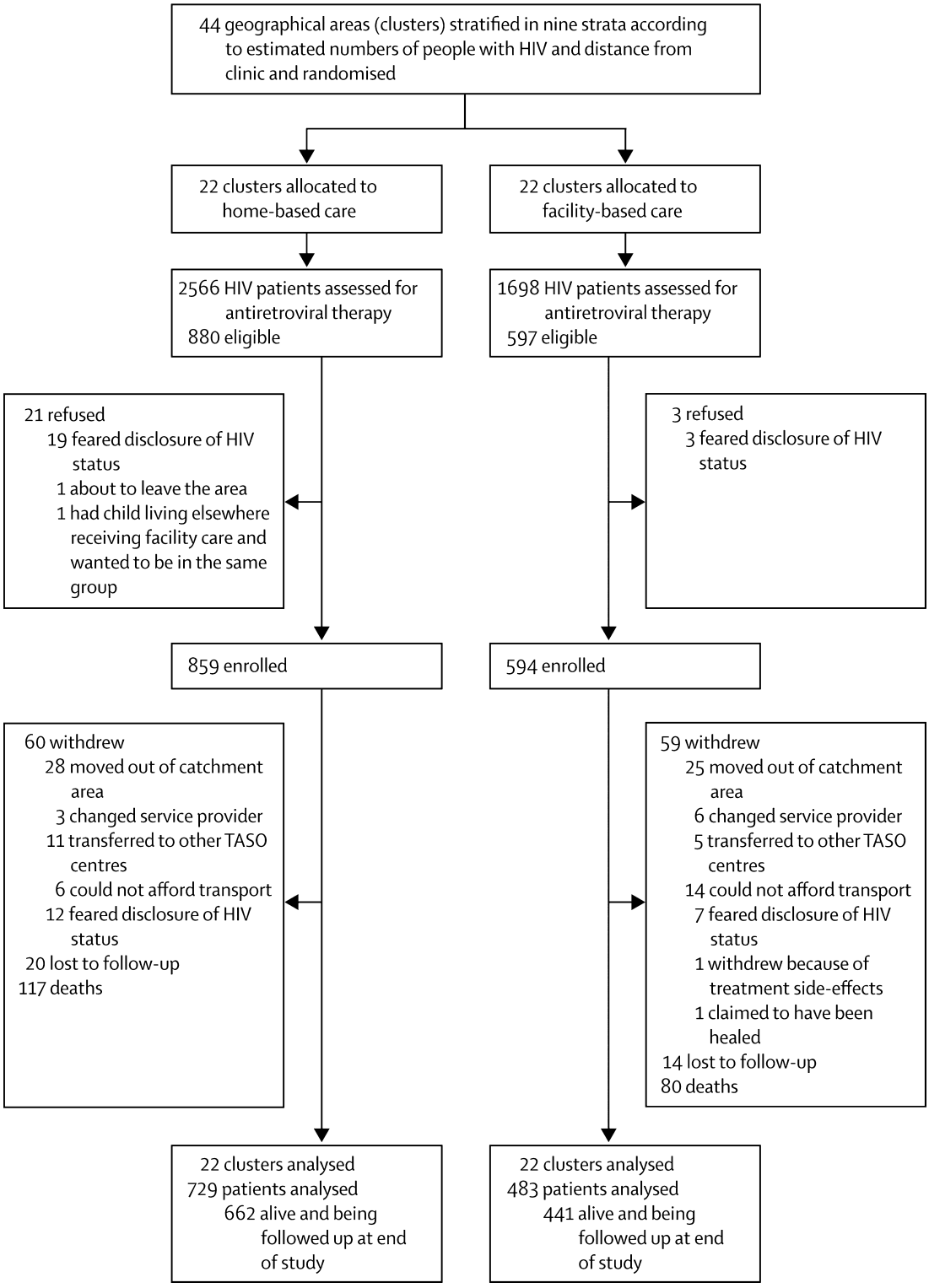

Figure 1.
Trial profile
TASO=The AIDS Support Organisation.

