Tropical Medicine and International Health doi:10.1111/j.1365-3156.2010.02620.x

VOLUME 15 NO 11 PP 1347–1356 NOVEMBER 2010

# Barriers to starting ART and how they can be overcome: individual and operational factors associated with early and late start of treatment

**Rosalind Parkes-Ratanshi[1,2,5], Leonard Bufumbo[2], Barbara Nyanzi-Wakholi[2], Jonathan Levin[2,4], Heiner Grosskurth[2,3], David G Lalloo[5] and Anatoli Kamali[2]**

1 *Imperial College, St Marys Medical School, London, UK*
2 *Medical Research Council/Uganda Virus Research Institute, Entebbe, Uganda*
3 *Liverpool School of Tropical Medicine, Liverpool, UK*
4 *School of Public Health, University of the Witwatersrand, Johannesburg, South Africa*
5 *London School of Hygiene and Tropical Medicine, London, UK*

**Summary**

OBJECTIVE Despite expanding access to antiretroviral therapy (ART) in Sub-Saharan Africa, there are few data on patients' perceptions about starting ART to explore issues affecting decisions to start ART in eligible individuals during the ART roll out.

METHODS We studied patterns of ART uptake for 957 participants in a trial of cryptococcal disease prevention and performed a qualitative cross-sectional study about issues affecting decisions to start ART in this cohort. In-depth interviews (IDIs) were conducted with 48 participants who started ART after variable time on the trial.

RESULTS Time to starting ART from trial enrolment decreased during the ART roll out (Median 83 days to 68 days). Multiple factors causing delay to ART were reported; awaiting home visit by service provider ($P = 0.025$), domestic issues ($P = 0.028$), moving from area ($P \leq 0.001$) and fear of side effects ($P = 0.013$) were statistically significant. In the IDIs, fear of side effects was the strongest factor for delay and observation of health improvement in others on ART was the strongest inducement to start. Information from patients already taking ART was the most valued source of information.

CONCLUSIONS This study provided novel information about factors encouraging people to start ART early; positive beliefs about ART were the most important. Whilst side effects of ART must not be downplayed, programmes should provide information in a balanced way to prevent unnecessary fear of starting ART. Those already receiving ART were found to be good advocates and should be utilised by ART programmes to educate others.

**keywords** starting ART, decisions, Uganda, Africa

## Introduction

As a result of international initiatives, the roll out of antiretroviral therapy (ART) in Sub-Saharan Africa has progressed rapidly; about 44% of those estimated to need ART have now started treatment (WHO, UNAIDS & UNICEF 2008). Adherence to ART and clinical outcomes has been studied (Orrell *et al.* 2003; Mills *et al.* 2006; Bell *et al.* 2007; Carlucci *et al.* 2008; Krebs *et al.* 2008; Vreeman *et al.* 2009; Watt *et al.* 2009; Tassie *et al.* 2010) but these data concentrate on patients within ART programmes, and we know relatively little about those who do not start or delay ART.

Most of those who delay or do not start ART have no access to drugs; others may be unaware of their HIV status and some have no knowledge about the existence of ART (Souza *et al.* 2007; WHO, UNAIDS & UNICEF 2008). However, there is a group who do not start ART despite knowing their HIV status, being aware of and having access to ART. A Tanzanian study of people referred for ART to a distant health centre after HIV diagnosis showed that lack of perceived susceptibility to HIV illnesses, lack of symptoms, visiting traditional healers and denial of HIV status were strong disincentives for accessing ART (Wringe *et al.* 2009). Negative beliefs about ART, unfamiliarity of dealing with chronic disease, HIV stigma and concern about relationships were all major factors in delaying ART in Zambian breast feeding mothers (Murray *et al.* 2009). In Uganda, a study of those attending screening for ART at a regional health centre found that time and costs involved

in accessing ART caused delays (Jaffar *et al.* 2008). Ethiopian factory workers stated lack of knowledge of eligibility and non-disclosure of serostatus barriers to initiating ART (Degefa *et al.* 2003). In Rwanda, reluctance to start ART was related to a fear of lack of food supplies: people felt that their appetite would increase (Au *et al.* 2006). These studies all explored delays before starting ART, and none studied factors that encouraged patients to start ART quickly. We studied the time it took to start ART in a rural Ugandan cohort who were already accessing HIV care and were eligible for ART in an area with easy access to ART and explored the issues surrounding the decision to start ART in those who started ART early as well as those who delayed.

## Population and methods

Patients were drawn from those enrolled in a trial of primary prevention of invasive cryptococcal disease using fluconazole prophylaxis in HIV-infected adults in Masaka District, South West Uganda (CRYPTOPRO), up to 31st May 2007. The trial is described elsewhere (Parkes-Ratanshi *et al.* 2009). Masaka district consists of one town and 1331 villages in south-western Uganda. Road access within the district is relatively poor; most people live in rural areas and live by subsistence farming and cash crops such as coffee and bananas.