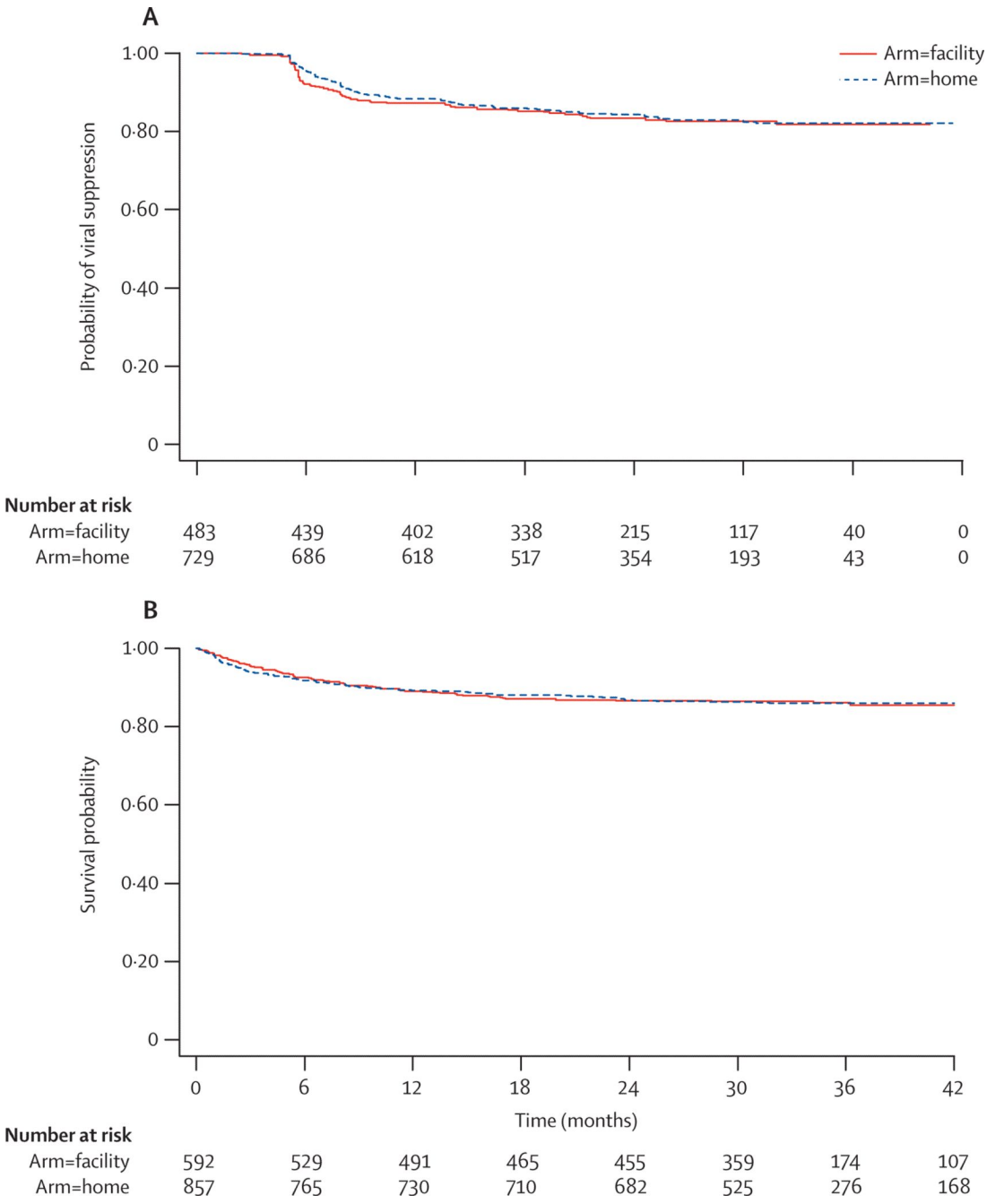

Figure 2.
Kaplan-Meier curve of HIV-RNA virological suppression (A) and survival (B)