Trial participants were recruited from two non-governmental organisations that provide HIV care and ART: The AIDS Support Organisation (TASO) and Kitovu Mobile AIDS Home Care and Orphans Programme (Kitovu). All participants had CD4 counts <200 cells/$\mu$l. At enrolment, the participants were counselled about their CD4 count and eligibility for ART and were told that they could either start ART without being enrolled in the cryptococcal trial or join the trial and start ART. Participants had a choice of three ART providers: the two sites of recruitment (TASO and Kitovu) and the Ministry of Health/Uganda Cares ART clinic at Masaka Regional Referral Hospital (MOH/Uganda Cares). All had reliable ART supplies and provided ART free of charge, but used different delivery systems. TASO and MOH provide ART at clinics close to the hospital: some TASO clients receive ART at home. Kitovu provides ART in outreach clinics in villages around Masaka. A treatment partner was required for support by those attending TASO.

Participants gave written informed consent for the CRYPTOPRO trial which had approval from the Ethics Committee of the Uganda Virus Research Institute, the Ugandan Council for Science and Technology, and the Liverpool School of Tropical Medicine Research Ethics committee. In-depth interviews for the qualitative research were performed at the participants' homes: only participants who had given permission for home visits and verbal consent for in-depth interviews were included in this substudy.

### Data collection

*Quantitative data*

All participants in CRYPTOPRO were seen 4 weeks after enrolment into the trial and then every 8 weeks. The quantitative data in this paper used data collected for the CRYPTOPRO trial. At each appointment, participants were asked whether they had started ART; counsellors explored reasons if they had not started. Medical officers also documented whether participants had started ART and reasons given for not starting. A delay was defined if anyone had not started ART within 3 months of CRYPTOPRO enrolment.

*Qualitative data*

For the qualitative analysis, the local investigator (RP), principal investigator (DL) and a social scientist (LB) used reasons for not starting ART given to the doctors and counsellors by the first 640 patients (Parkes *et al.* 2005) to develop an in-depth topic guide to explore issues surrounding the decision to start ART. Table 1 shows the topic guide; this was piloted on four participants, then reviewed and refined to produce the final in-depth interview (IDI) plan. For the IDIs, participants were selected from three categories: those who had started promptly i.e. started within 3 months of trial enrolment (<3 months), those who delayed for more than 6 months but had started before the interview (>6 months delay) and those who delayed for more than 6 months and had not started at the time of the interview (>6 months delay, not started). Enrolled participants who fitted each category were approached in order of their trial participation number. If the chosen respondent was not available or did not consent, the next available participant was chosen.

The number of IDI participants was guided by the principle of saturation; the limit being reached when responses became repetitive during data collection. Interviews were conducted in the local language by trained interviewers at participants' homes in private. Confidentiality was assured and respected. Interview sessions were captured on audiotapes, then transcribed and translated to English.

### Statistical methods

To find factors associated with delayed time to starting ART, survival analysis methods (Cox regression models) were used, with subjects who died before starting ART

**Table 1** IDI topic guide organised by themes which emerged in analysis

| Topic guide | Main themes |
|---|---|
| ART Knowledge<br>Observations of other people on ART<br>ART education<br>Service Provider/ doctor flexibility | Knowledge from personal experience with HIV |
| Beliefs/feelings about ART<br>Recommendations to others about ART | Attitude/belief towards ART |
| Transport/logistical issues<br>Disclosure<br>Other non-ART HIV treatments | Practices regarding ART |

IDI, in-depth interview.

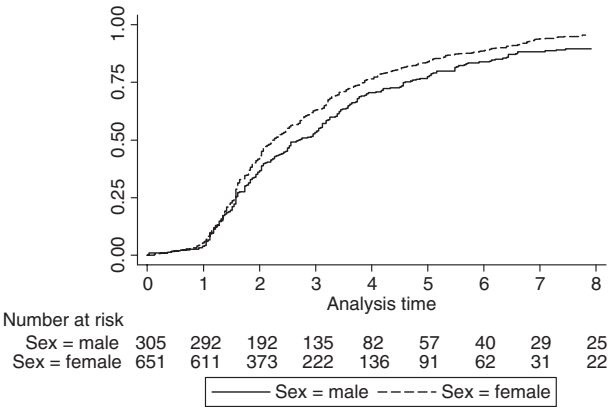


**Figure 1** Time (months) to starting ART by gender.

regarded as being censored at date of death. The following explanatory factors were considered of substantive interest and included in the final model irrespective of statistical significance: gender, baseline CD4 group, baseline WHO stage, Age (grouped), ART site and period of enrolment. We present unadjusted hazard ratios for each factor, as well as hazard ratios adjusted for all of the other factors in the final model. The reasons for delaying ART were compared between two groups, namely those who began ART between 3 and 6 months and those who had not begun by 6 months, for each possible reason, using a Fisher exact test. There was no adjustment made for multiple testing in this analysis. All quantitative analyses were carried out using Stata release 10.1.