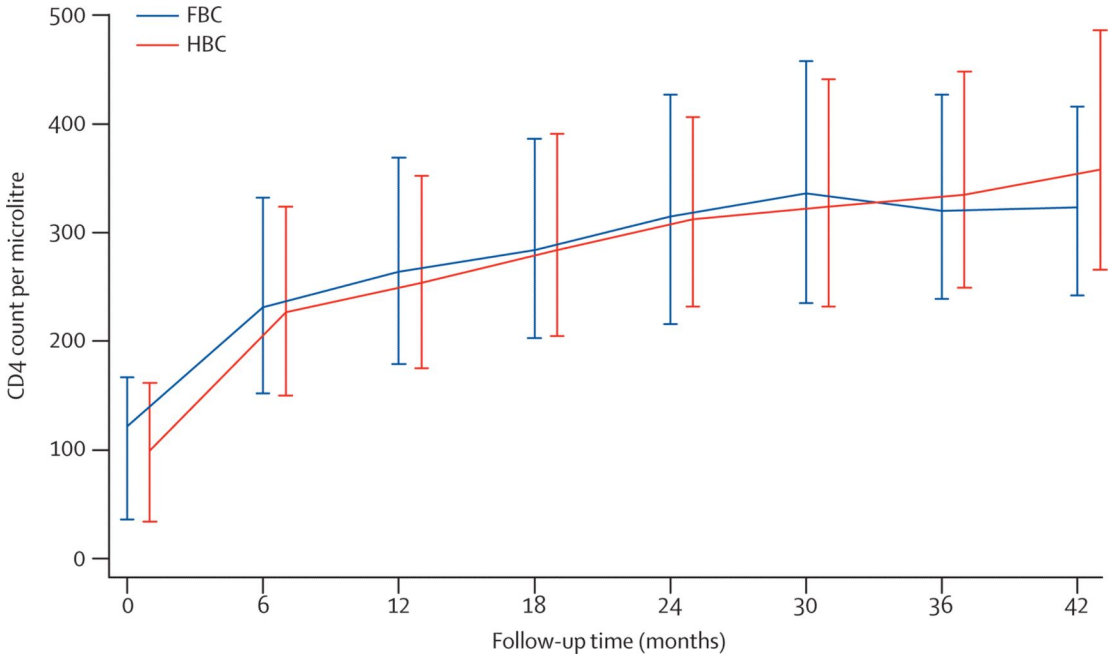

Figure 3.
Median (IQR) CD4-cell counts

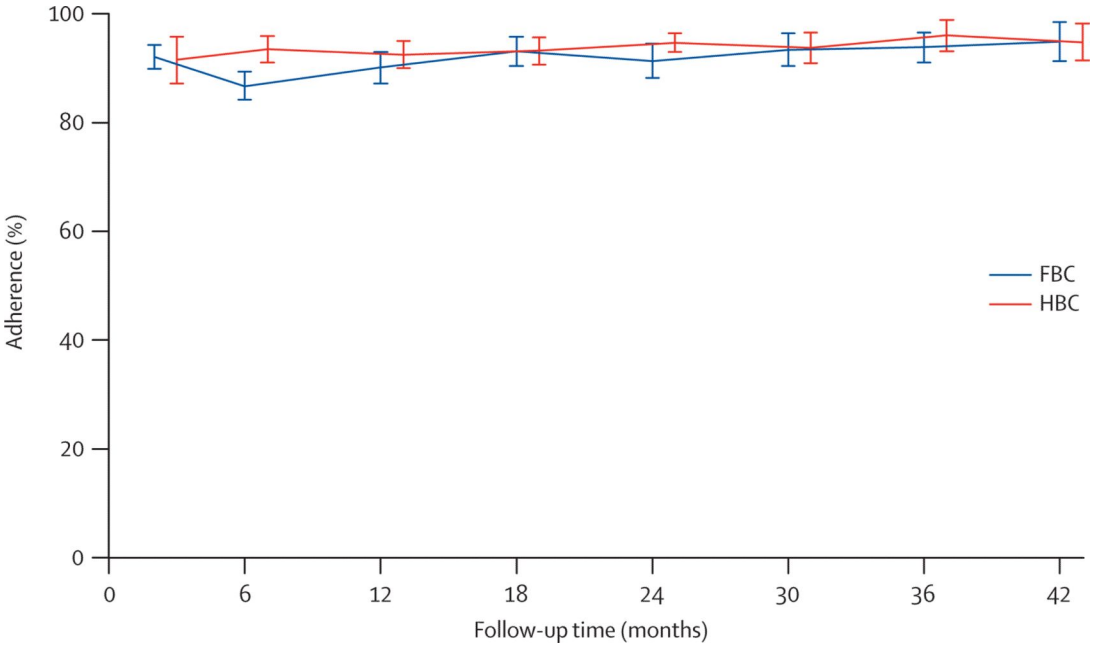

Figure 4.
Proportion (95% CI) of patients reporting complete adherence in the past 28 days

Table 1

Baseline social and demographic characteristics of home-based and facility-based care groups

	Home-based care (n=859)	Facility-based care (n=594)
Female sex	625 (73%)	406 (68%)
Age (years)	37 (32–44)	38 (33–44)
Education		
No education	151 (18%)	83 (14%)
Primary	484 (56%)	332 (56%)
Secondary or tertiary	224 (26%)	179 (30%)
Marital status		
Married or cohabiting	300 (35%)	216 (36%)
Widowed	351 (41%)	232 (39%)
Divorced or separated	194 (23%)	137 (23%)
Single	14 (2%)	9 (2%)
Median time taken to reach clinic (h)	1·0 (0·5–2·0)	1·25 (1·0–2·0)
Main form of transport to clinic		
Walking	36 (4%)	31 (5%)
Minibus or car taxi	716 (83%)	479 (81%)
Motorbike or bicycle taxi	66 (8%)	51 (8%)
Other	41 (5%)	33 (5%)
WHO stage		
I	14 (2%)	6 (1%)