Statements collected during IDIs were coded independently by the local investigator (RP) and 2 social scientists (LB and BN) after transcription and translation to English. A manual coding frame of themes and subthemes was developed guided by the inclusion of the main question topics and other topics which emerged. The main themes are seen in Table 1. Finally, all the data was categorized into two additional themes: 'factors leading to delaying ART' and 'factors which encouraged starting ART'.

## Results

### Pattern of access to ART

We found that 879 (91.8%) of 957 participants enrolled in the study until 31st December 2007 had started ART by 31st May 2008. Of all patients, 557 (58.2%) had started within 3 months, 235 (24.5%) within 3–6 months, and 87 (9.1%) took longer than 6 months to start. The median time between enrolment and starting ART was 73 days [Interquartile range (IQR) 48–123 days]. The median time in those who delayed more than 6 months was 222 days (IQR 198–300). Figure 1 shows the cumulative probability of starting ART since enrolment: 53 (73.1%) of the 78 patients who did not start on ART died. The remaining 21 patients withdrew from the study (abnormal liver function (1), loss to follow-up (9), non-adherence to trial drug (2), wanting to leave the trial (6) and other reasons (3). We know that 11 of these 21 started ART elsewhere.

### Factors associated with delayed start of ART

Table 2 summarizes the proportion starting ART, deaths before ART and median times to ART by baseline CD4 group, baseline WHO stage, sex, age, site of recruitment and period of trial (four equal periods of 8 months). Table 3 shows the results of fitting Cox regression models to the variables shown in Table 1 (a hazard ratio <1 is seen if ART initiation was delayed). Women initiated earlier than men [Hazard ratio (HR) = 1.3; $P = 0.001$] and those than 25 years took longer to initiate than others. Those with a baseline CD4 count <50 initiated earlier than those with a CD4 count >50, but those in advanced WHO stages (3 and 4) took longer to begin ART. This apparent inconsistency may reflect the lack of specificity of WHO stage; 38% of those in stage 1 and 2 had CD4 counts <100 (and participants with CD4 counts <100 started earlier than those with CD4 counts >100). Participants enrolled later in the study started ART more quickly than those enrolled in the early months. There was a significant difference between two main service providers: those in Masaka started earlier than in Kitovu Mobile ($P = 0.007$).

**Table 2** Proportion starting ART, Deaths before starting ART and median time to starting ART by explanatory factors

| Factor | Level | *n* | Started ART (%) | Died before ART (%) | Median days to ART | IQR |
|---|---|---|---|---|---|---|
| Overall | | 957 | 879 (91.8) | 57 (5.8) | 73 | 48–123 |
| Baseline CD4 count cells/mm$^3$ | <50 | 260 | 226 (86.9) | 30 (11.5) | 63 | 42–109 |
| | 50–99 | 194 | 178 (91.8) | 12 (6.2) | 77 | 48–130 |
| | 100–149 | 212 | 200 (94.3) | 7 (3.3) | 85 | 49–132 |
| | 150–199 | 291 | 275 (94.5) | 8 (2.7) | 75 | 49–126 |
| Baseline WHO stage | 1/2 | 224 | 212 (94.6) | 5 (2.2) | 70 | 47–116 |
| | 3 | 663 | 603 (91.0) | 47 (7.1) | 74 | 48–126 |
| | 4 | 70 | 64 (91.4) | 5 (7.1) | 76 | 47–123 |
| Sex | Male | 305 | 275 (90.2) | 20 (6.6) | 83 | 48–140 |
| | Female | 652 | 604 (92.6) | 37 (5.7) | 69 | 47–118 |
| Age group | <25 | 60 | 51 (85.0) | 5 (8.3) | 116 | 57–183 |
| | 25–34 | 393 | 365 (92.9) | 26 (6.6) | 71 | 47–118 |
| | 35–44 | 339 | 322 (95.0) | 12 (3.5) | 69 | 48–114 |
| | 45+ | 165 | 141 (85.4) | 14 (8.5) | 77 | 48–133 |
| Site | Masaka Hospital | 799 | 733 (91.7) | 47 (5.9) | 69 | 47–121 |
| | Kitovu Mobile | 158 | 146 (92.4) | 10 (6.3) | 85 | 53–129 |
| Time of enrolment | Up to 31/5/05 | 298 | 272 (91.3) | 18 (6.0) | 83 | 47–146 |
| | 1/6/05–31/1/06 | 303 | 280 (92.4) | 16 (5.3) | 74 | 49–119 |
| | 1/2/06–30/9/06 | 181 | 167 (92.3) | 11 (6.1) | 67 | 40–113 |
| | 1/10/06–31/5/07 | 175 | 160 (91.4) | 12 (6.9) | 68 | 48–105 |

**Table 3** Results of fitting Cox proportional hazards regression models to find factors associated with time to starting ART

| Factor | Level | Unadjusted Hazard ratio (95% CI) | Adjusted Hazard Ratio (95%CI)* | *P*-value |
|---|---|---|---|---|
| Sex | Male | 1 (Reference level) | 1 (Reference level) | – |
| | Female | 1.25 (1.08–1.44) | 1.30 (1.12–1.52) | 0.001 |
| Baseline CD4 count cells/mm$^3$ | <50 | 1 (Reference level) | 1 (Reference level) | – |
| | 50–99 | 0.77 (0.63–0.94) | 0.76 (0.63–0.93) | 0.008 |
| | 100–149 | 0.79 (0.65–0.95) | 0.71 (0.58–0.87) | 0.001 |
| | 150–199 | 0.79 (0.66–0.94) | 0.72 (0.60–0.87) | 0.001 |
| WHO stage | 1 or 2 | 1 (Reference level) | 1 (Reference level) | – |
| | 3 | 0.94 (0.81–1.11) | 0.87 (0.74–1.02) | 0.09 |
| | 4 | 1.02 (0.77–1.34) | 0.83 (0.62–1.15) | 0.22 |
| Age in years (grouped) | <25 | 1 (Reference level) | 1 (Reference level) | – |
| | 25–34 | 1.51 (1.12–2.02) | 1.56 (1.16–2.09) | 0.003 |
| | 35–44 | 1.49 (1.10–2.00) | 1.64 (1.21–2.21) | 0.001 |
| | 45+ | 1.35 (0.98–1.86) | 1.54 (1.11–2.14) | 0.010 |
| Site | Masaka Hospital | 1 (Reference level) | 1 (Reference level) | – |
| | Kitovu Mobile | 0.88 (0.74–1.06) | 0.77 (0.63–0.93) | 0.007 |
| Time of enrolment | Up to 31/5/05 | 1 (Reference level) | 1 (Reference level) | – |
| | 1/6/05–31/1/06 | 1.12 (0.95–1.32) | 1.23 (1.04–1.47) | 0.019 |
| | 1/2/06–30/9/06 | 1.27 (1.05–1.54) | 1.40 (1.14–1.72) | 0.001 |
| | 1/10/06–31/5/07 | 1.18 (0.97–1.44) | 1.39 (1.12–1.71) | 0.002 |

*Adjusted for all other terms in the model.

### Factors involved in the decision to start ART

*Factors leading to delaying ART – reported to medical staff*
There were 400 people who delayed ART for >3 months; in the routine clinic questioning, 323 participants who delayed gave a total of 379 reasons to the doctors and counsellors at routine appointments for not having started ART and these are shown in Table 4. The most common reason was being on tuberculosis (TB) treatment or having other medical treatment (17.3%). Awaiting home visit by

**Table 4** Reasons for delaying ART reported by participants at routine appointments

| | Number who gave reason for delay (% of those who delayed) | | | | | |
|---|---|---|---|---|---|---|
| Reason | All who delayed >3 months ($n$ = 400) | Started ART within 3–6 months ($n$ = 235) | Started ART >6 months ($n$ = 87) | Had not started after >6 months ($n$ = 21) | Died before starting (>3 months on trial ($n$ = 57) | *$P$-value |
| Awaiting home visit by service provider | 56 (14.0) | 44 (18.7) | 10 (11.5) | 0 | 2 (3.5) | 0.025 |
| On TB treatment | 42 (10.5) | 21 (8.9) | 12 (13.8) | 2 (9.5) | 7 (12.3) | 0.25 |
| Awaiting choice of service provider | 39 (9.8) | 25 (10.6) | 13 (14.9) | 0 | 1 (1.8) | 0.70 |
| No clear reason | 32 (8.0) | 20 (8.5) | 8 (9.2) | 1 (4.8) | 3 (5.5) | 0.96 |
| Domestic problems | 29 (7.3) | 14 (6.0) | 12 (13.8) | 2 (9.5) | 1 (1.8) | 0.028 |
| Other medical reasons | 27 (6.8) | 12 (5.1) | 7 (8.1) | 1 (4.8) | 7 (12.3) | 0.40 |
| Fear of stigma | 24 (6.0) | 11 (4.7) | 7 (8.1) | 1 (4.8) | 5 (9.6) | 0.30 |
| Drug/personnel shortage | 23 (5.8) | 16 (6.8) | 7 (8.1) | 0 | 0 | 0.91 |
| Clinic admin issues | 22 (5.5) | 16 (6.8) | 2 (2.3) | 1 (4.7) | 3 (5.3) | 0.13 |
| Difficulty in understanding sensitisation | 22 (5.5) | 14 (6.0) | 7 (8.1) | 1 (4.8) | 0 | 0.61 |
| Moved out of area/Lost to follow-up | 18 (4.5) | 2 (0.9) | 5 (5.8) | 8 (38.0) | 3 (5.3) | <0.001 |
| Fear/concern about side effects | 17 (4.3) | 7 (3.0) | 9 (10.3) | 1 (4.8) | 0 | 0.013 |
| Cost and transport issues | 15 (3.8) | 9 (3.8) | 5 (5.8) | 0 (00) | 1 (1.8) | 0.73 |
| Non-compliant with medication | 7 (1.8) | 3 (1.3) | 2 (2.3) | 1 (4.8) | 1 (1.8) | 0.33 |
| Believed healed by God | 2 (0.5) | 1 (0.4) | 1 (1.2) | 0 | 0 | 0.57 |
| Pill burden | 1 (0.3) | 0 | 1 (1.2) | 0 | 0 | 0.14 |
| Not enough food | 3 (0.8) | 0 | 3 (3.5) | 0 | 0 | 0.03 |
| Reason not documented | 77 (19.2) | 41 (17.5) | 2 (2.4) | 5 (23.8) | 29 (50.9) | 0.007 |