II	384 (45%)	258 (43%)
III	390 (45%)	283 (48%)
IV	71 (8%)	47 (8%)
CD4-cell count (cells per μL)		
<50	272 (32%)	172 (29%)
50–99	159 (19%)	73 (12%)
100–149	170 (20%)	136 (23%)
150–199	171 (20%)	168 (28%)
≥200	87 (10%)	45 (8%)
Median (IQR)	99 (34–162)	122 (30–167)
Plasma viral load copies per mL		
<1000	12 (1%)	9 (2%)
1000–9999	21 (2%)	19 (3%)
10 000–99 999	252 (29%)	202 (34%)
100 000–999 999	514 (60%)	318 (54%)
≥1 000 000	60 (7%)	46 (8%)
Median (IQR)	173 000 (69 000–380 000)	151 700 (58 600–359 000)
Antiretroviral therapy prescription at enrolment		
Stavudine, lamivudine, nevirapine	401 (47%)	269 (45%)
Stavudine, lamivudine, efavirenz	75 (9%)	61 (10%)

	Home-based care (n=859)	Facility-based care (n=594)
Zidovudine, lamivudine, nevirapine	253 (29%)	188 (32%)
Zidovudine, lamivudine, efavirenz	129 (15%)	75 (13%)
Tenofovir, lamivudine and nevirapine	0	1 (<1%)
Tenofovir, lamivudine and efavirenz	1 (<1%)	0

Data are n (%) or median (IQR).