*The $P$-value refers to the comparison of those delaying for 3–6 months with those delaying for >6 months. The calculation did not include those who died.

service provider, obligatory for those receiving ART at home (14.0% of those delaying) and awaiting choice of service provider (9.8%) were the next most common. TASO started their ART scale up on a 'first come first served' basis (longest enrolled participants were the first to access ART) which meant that some participants were not eligible for ART at TASO immediately. However, they were eligible to access ART at the MOH clinic but chose to wait their turn at TASO. Kitovu scaled up ART on a village by village basis; participants were also eligible to go to the MOH clinic, but many preferred to wait for ART to reach their village rather than travelling to Masaka.

Fear of stigma (no treatment partner and non-disclosure at home) was cited by 6.0%. Participants also identified initial difficulties with communication between the trial team and service providers such as lost files or lost or absent referral forms. However, this was relatively rare (5.5%). Occasional interruptions in ART services for a few weeks were reported, but this was usually because of holiday periods, rather than lack of drug supply (4%). Occasionally personnel shortages resulted in a delay (1.8%).

No clear reason was given by 15.5% of those who delayed; this included 'reluctant to start', 'did not take referral letter' and 'has not attended ART sessions'. It is unclear whether the study staff did not have time to explore reasons fully in busy trial clinics, or whether participants had reasons that they did not wish to disclose. Surprisingly, time and cost involved in accessing ART was mentioned only a few as a reason for delay.

Issues which were significantly associated with a long delay (>6 months compared with 3–6 months) were awaiting home visit by service provider ($P = 0.025$), domestic issues ($P = 0.028$), moving out of the area ($P < 0.001$) and fear of side effects ($P = 0.013$).

*Factors leading to delaying ART – IDIs*

Overall, analysis of the IDIs found trends in those who started early (<3 months) and those who delayed starting (>6 months). Most prominent were expression of fear of side effects in those who delayed and positive beliefs about ART (such as improvement in health) in those who started early. The most striking finding was the considerable influence that other people living with HIV/AIDS (PHA) had on attitudes to starting. These PHAs were people that the participants knew from the community, or people that they had met at the service provider clinics. Table 5 summarises some of the positive and negative information received by participants and highlights the information received from other PHAs.

Many of those who delayed mentioned witnessing illness and side effects after starting ART in relatives, friends or acquaintances.

> *It was because of fear, created by those who had already started on ART before me. My friends said 'ART is very difficult'. Even here in this home my uncle for example took ART wrongly and he was affected badly and died badly.* (Female, 44, farmer, >6 months delay)

Participants in the groups that delayed also reported being told about side effects more frequently than those who started early. Illness was often given as a reason for delaying ART; all participants were very immunosuppressed and many had opportunistic infections. TB is common and Ugandan National guidelines suggested completing 2 months intensive TB treatment before starting ART. Service providers could not start ART in patients in hospital, and many participants had multiple or prolonged hospital admissions. Some participants chose to wait until their high pill burden was reduced.

> *It was about one year before I started taking ART because I had TB. I took the TB drug for 8 months and I was still on the meningitis drugs as well.* (Female, 47, farmer, >6 months delay)

Domestic issues requiring attention prior to starting ART were a frequent factor causing delays. Female participants often had to care for sick relatives.

> *I decided to start ART in December because by the time they gave me that referral letter I had my child who was supposed to undergo a leg operation. I decided to first finish up with that so that I start ART afterwards without any problem.* (Female 27, unemployed, >6 months delay)

Whilst all of the participants had a good understanding of ART, the number of ART education sessions varied; service providers would not start ART if they did not feel that patients understood how to take it properly.

> *He asked me the questions in the doctors' office in the clinic. He advised me to return, saying 'come back after you have grasped what is taught in the sessions'. I went back the second time and I failed two questions and he sent me away again.* (Male, 29, unemployed, >6 months delay, not started)

Participants who were unwell found the education sessions difficult.