Table 2

Rates of virological failure, mortality, and admission by group

	Home-based care (n=859)		Facility-based care (n=594)		Adjusted rate ratio (95% CI)*
	Number of events (%)	Rate per 100 person-years (95% CI)	Number of events (%)	Rate per 100 person-years (95% CI)	
Plasma RNA VL >500 copies per mL†‡	117/729 (16%)	8·19 (6·84–9·82)	80/483 (17%)	8·67 (6·96–10·79)	1·04 (0·78–1·40)
Either plasma RNA VL >500 copies per mL‡ if undetectable at 6 months, or an increase of 1000 copies between two consecutive tests if RNA detectable at 6 months†	106/729 (15%)	7·33 (6·06–8·86)	74/483 (15%)	7·88 (6·28–9·90)	0·99 (0·73–1·34)
All-cause mortality§	117/857 (14%)	5·40 (4·51–6·47)	80/592 (14%)	5·51 (4·42–6·86)	0·95 (0·71–1·28)
Mortality or plasma RNA VL >500 copies per mL‡§	226/857 (26%)	11·29 (9·91–12·86)	152/592 (26%)	11·45 (9·76–13·42)	1·03 (0·83–1·27)
Admitted on one or more occasions§‖	97/857 (11%)	5·16 (4·23–6·29)	75/592 (13%)	6·11 (4·87–7·66)	0·91 (0·64–1·28)
All admissions	116	5·86 (4·89–7·03)	84	6·37 (5·14–7·89)	0·99 (0·69–1·42)
Death, first admission, or change to second-line therapy§	170/857 (20%)	9·04 (7·78–10·51)	138/592 (23%)	11·24 (9·52–13·29)	0·81 (0·64–1·02)

VL=viral load.

*Adjusted for study stratum and CD4-cell count categorised as 0–49, 50–99, 100–149, and 150 or more cells per μL.

†Patients not followed up for 1 year were excluded. Home-based group, 93 (11%) died, 29 (3%) withdrew, and eight (1%) lost to follow-up; facility-based group 66 (11%) died, 36 (6%) withdrew, and nine (2%) were lost to follow-up.

‡After 6-monthly visit.

§74 (9%) deaths in home-based and 57 (10%) in facility-based care took place at home. Two home and two facility patients were immediately lost to follow-up.

‖Variable analysed is the time to first admission.

Table 3

Diagnoses at first admission after start of antiretroviral therapy

	Home-based care (n=859)	Facility-based care (n=594)
Malaria	24 (25%)	28 (37%)
Bronchopneumonia	17 (18%)	14 (19%)
Lobar pneumonia	1 (1%)	1 (1%)
Anaemia	12 (12%)	3 (4%)
Pulmonary tuberculosis	7 (7%)	5 (7%)
Extrapulmonary tuberculosis	2 (2%)	0
Kaposi's sarcoma	3 (3%)	2 (3%)
Bacterial meningitis	4 (4%)	1 (1%)
Cryptococcoccal meningitis	2 (2%)	2 (3%)
Gastroenteritis	2 (2%)	3 (4%)
Dehydration	1 (1%)	1 (1%)
Diarrhoea	1 (1%)	0
Abscess	2 (2%)	0
Oesophageal candidosis	1 (1%)	1 (1%)
Stevens-Johnson syndrome	2 (2%)	0
Pleural effusion	1 (1%)	1 (1%)
Psychosis	2 (2%)	0
Herpes simplex labial	1 (1%)	0
Herpes zoster	0	1 (1%)
Arthritis	0	1 (1%)
Cervical cancer	0	1 (1%)
Congestive cardiac failure	1 (1%)	0
Enteric fever	0	1 (1%)
Fibroids	1 (1%)	0
HIV wasting syndrome	1 (1%)	0
Hypertension	0	1 (1%)
Intrauterine fetal death	0	1 (1%)
Liver cirrhosis	1 (1%)	0
Osteomyelitis	0	1 (1%)
Tetanus	1 (1%)	0
Toxoplasmosis	1 (1)	0
Urinary tract infection	0	1 (1%)
Other diagnoses	6 (6%)	5 (7%)

Data are n (%).

Table 4

Frequency of outpatient attendance overall and in which a physician was seen and a new clinical disorder diagnosed

	Home-based care (n=859)	Facility-based care (n=594)
Outpatient presentations (visits/patients)	6691 (8/1)	15 242 (26/1)
New disorder diagnosed* (diagnoses/patients)	3908 (5/1)	5751 (10/1)
Diagnosis by classification†		
Infectious and parasitic	2063 (53%)	3086 (54%)
Nervous system	521 (13%)	676 (12%)
Skin and subcutaneous tissue	447 (11%)	597 (10%)
Musculoskeletal system and connective tissue	343 (9%)	548 (10%)
Digestive system	128 (3%)	209 (4%)
Respiratory system	98 (3%)	193 (3%)
Genitourinary system	65 (2%)	73 (1%)
Circulatory system	61 (2%)	117 (2%)
Endocrine, nutritional, and metabolic	60 (2%)	80 (1%)
Mental and behavioural disorders	38 (1%)	56 (1%)
Blood and blood-forming organs and some disorders affecting immune mechanisms	31 (1%)	30 (<1%)
Neoplasms	25 (1%)	24 (<%)
Pregnancy, childbirth, and puerperium	18 (<1%)	54 (1%)
Other	10 (<1%)	8 (<1%)

Data are n (%) unless otherwise stated.