> *I took longer because whenever I would go there, the health workers would make me feel uneasy. I would be in a lot of pain, so whenever I would go for sessions*

**Table 5** Examples of negative and positive statements recorded during IDIs on information received from various sources

| | Source: Health workers | Source: Other patients (PHAs) | Source: Other community members |
|---|---|---|---|
| Negative effects of ART | The medicine might cause hallucination, it might cause some skin irritation. *F, 36, farmer, >6 months, delay* | What worried me was that those (mates) taking the drugs said that I will get a skin irritation, I might get hallucinations and become very sick. *F,41, alcohol trader >6 months, delay* | Okay I really feared, .because people say it is deadly, it weakens *F, 31, trader >6 months, delay* |
| | The counsellors at TASO would even tell us that your eyes would turn yellow and at times one would get nausea as if one is pregnant. *F, 23, waitress, >6 months, delay* | It will bring skin irritation and you may have diarrhea, you will get sores in the mouth and even get paralysis. If you get some of those signs you report immediately to a health worker. *F, 42, Farmer, >6 months, delay* | |
| | | Most of them [PHAs] fear going to Masaka and they say that TASO will kill people. *M, 36, farmer, >6 months, delay* | |
| Positive effects of ART | My mates and the counsellor told me that if you start ART you will be okay and that might also help to prolong your life span *F, 42, peasant farmer, <3 month started* | They talked to me and said that if I started on ARVs, I would notice all the current ailments reduce. *F, 42, farmer, 3–6 month started* | |
| | | There were also patients at the hospital who used to say that they had spent six months unable to walk and now they were walking. They could not eat and now they were eating. *M 35, shop attendant, <3 month started* | |
| Encouragement to start | The way they reassure us. They treat us well and do not want us to be worried. They will tell you to decide whether to start the ART or not. So I realized that starting the ART was an important thing and I decided to start taking them. *F, 38, farmer, >6 months, delay* | I asked them 'when I take the ART won't they be bad for my health?' They told me, 'No do not fear they will not affect you, for us, we have been taking it' So I tried it. *F,38 peasant farmer, >6 months, delay* | |

IDI, in-depth interview; PHA, people living with HIV/AIDS.

*I would fall asleep. A mate would wake me up when they would hear the health worker directing a question to me and I would not be in position to give a correct answer.* (Female, 32, charcoal seller, >6 months delay)

Although comparatively few patients reported transport problems during routine visits, several IDIs identified both a lack of money for transport and difficult logistics, such as bad roads to the clinic as problematic.

*The problem I had as an individual was poverty because I had to sell my only plot of land to get money for transport since I had to go to Masaka every week.* (Male, 34, unemployed >6 months delay)

*Factors which encouraged starting ART*

Only the qualitative study addressed this issue. A strong inducement to start ART was the observation of positive

effects of ART in other PHAs; around half of all participants mentioned this.

> *I saw some of them* (PHAs) *and their health condition was terrible. But then they started taking ART, they got better and they are now working very well.* (Male, 38, farmer, >6 months delay)

There was a great deal of emphasis placed on the views of other PHAs; participants often reported being told by health workers and PHAs about the positive effects of ART on their health. This was common those starting within 3 months, but was rarely mentioned by those that had not started. An interesting finding was the self-defined role of PHAs who were already established on ART in specifically encouraging others to start. We saw marked effects of this influence throughout the interviews.

> *I refused because I feared rumours about ART. When we discussed with my mate, she said 'You are making a mistake, you are becoming very sick, go for a CD4 test and make sure you start ART. Don't you see me? I don't have any problem at all and even my CD4 cell count has increased' So that is how I started ART.* (Female, 33, unemployed, <3 months, started)

Some participants acted as advocates for other patients to assist them in accessing care.

> *A PHA friend found me at MOH after I had attended three educational sessions, so when she found me there on the fourth educational session she said to the health workers 'this person has attended three sessions, why is she not on ART as yet?' The doctor then asked me how many sessions I had attended, and I replied that I had attended three sessions. That is how I started on ART.* (Female, age 34, shop attendant, <3 months, started)

Worsening health, fear of illness and death because of HIV was the motivation for starting ART.

> *… what motivated me most was the pain the disease inflicted on me without any moments of relief whatsoever.* (Male, 32, forestry worker, <3 months started)

The desire to survive was also a strong motivator for starting:

> *I was feeling very weak and they had already explained that ART would improve my immunity and might even prolong my life span. That is why I went for the drugs immediately.* (Male, 37, self-employed, <3 months, delay)

Flexibility and an accommodating approach by health care workers and the health care system enabled some people to start quickly. Encouragement for people who were wavering was also acknowledged as helpful.

> *I have a small child, who is now getting her ART from Uganda Cares. I cannot afford transport for two different days. I had told the doctors that I would not afford transport, so they gave me the same day for reporting as my child.* (Female, 36, unemployed, <3 months delay)

Some explained how counselling helped them overcome negative feelings towards ART:

> *But after sometime my counsellor convinced me. She said, 'Take courage. ART is not bad at all they are very good. Every sickness that bothers you will be cleared' and explained to me all the procedures in detail.* (Female, age 43, farmer, >6 months delay)

## Discussion

This study explored issues surrounding the uptake of ART in an area with a good supply of ART drugs at the beginning of an ART rollout programme. CRYPTOPRO started enroling at the same time, ART was becoming available free of charge in Masaka, Uganda. Whilst the median time to starting ART fell during the study, the median time was still 68 days at the time our study ended. The fact that delays were less common in those with lower CD4 counts do suggest that either clinicians are prioritizing the most immuno-compromised patients or ill patients want to start quicker. Conversely, perhaps people who delayed did so because they knew their CD4 cells/$\mu$l count was near to 200, or because they felt well, as observed in Tanzania (Wringe *et al.* 2009).