*During outpatient presentation in which a medical officer was seen.

†Diagnoses classified according to WHO International Classification of Diseases. Only primary diagnosis listed.

Table 5

Distribution of drug substitutions to first-line regimens according to initial regimen

	Stavudine		Zidovudine		Lamivudine		Nevirapine		Efavirenz	
	HBC	**FBC**	**HBC**	**FBC**	**HBC**	**FBC**	**HBC**	**FBC**	**HBC**	**FBC**
Starting ART	476 (55%)	330 (56%)	382 (44%)	263 (44%)	859 (100%)	594 (100%)	655 (76%)	457 (77%)	204 (24%)	137 (23%)
Changed to another ART	70 (15%)	56 (15%)	33 (9%)	22 (9%)	7 (1%)	2 (<1%)	38 (6%)	37 (8%)	18 (9%)	25 (18%)
Main reason for change										
Adverse reaction	65 (93%)	53 (95%)	26 (79%)	20 (91%)	6 (86%)	2 (100%)	16 (42%)	14 (38%)	8 (44%)	10 (40%)
Intolerance*	1 (1%)	0	2 (6%)	2 (9%)	0	0	0	1	1 (6%)	0
ART out of stock	1 (1%)	0	0	0	0	0	0	1	0	0
Patient sick, drug burden reduced	0	0	1 (3%)	0	0	0	0	0	0	0
Pregnancy	0	0	0	0	0	0	0	0	8 (44%)	15 (60%)
Started tuberculosis drug	0	0	0	0	0	0	22 (58%)	21 (57%)	1 (6%)	0
Other reasons	3 (4%)	3 (3%)	4 (12%)	0	1 (14%)	0	0			
Time to change (months)†	23 (8–28)	22 (9–26)	2 (2–5)	2 (1–5)	8 (2–12)	3,4	3 (3–11)	4 (3–11)	9 (4–17)	11 (4–22)

Data are n (%) or median (IQR). HBC=home-based care, n=859. FBC=facility-based care, n=594. One home-care and one facility-care patient started treatment with tenofovir and neither had a drug substitution. ART=antiretroviral therapy.

*Mostly vomiting, nausea, headache, and changes in nail pigmentation.

†Actual times for the two patients in facility-based care who started on lamivudine and changed are given.

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Table 6

Costs of health-service delivery and costs incurred by patients to access care (in US$)

	Home-based care	Facility-based care
Health-service costs		
Staff*	359 139 (23·0%)	319 016 (29·1%)
Transport	66 859 (4·3%)	29 204 (2·7%)
Drugs	822 509 (52·8%)	548 339 (50·1%)
Laboratory and clinical	80 850 (5·2%)	53 900 (4·9%)
Sensitisation	31 000 (2·0%)	20 666 (1·9%)
Training and workshops	33 472 (2·2%)	22 315 (2·0%)
Utilities	17 313 (1·1%)	11 542 (1·1%)
Supervision and overheads	84 452 (5·4%)	55 818 (5·1%)
Capital	61 970 (4·0%)	35 073 (3·2%)
Total	1 557 564 (100%)	1 095 873 (100%)
Cost per patient per year (mean)	793	838
Patient costs to access care (per patient)		
Transport, lunch, and childcare costs (median)	9	39
Lost work time (yearly)	9	15
Total (first year)	29	60
Total per year (after first year)	18	54

Data are US$ (%) or US$ (SD), unless otherwise indicated.

*Includes all staff. Calculated from 2005–08 mean exchange rate of 1732 Ugandan shillings to US$1.