One of the study's limitations was that it was carried out in the early roll out of ART. However, although ART is now well established in Sub-Saharan Africa, there are still many areas where there is limited penetration of ART and our findings are highly relevant to these areas. Those areas with limited access to ART are mainly rural or geographically isolated areas, similar to this study population. Another limitation is that these patients were already enrolled in a trial for cryptococcal disease and so are likely to be motivated to look after their health. The study does not capture those who are avoiding all HIV care. However, despite this bias towards accessing services, many of the enrolled participants delayed starting ART which highlights the importance of understanding

concerns/issues surrounding ART, above and beyond regular HIV care.

The reasons given for a delay in starting ART to the medical officers and counsellors (Table 4) had a different emphasis to the IDIs, highlighting the importance of performing in-depth qualitative work. The IDIs showed that there were many different factors influencing decisions to start ART which these varied considerably between individuals. Most influential was fear of side effects, either through witnessing this first-hand or from information gathered from other PHAs. There is a genuine risk of side effects or morbidity in the first six months of ART *(Lawn et al.* 2008) and health care workers should not play down this risk, but there is a crucial role for augmented counselling in those scared of starting ART. It is important for counsellors to specifically explore this issue with people who delaying starting ART; some people who initially gave vague responses about reasons for delaying later admitted that this was because of fear of side effects.

Flexibility and sensitivity of the service providers and the attitude of the staff to the patients made a big difference in participants who were hesitant to start. This was highlighted by examples such as the participant who needed to come to clinic on the same day as her child, and the participant who experienced renewed hope in ART as the health workers encouraged her. This emphasises the importance of understanding the different demands on each individual, although this can be difficult in resource poor settings with large numbers of patients and few health workers. The observation that one of the main reasons for delayed start of ART was to access it from a specific service provider is important as in Sub-Saharan Africa there are often different service providers in one area e.g. NGOs providing ART alongside government-based services: Perceived staff attitudes may have contributed to participants waiting for their choice of service provider, as they felt that they received a better service overall from one particular provider who they knew and trusted; understanding patient preferences will help improve services.

We are unsure why lack of food was rarely an issue for this cohort in contrast to Rwanda (Au *et al.* 2006). There has been a strong emphasis on eating well from their first positive HIV test result in Uganda, and therefore, concerns about food may apply to all patients with HIV and are not associated with ART alone. HIV stigma was mentioned to doctors and counsellors by only 7.4% of those who delayed and was not a strong theme in the IDIs. This is different to the Tanzanian and Malawi experience where it was an important factor(Murray *et al.* 2009; Wringe *et al.* 2009). This may be because of efforts in Uganda to tackle stigma (Green *et al.* 2006). Another study in Uganda found 44% of people screened for ART who were eligible did not start, and a major reason for this was transport costs and lack of time were a major factor in the 44% who did not start ART in one Ugandan study (Jaffar *et al.* 2008). We did not find this but participants in our study were reimbursed for trial visits and may have used this opportunity to visit ART clinics on the same day.

This study is novel in the exploration of factors that encourage people to start ART early. The most marked finding was the strong positive influence of observing or hearing from other people already taking ART, especially in those who started early. Although there may have been an element of recall bias of those who had started ART and had noticed an improvement in their own health, this group often recalled seeing people do well or being told by other patients or health staff about the benefits. The potential value of involvement of PHAs in HIV prevention programmes has already been recognised (Bassett 1998; Ronald Hope 2003, Sloan & Myers 2005). Many programmes now use PHAs in the provision of care/ART, but there is limited published information about the efficacy of this approach (Sankar *et al.* 2006). This study emphasises the potentially important role of PHAs in assisting health care workers in the specific area of ART education in the roll out programme. Given the limits on resources in Sub-Saharan Africa, maximizing the existing knowledge and experience in PHAs could be of great assistance in scaling up ART.

> *I could even sacrifice my time taking my colleagues to go for ART, and even help then through the procedures so that they would attain what I now have. I was assisted by health workers but I can also help others.* (Male, age 28, mechanic, <3 months delay).

## Acknowledgements

We thank the Cryptococcal trial participants and staff for their time and effort, and our colleagues from TASO, Kitovu Mobile, Masaka Regional Referral Hospital and UgandaCares for their support and close collaboration. This work was undertaken as part of the trial of Primary Prophylaxis of Cryptococcal Disease in HIV-positive Ugandan Adults funded by the UK Medical Research Council.

## References

Au JT, Kayitenkore K, Shutes E *et al.* (2006) Access to adequate nutrition is a major potential obstacle to antiretroviral adherence among HIV-infected individuals in Rwanda. *AIDS* **20**, 2116–2118.

Bassett M (1998) Impact of peer education on HIV infection in Zimbabwe. *Sexual Health Exchange* **4**, 14–15.

Bell DJ, Kapitao Y, Sikwese R, van Oosterhout JJ & Lalloo DG (2007) Adherence to antiretroviral therapy in patients receiving free treatment from a government hospital in Blantyre, Malawi. *Journal of Acquired Immune Deficiency Syndromes* **45**, 560–563.

Carlucci JG, Kamanga A, Sheneberger R *et al.* (2008) Predictors of adherence to antiretroviral therapy in rural Zambia. *Journal of Acquired Immune Deficiency Syndromes* **47**, 615–622.

Degefa A, Sanders EJ, Mekonnen Y *et al.* (2003) Knowledge and attitudes towards antiretroviral therapy among factory workers participating in a cohort on HIV and AIDS, Addis Ababa, Ethiopia. *Ethiopian Medical Journal* **41**(Suppl. 1), 75–87.

Green E, Halperin D, Nantulya V & Hog J (2006) Uganda's HIV Prevention Success: The Role of Sexual Behavior Change and the National Response. *AIDS and Behaviour* **10**, 335–346.

Jaffar S, Birungi J, Grosskurth H *et al.* (2008) Use of WHO clinical stage for assessing patient eligibility to antiretroviral therapy in a routine health service setting in Jinja, Uganda. *AIDS Research and Therapy* **5**, 4.

Krebs DW, Chi BH, Mulenga Y *et al.* (2008) Community-based follow-up for late patients enrolled in a district-wide programme for antiretroviral therapy in Lusaka, Zambia. *AIDS Care* **20**, 311–317.

Lawn SD, Harries AD, Anglaret X, Myer L & Wood R (2008) Early mortality among adults accessing antiretroviral treatment programmes in Sub-Saharan Africa. *AIDS* **22**, 1897–1908.

Mills EJ, Nachega JB, Buchan I *et al.* (2006) Adherence to antiretroviral therapy in Sub-Saharan Africa and North America: a meta-analysis. *JAMA* **296**, 679–690.

Murray LK, Semrau K, McCurley E *et al.* (2009) Barriers to acceptance and adherence of antiretroviral therapy in urban Zambian women: a qualitative study. *AIDS Care* **21**, 78–86.

Orrell C, Bangsberg DR, Badri M & Wood R (2003) Adherence is not a barrier to successful antiretroviral therapy in South Africa. *AIDS* **17**, 1369–1375.

Parkes R, Namakoola I, Todd J *et al.* (2005) Barriers to initiation of ART in a cohort of HIV positive Ugandan adults with CD4 counts of less than 200. *World AIDS Conference, Toronto. WEPE 0079*

Parkes-Ratanshi R, Kamali A, Wakeham K *et al.*(2009) Successful Primary Prevention of Cryptococcal Disease Using Fluconazole Prophylaxis in HIV-infected Ugandan Adults. *Conference on Retroviruses and Opportunisitc Infections, Montreal* Oral O26.

Ronald Hope K Sr (2003) Promoting behavior change in Botswana: an assessment of the Peer Education HIV/AIDS Prevention Program at the workplace. *Journal of Health Communication* **8**, 267–281.

Sankar A, Golin C, Simoni JM, Luborsky M & Pearson C (2006) How qualitative methods contribute to understanding combination antiretroviral therapy adherence. *Journal of Acquired Immune Deficiency Syndromes* **43**(Suppl 1), S54–S68.

Sloan NM & Myers JE (2005) Evaluation of an HIV/AIDS peer education programme in a South African workplace. *South African Medical Journal* **95**, 261–264.

Souza PR Jr, Szwarcwald CL & Castilho E A (2007) Delay in introducing antiretroviral therapy in patients infected by HIV in Brazil 2003-2006. *Clinics (Sao Paulo)* **62**, 579–584.

Tassie J-M, Baijal P, Vitoria M *et al.* (2010) Trends in retention on Antiretroviral Therapy in National Programs in Low-income and Middle-Income Countries. *Journal of Acquired Immune Deficiency Syndromes* DOI:10.1097/QAI.0b013e3181d73e1b. Published ahead of print.

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

Watt MH, Maman S, Earp JA *et al.* (2009) "It's all the time in my mind": facilitators of adherence to antiretroviral therapy in a Tanzanian setting. *Social Science and Medicine* **68**, 1793–1800.

WHO, UNAIDS & UNICEF (2008) Towards Universal Access: Scaling up priority HIV/AIDS interventions in the health sector. Progress Report. *WHO Library Cataloguing-in-Publication*, 1–140.

Wringe A, Roura M, Urassa M *et al.* (2009) Doubts, denial and divine intervention: understanding delayed attendance and poor retention rates at a HIV treatment programme in rural Tanzania. *AIDS Care* **21**, 632–637.

**Corresponding Author** **Rosalind Parkes-Ratanshi**, Imperial College, St Marys London, Medical School, Campus, Norfolk Place, London W2 1NY, UK. Tel.: +256 782323; E-mail: r.parkes@imperial.ac.uk